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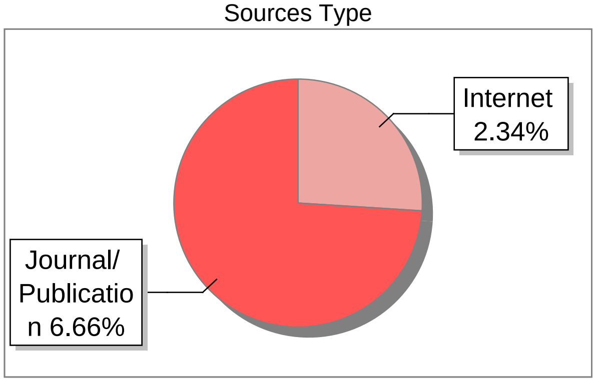

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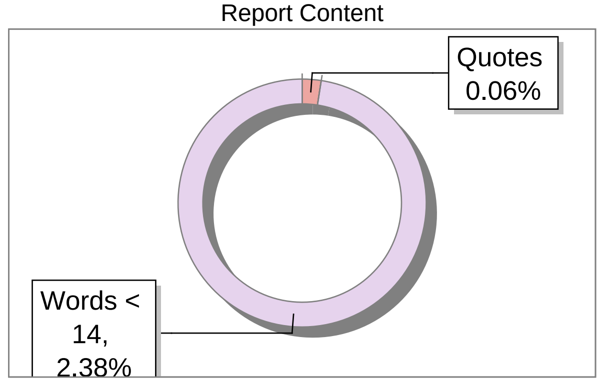

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A

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Abstract

Heterocyclic moieties play an indispensible part in the field of medicinal chemistry as high number of heterocyclic compounds is employed in the development of many important drug molecules. Indole ring is one such moiety which is researched in the search of many potent ant-cancer and antimicrobial agents. In the present study we designed two series of indole-amantadine based compounds and further evaluated them for their anti-bacterial, anti-fungal and anticancer activity. The designing of the compounds was done with the computer aided drug designing approaches such as ligand based approach 2D-QSAR and the structural based drug designing approach including molecular docking and molecular dynamics simulations.

The study is initiated with the generation of separate 2D-QSAR model against the both the scheme and then these models were used for screening of the compounds by predicting their anti-cancer activity. Further screening of the compounds is performed using the molecular docking simulations. The compounds which had shown good results from the 2D-QSAR and molecular docking based virtual screening were then opted for performing the synthesis. The synthesis of the compounds was then confirmed from the spectroscopic techniques including IR, NMR and mass spectrometry. These molecules were then further evaluated for their anti-microbial and anticancer potential.

From the biological evaluation, it is confirmed that the compound SS-1H has shown best antibacterial activity compared to the other analogues of the scheme. In the anti-fungal activity the synthesised compounds didn't show as much promising activity and the compound SS-1O has shown some moderate activity. The anti-cancer potential of the synthesised compounds were evaluated against various cell lines and from the evaluation it is observed that here compounds SS-III, SS-IIK and SS-IIU emerged out as most potent against the maximum cell lines. Therefore the interaction and probable mechanism of action of these three compounds were further evaluated through the molecular dynamic simulations. The molecular dynamic simulations also further reinforced the *in-vitro* anticancer studies and shown that all the three ligands were stable inside the binding site of the receptor.

From our study, it is concluded that the molecules SS-IH, SSIO, SSIII, SS-IIK and SS-IIU are the uppermost active compounds from our study against the various activities. These molecules possibly be further explored and studied by changing substitutions for obtaining the more potent molecules.

CHAPTER-1

INTRODUCTION

In the recent decades, the emergence of the multiple drug resistance has posed an eminent challenge in front of the medicinal chemists [1-2]. Nosocomial infections have also increased dramatically in the past few years. Combination of many factors pose many challenges in the treatment of infectious diseases which include development of resistance to current antibacterial therapy and a very rapid increase of primary and opportunistic fungal infections in immune compromised patients with AIDS orundergoing anticancer therapy and organ transplants [3-4]. Despite of large number of antibiotics and chemotherapeutics accessible for medical use, the appearance of old and new antibiotic resistance developed in thelast decades, has created a substantial medical needfor new classes of antibacterial [5-7]. As per the WHO data, it was estimated that there were 1.27 million global deaths due to the anti-microbial resistance globally in the year 2019 [8]. The resistance by the microbes to the drugs is believed to be acquired through several pathways briefly explained in the fig. 1.1.

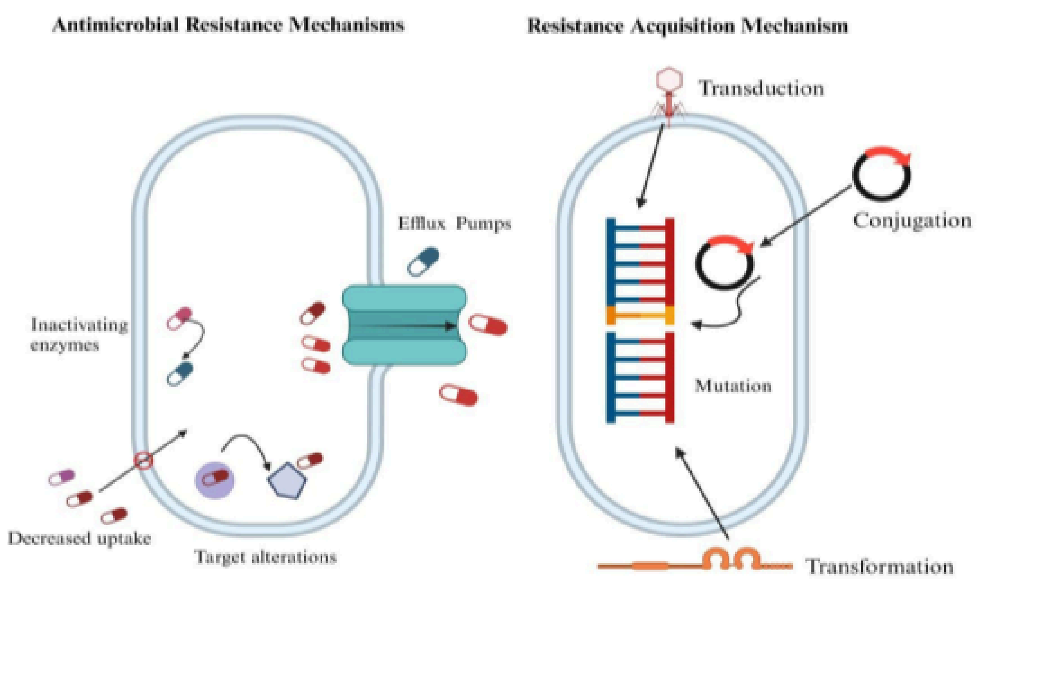


Fig. 1.1: Mechanism of Antimicrobial resistance

Cell cycle and apoptosis are two utmost important processes of human cell growth and programmed cell death [9-10]. Cancer is considered a complex disease which occurs when human body fails to regulate these two processes [11-13]. These uncontrolled dividing cancer cells hijacks the process of normal cell division (Fig. 1.2).

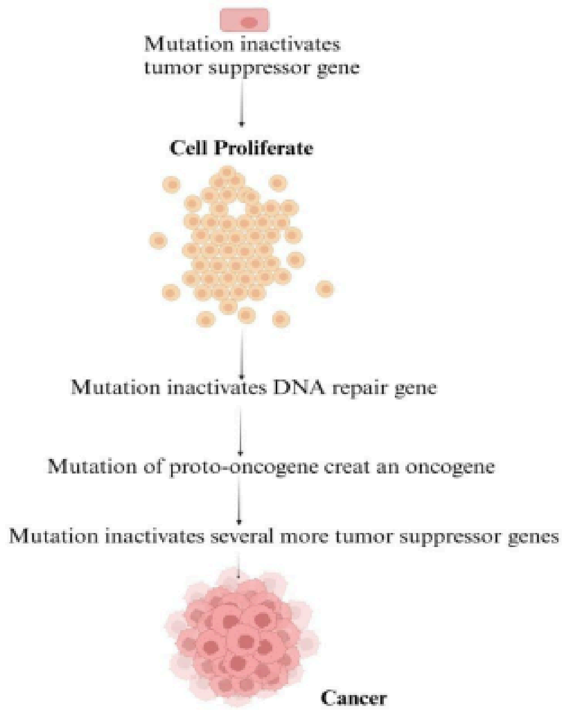


Fig. 1.2: Illustration of the growth of tumor cells inside the body

As per the WHO, cancer has accounted for around 10 million deaths worldwide in 2020. Most common types of cancers are rectum, lung, breast, prostate and colon tumors. It has also been projected by the WHO that by 2040, there will be around 16.3 million deaths per year worldwide due to this deadly disease [14].

This has posed an eminent threat and challenge to the medicinal chemists to develop novel molecules which can more effectively treat the occurrence of cancer [15-16]. To serve this purpose, heterocyclic moieties have played an indispensible role in the development of many lifesaving drugs against several ailments. Indole scaffold is one of the promising heterocycles present in many drugs employed in the treatment of cancer including naturally occurring alkaloids vincristine and vinblastine [17].

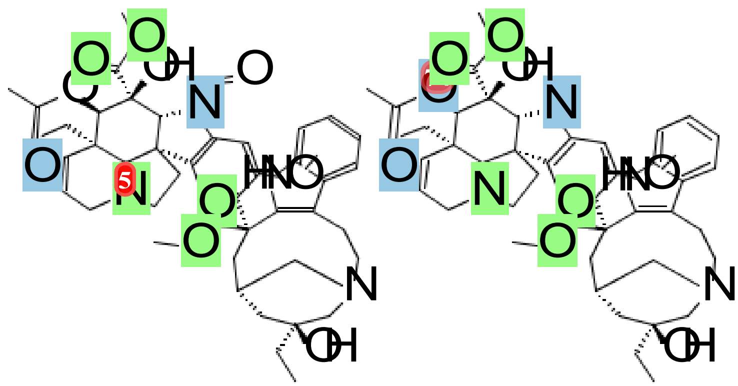


Fig. 1.3: Structure of Vincristine and Vinblastine

Drug design is a process which involves the identification of a compound that displays a biological profile and ends when the biological profile and chemical synthesis of the new chemical entity are optimized. Drug designing is otherwise known as rational drug design and it is a method of finding new medications based on the biological receptors and target molecules [18]. It involves the designing of small molecules which is complementary to the biological receptor to which they bind and interact to cause the pharmacological actions [19]. Natural products (including plants, animals and minerals) have been the basis of treatment of human diseases. But due to the lack of potential action and definitive cure and sometimes more toxicity, the discovery of new drugs that are more potential and less toxic is essential [20-21]. The synthesis of derivatives has been an important part and is aimed at modifying theaction of drugs, particularly to reduce the side effects and to potentiate the drugaction. Today more than 60% drugs used in practice are synthesized derivativesand day-by-day the scope of synthetic medicinal chemistry is broadening [22-23]. Medicinal chemistry is concerned with discovery, development, synthesis in laboratory and assessing the pharmacological action of the synthesized molecules. In addition to the experimental techniques, a variety of computational approaches have been applied at the various stages of the drug-design process: in the early stages these approaches focused on reducing the number of possible ligands, whereas in the later stages, during lead-optimization, the emphasis is on decreasing experimental costs and reducing the period of discovery [24-25].

Traditional drug discovery process is linked with high cost and consumes lots of time in getting any novel potential drug. To overcome this, computer aided drug designing (CADD) approaches are employed by the medicinal chemists for reducing this cost and to reduce the overall time for the development of a new drug moiety. Quantitative Structural Activity Relationship (QSAR) technique is a ligand-based drug designing (LBDD) approach of CADD in which a mathematical relationship is developed for the chemical properties of already reported compounds and their biological activities. In the similar manner, molecular docking simulation is structure-based drug designing (SBDD) method of CADD which works on lock & key mechanism in which proposed ligand is placed inside the active cavity of the receptor and Gibbs free energy (Dock Score) of the system is calculated [26-27].

When we see the above two problems in a combined manner, the solution lies in the development of novel heterocyclic moieties which can be utilised not only for the treatment of antimicrobial resistant cases but also for the cure of the deadly disease cancer. The heterocyclic moieties served as a boon to the medicinal chemist's fraternity from the decades. Till date, there have been numerous marketed heterocyclic compounds employed for the treatment of many ailments such as cancer, AIDS, diabetes, cardiovascular diseases, anti-psychotic etc. Among all the heterocyclics, indole derivatives being a special category which gave many successful marketed drugs such as Indomethacin (NSAID) [28], Ergotamine (anti-psychotic) [29], Zafirlukast (anti-asthmatic) [30], Reserpine (Anti-hypertensive) [31], Delavirdine (anti-viral) [32], Oxypertine (anti-psychotic) [33], Tulongicin (anti-bacterial) [34] etc. Due to the high utility of the indole ring in the heterocyclic medicinal chemistry we planned to explore further the potential of this moiety for the development of the potential anti-microbial and the anti-cancer agents.

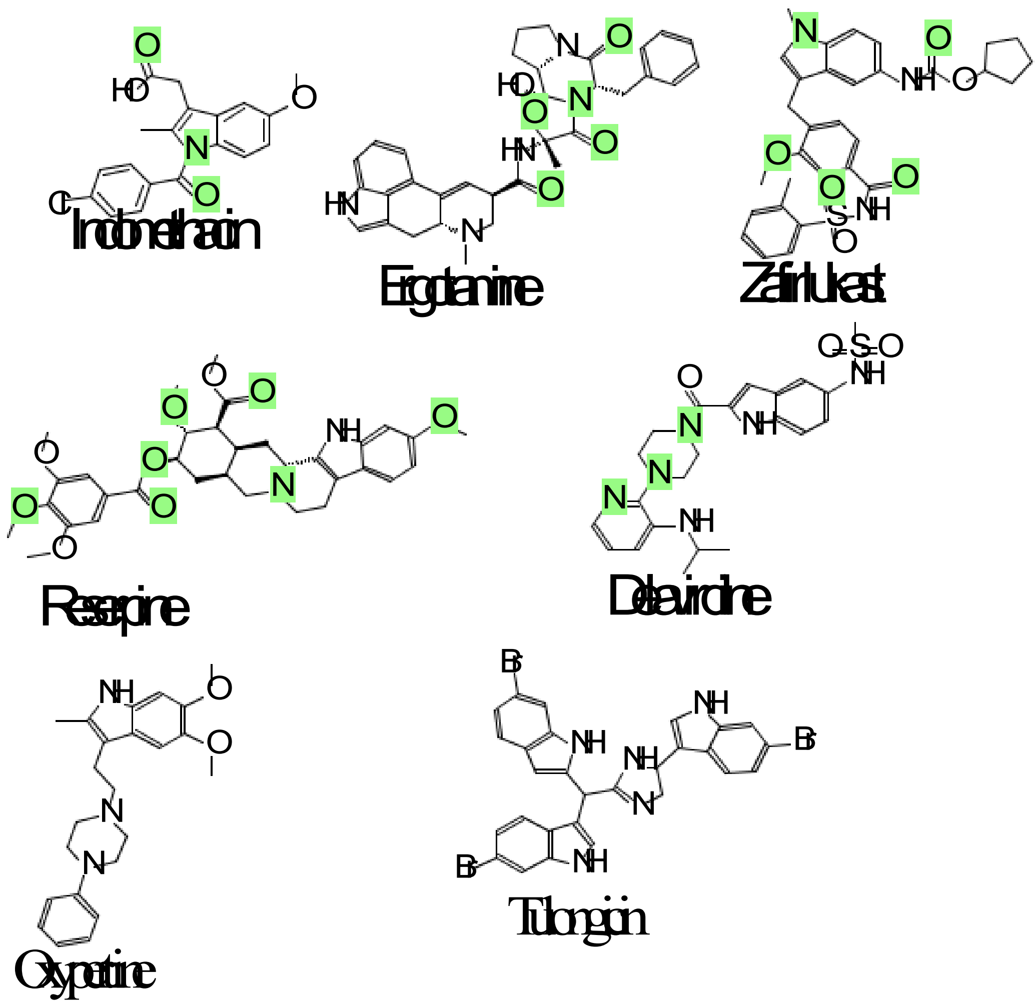


Fig. 1.4: Marketed Indole Based Drugs

1.1 Nucleus profile

1.1.1 Structural Studies: Indole, with the chemical formula $C_6H_4CCNH_3$, is an organic compound classified as an aromatic heterocycle. Its structure comprises a six-membered benzene ring fused to a five-membered pyrrole ring, forming a bicyclic arrangement. Indoles occur naturally and are prevalent in biological molecules such as the amino acid tryptophan and the neurotransmitter serotonin. Derivatives of indole are formed by replacing one or more hydrogen atoms with other groups, and they exhibit diverse chemical reactivity [35].

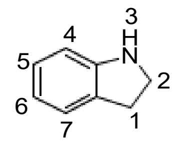


Fig. 1.5 : General Structure of Indole

It is a hetero-atomic planar molecule comprising of benzene ring fused to a pyrrole ring at -2 & -3 position. The chemistry of indole dates back to mid-19th century due to extensive research on a natural violet-blue dye named indigo which leads to the synthesis of indole in 1866 by zinc distillation of Oxindole [36].

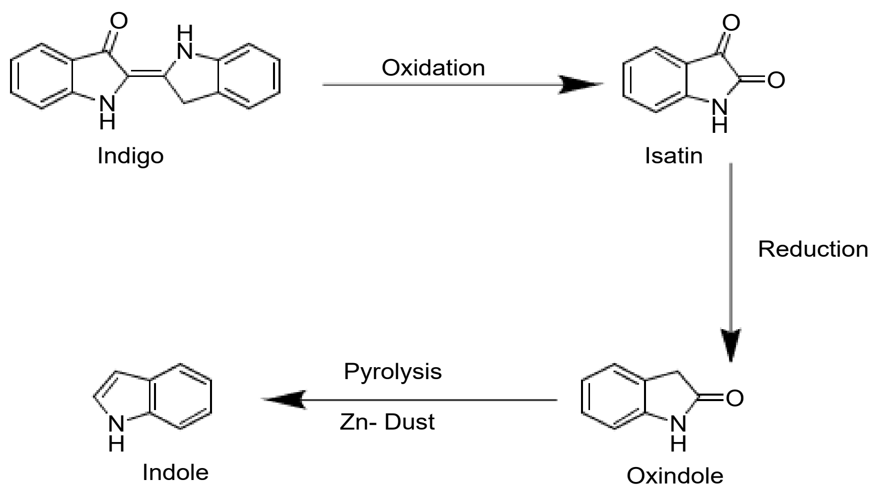


Fig.1.6: Discovery of Indole

1.1.2 Physical Properties:

Name: Indole (2,3-benzopyrrole), ketole, 1- benzazole

Chemical Formula: C8H7N

Molar Mass: 117.14788g

State of Matter: White solid

Mass Percent: C 82.020 %; H 6.0227 %; N 11.956 %.

Isomers: p-tolunitrile

1.1.3. Chemical Properties of Indole:

1.1.3.1 Basicity: Indole, unlike typical aromatic amines, is not basic due to its aromaticity and resonance stabilization. Its bonding situation is analogous to that of pyrrole. While strong acids such as hydrochloric acid can protonate indole, it primarily occurs at the C-3 position ratherthan N-1. This preference arises from the enamine-like reactivity of the portion of the molecule located outside the benzene ring. The protonated form of indole has a pKa of 3.6 [37].

1.1.3.2 Electrophilic Aromatic Substitution (EAS): Indole undergoes electrophilic aromatic substitution reactions at the 2, 3, 5, and 7 positions due to its aromatic nature. Common electrophiles used in EAS reactions with indole include halogens (e.g., bromine, chlorine), nitro groups, acyl groups, and alkylating agents.

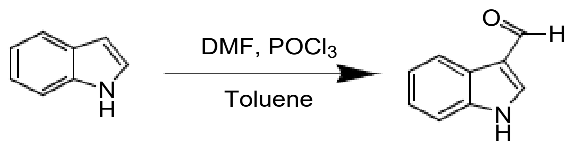


Fig. 1.7: Electrophilic Aromatic Substitution (EAS)

1.1.3.3 Reaction with carbene: Halocarbenes, such as dichlorocarbene (CCl2), can react with indole to add onto the 2,3 carbon-carbon double bond, resulting in the formation of a mixture of two products: 2-chloro-3-(chloromethylene) indole and 3-chloro-2-(chloromethylene)indole.

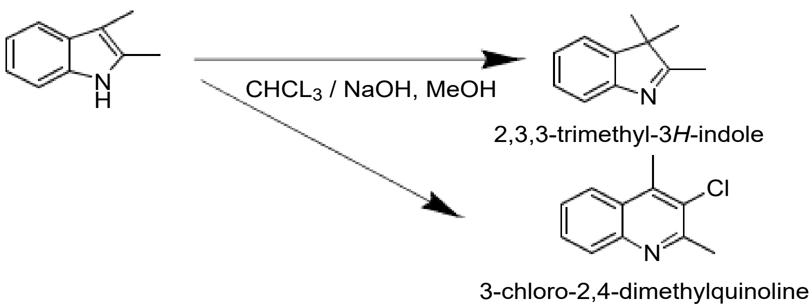
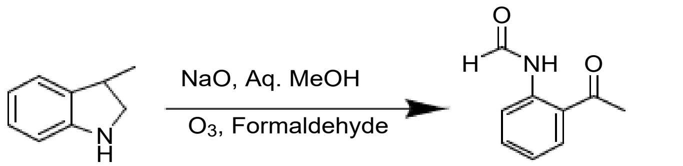


Fig. 1.8 : Reaction with carbene

1.1.3.4 Oxidation Reaction of Indole: The C2-C3 double bond in indole can be cleaved using oxidative reagents such as ozone, sodium periodate, potassium superoxide, or CuCl2 in an oxygen atmosphere. These reagents induce oxidation of the double bond, resulting in its cleavage. This process allows for the fragmentation of the indole molecule at the C2-C3 position, leading to the formation of two separate products.

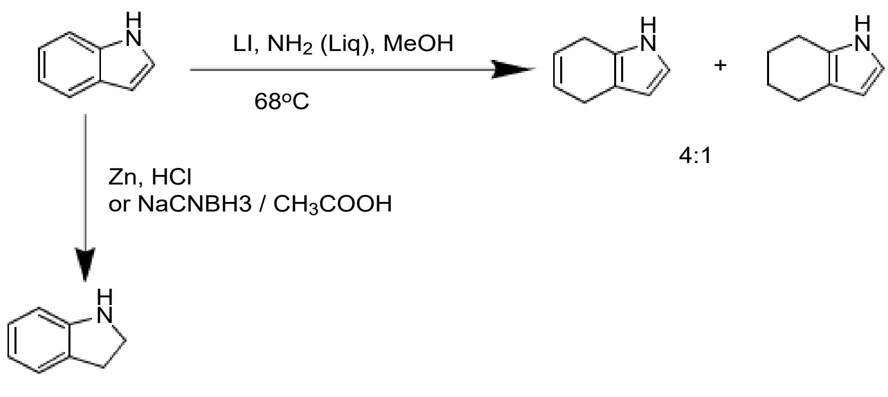


N-(2-acetylphenyl)formamide

Fig. 1.9: Oxidation Reaction of Indole

1.1.3.5 Reduction Reaction of Indole:

Selective reduction of the indole ring can be achieved using different reducing agents. Nucleophilic agents like LiAlH4 or NaBH4 do not affect the indole nucleus, leaving it intact. However, lithium in liquid ammonia selectively reduces the benzene ring to produce 4,7-dihydroindole as the major product. On the other hand, acidic reagents such as Zn/HCl or NaCNBH3/CH3COOH can reduce the heterocyclic ring to yield indoline.



Indoline

Fig. 1.10: Reduction Reaction of Indole

1.1.3.6 Reaction of N-metallated Indoles:

In the presence of very strong bases, such as alkali metal amides or hydrides, indoles act as weak acids. Consequently, they can be deprotonated to form N-metallated derivatives. These N-metallated indoles possess nucleophilic properties and can react with appropriate electrophiles either at the nitrogen atom (N) or at the carbon-3 position (C-3) [38-40].

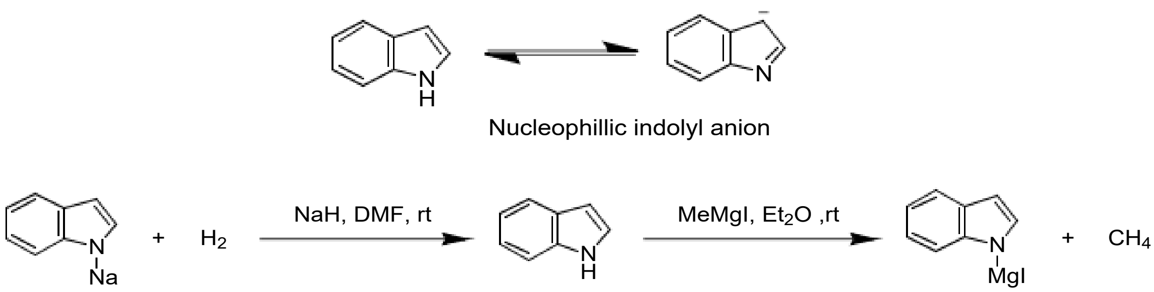


Fig. 1.11: Reaction of N-metallated Indoles

1.1.4. Spectral Data: The spectroscopic characterization of indole has been established by various instrumental method of analysis like, ultraviolet (UV), infrared (IR), nuclear magnetic resonance (NMR) and mass spectroscopy.

Brief discussion of spectral features is presented as follows:

1.1.4.1 U.V. spectra of indole: Indole exhibits fluorescence with an excitation peak at 274 nm and an emission peak at 332 nm, resulting in a Stokes' Shift of 58 nm.

1.1.4.2IR Spectroscopy: The IR (KBr) spectrum of indole NH-band at 3389 cm -1, hydrogen bonded -OH stretching band between (2730 to 3127) cm -1 and carboxylic group (C = O) stretching at 1701 cm -1.

1.1.4.3 NMR : For proton NMR, the chemical shifts usually fall within the range of 0-10 ppm, with the hydrogen attached to the nitrogen atom (N-H) typically appearing around 7-8 ppm. For carbon-13 NMR, the chemical shifts can range from 0 to 200 ppm, with the carbon attached to the nitrogen atom (C-N) often appearing around 120-140 ppm [41-42].

1.1.4.4. Mass Spectrometry:

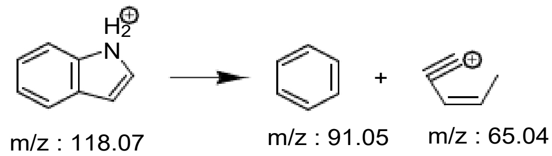


Fig. 1.12: Fragmentation pattern of indole

In our current study, we initially employed the computer aided drug designing approaches for the finding out the potential indole based moieties which can be synthesized further against the anti-microbial agents and for the treatment of tumor. The potent moieties through the CADD approaches will further be synthesized using the well established organic chemistry synthetic routes. In the last step the synthesized compounds will be put under biological evaluation against the various stains of the microbes and against the various cancer cell lines.

CHAPTER-2

AIM AND PLAN OF WORK

The increasing clinical implication of drug resistance and adverse effect of cancer has lent additional urgency to infectiousresearch and new drug development. Drug design in heterocyclic chemistry is created asa multidisciplinary and innovative role in development of such types of drugs. We are focusing on the produce new molecules that can successfully fight cancer and infections by synthesizing antibacterial and anticancer indole derivatives. The goal is to create molecules that are potent against cancer cells, overcome drug resistance, improve selectivity and potency while having the fewest negative effects possible.

The following goals can help accomplish the aforementioned goal:

- Thorough review of the literature to learn about the situation today and what the needs are for the future.
- To perform the *in-silico* studies such as 2D-QSAR, Molecular docking & Molecular Dynamics for screening of the large number of compounds having antimicrobial and anticancer activity.
- To perform the synthesis of those compounds which show promising antimicrobial and anticancer activity.
- Establishing physical parameters such as solubility, melting point, and thin layer chromatography.
- Using mass spectroscopy, 1H NMR spectra, IR, and 12CNMR to characterise synthesised chemicals.
- To perform the *in-vitro* [26] evaluation of the compounds for the treatment of AD.

- Analysis and compilation of the results.

PLAN OF WORK:

Stage	Activities	Time Duration (In Months)					
		0-6	6-12	12-18	16-24	24-30	30-36
Course Work	Develop advanced research skills,	→					
Literature Review	understand current progress and identify gaps		→				
Design Phase	CADD			→			
Synthesis & Characterisation	Synthesize target indole derivatives and Characterization				→		
Biological Evaluation	Antimicrobial & Anticancer					→	
Pharmacokinetics	Evaluate ADME and safety profile					→	

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CHATPER-3

REVIEW OF LITERATURE

3.1 REVIEW ON INDOLE DERIVATIVES

Indole is an aromatic, heterocyclic organic compound. Its bicyclic structure consists of a six-membered benzene ring fused to a five-membered nitrogen-containing pyrrole ring. Indole is the base for many pharmaceuticals and a popular element in fragrances. Compounds containing an indole ring are known as indoles. Interestingly, tryptophan is an indolic amino acid that is converted into the neurotransmitter serotonin. Moreover, a wide range of naturally occurring terrestrial or marine compounds with advantageous biological properties contain the indole ring [43].

3.1.1 Method of synthesis:

3.1.1.1Fischer Indole Synthesis: This reaction was discovered in 1983 by Emil Fischer. It involves the cyclization of arylhydrazones under heating conditions in the presence of either protic acids (like HCl, H2SO4, or TsOH) or Lewis acids (such as ZnCl2, PCl3, or FeCl3). This reaction mechanism, facilitated by acidic conditions, leads to the formation of indole molecules [44].

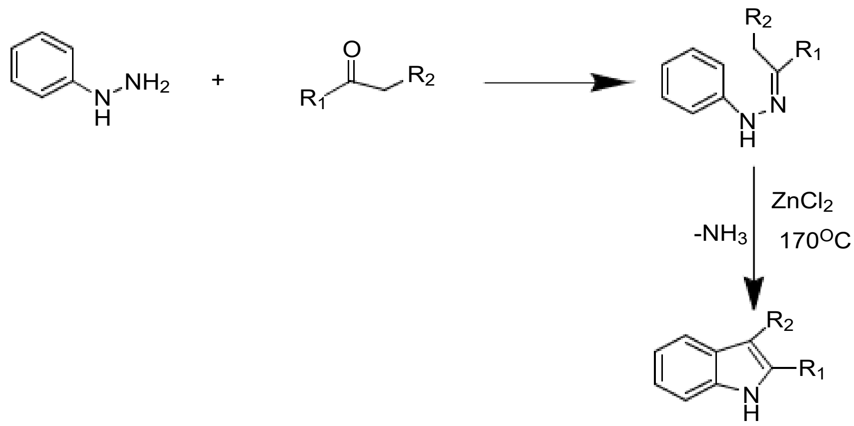


Fig. 3.1: Fischer Indole Synthesis

3.1.1.2 Reissert Synthesis: This method was developed by German chemist Siegmund Reissert in 1881. The Reissert synthesis typically involves the reaction of aniline derivatives with isatin (2,3-dioxoindole) or its derivatives, resulting in the formation of substituted indoles [45].

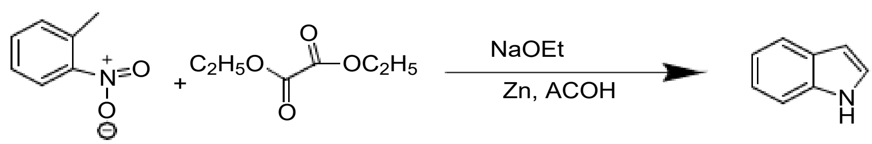


Fig. 3.2: Reissert Synthesis

3.1.1.3 Madelung Synthesis: It was developed by German chemist Philip Madelung in 1886. This synthesis involves the condensation reaction of an aryl ketone (usually acetophenone or its derivatives) with a primary amine and an aldehyde using an acid catalyst, typically sulfuric acid or hydrochloric acid. The reaction proceeds via a series of condensation, cyclization, and dehydration steps, ultimately resulting in the formation of an indole derivative [46].

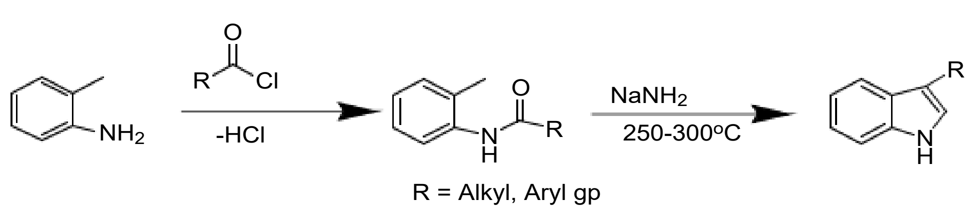


Fig. 3.3 :Madelung Synthesis

3.1.1.4 Bartoli indole synthesis: The Bartoli indole synthesis is a powerful method for the synthesis of indoles, which was developed by Italian chemist Carlo Bartoli in the 1970s.Ortho-substituted nitrobenzenes react with three mole equivalents of vinyl magnesium bromide (Grignard reagent) to give 7-substituted indoles .

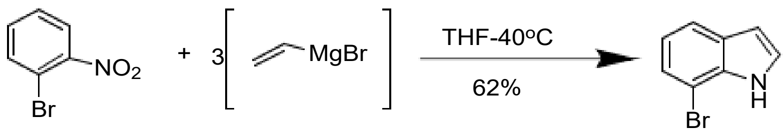


Fig.3.4 : Bartoli indole synthesis

3.1.1.5 Nenitzescu indole synthesis: The Nenitzescu indole synthesis is a significant method for the synthesis of indoles, developed by Romanian chemist Radu Nenitzescu in the 1930s. ortho-aminobenzaldehyde and a ketone, undergo a condensation reaction in the presence of an acid catalyst, such as concentrated sulfuric acid or polyphosphoric acid. The reaction proceeds through a series of steps involving nucleophilic addition, cyclization, and dehydration, ultimately leading to the formation of the indole ring[47].

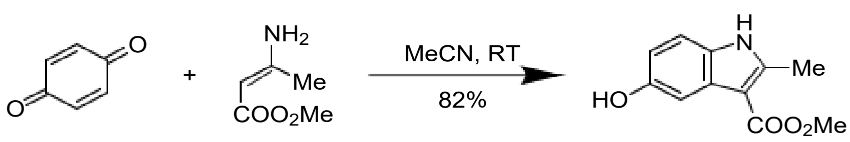


Fig.3.5: Nenitzescu indole synthesis

3.1.1.6 Bischler Indole Synthesis: It was developed by the German chemist Bernhard Bischler in 1903. The reaction involves the cyclization of a β-arylethylamine with a ketone or aldehyde using an acid catalyst, typically sulfuric acid. The reaction proceeds through an iminium intermediate followed by intramolecular electrophilic aromatic substitution to form the indole ring system [48].

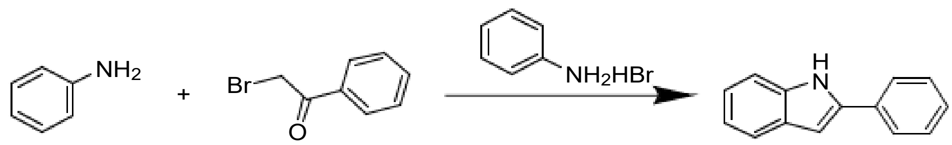


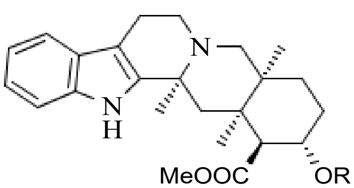
Fig. 3.6 : Bischler Indole Synthesis

3.1.2 Biological Activities:

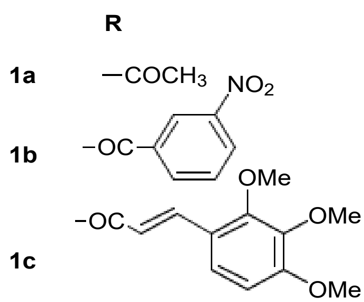
Literature survey states that Indole and its various substituent's derivatives were medicinally important and shows biological effect which are mentioned below.

3.1.2.1 Antimicrobial Activities:

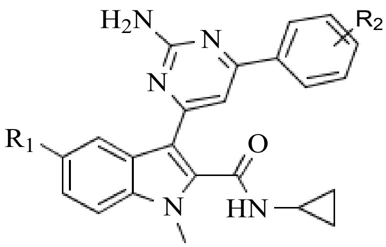
Dwivedi GR*Et al*(2015) A-yohimbine underwent chemical transformation to produce semisynthetic derivatives, which were then evaluated for their antibacterial activities and synergy potential when combined with nalidixic acid (NAL) against E. coli strains CA8000 and DH5a. Among these derivatives, derivative **1c** exhibited an eightfold reduction in minimum inhibitory concentration (MIC) of NAL against DH5a and a four- to eightfold reduction against CA8000. Additionally, these alkaloids lowered the MIC of tetracycline by up to eightfold against MDREC-KG4, a multidrug-resistant clinical isolate of *E. coli.*[49.].



(1)



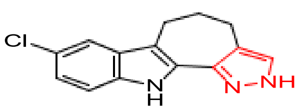
Some series of indole-pyrimidines studied by **Hanane Zaki et. al. (2018).** He developed 3D-QSAR for this series, using Comparative Molecular Field Analysis (CoMFA) and Comparative Molecular Similarity Index Analysis (CoMSIA) methods. The model has shown good statistical results i.e. R^2 = 0.922 and R^2 =0.876 for CoMFA and CoMSIA respectively. To validate the predictive power of the resulting models, external validation multiple correlation coefficient was calculated and we have noted a favorable estimation of stability for the two methods (Q2 = 0.502 and Q 2 =0.530 for CoMFA and CoMSIA methods, respectively). Basing on 3D-QSAR results new molecules were designed and the ADMET proprieties were predicted to select the potential hits. According to the ADMET and Drug liknes prediction results we have proposed two new heterocyclic molecules with a strong anti-fungal activity against *C. albicans*[50].



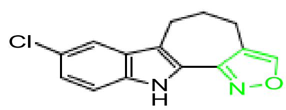
(2)

	R_1	R_2
2a.	$C(CH_3)_3$	4-F
2b.	Cl	4-F
2c.	C_2H_5	3-F
2d.	$C(CH_3)_3$	3-F

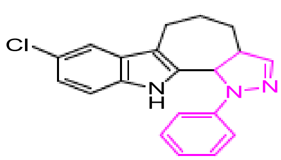
Ezhumalai Yamuna et. al. (2012) A novel class of heterocycles, including substituted pyrazolo-, isoxazolo-, and pyrimidocyclohepta[b]indoles, was synthesized through the condensation of substituted 7-(hydroxymethylene)-7,8,9,10-tetrahydrocyclohepta[b]indol-6(5H)-ones with various reagents such as hydrazine hydrate, hydroxylamine hydrochloride, phenylhydrazine, urea, and thiourea. These molecules were then evaluated for their in vitro antimicrobial and antimycobacterial potential against Mycobacterium tuberculosis H37Rv (MTB). Among the compounds tested, following showed a minimum inhibitory concentration (MIC) of 3.12 mg/ml or higher against MTB [51].



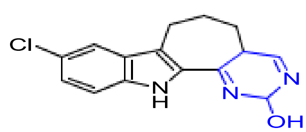
(3)



(4)

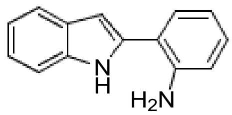


(5)



(6)

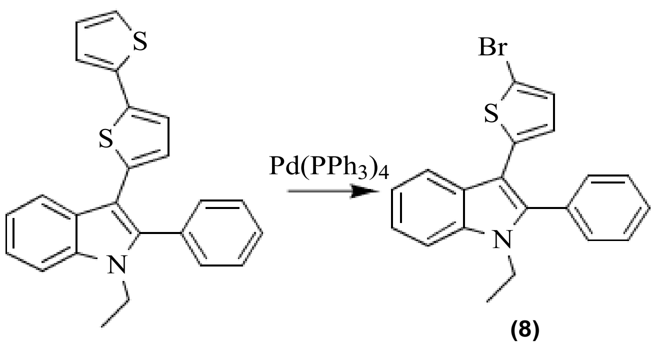
Rushikesh Tambat et. al. (2019) In this study, a series of new Schiff bases incorporating the indole moiety were synthesized and characterized through elemental analyses, IR, 1H and 13C NMR, and mass spectral studies. These compounds underwent screening for both antioxidant and antimicrobial activities. One compound **(7)** showed notable efficacy in both antioxidant and antimicrobial assays[52].



2-(1*H*-indol-2-yl)aniline

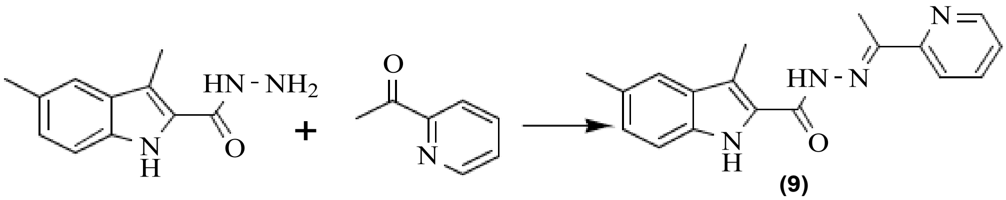
(7)

Metin Konus et. al. (2022) In this study, the biological properties of heteroaromatic indoles, including antioxidant, antimicrobial, cytotoxic, and apoptosis-induced anticancer effects, were investigated for the first time. However, compound **(8)** displayed high reducing activity and potent antibacterial effects against *Enterococcus faecalis*[53].



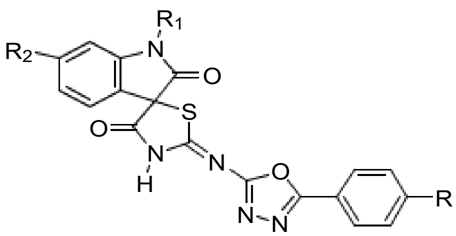
(8)

Fazlur Rahaman et.al. (2014) A new series of transition metal complexes comprising Co(II), Ni(II), Cu(II), Zn(II), Cd(II), and Hg(II) coordinated with a tridentate ligand, 3,5-dimethyl-N-[(1E)-1-pyridin-2-ylethylidene]-1H-indole-2-carbohydrazide (L), was synthesized. The ligand and its complexes were assessed for antibacterial activity against *Escherichia coli* and *Staphylococcus aureus*, as well as antifungal activity against *Aspergillus niger* and *Candida albicans*[54].



(9)

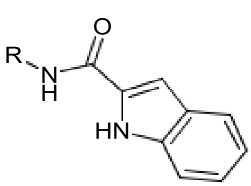
Handan Altıntas et. al. (2006). In this study, new compounds were made and evaluated for their antimicrobial activity against various bacterial and fungal strains. Among them, compound **(10a)** showed higher activity than the standard cefuroxime sodium against Staphylococcus aureus, while compound **(10b)** exhibited comparable activity against Staphylococcus epidermidis. These findings suggest the potential of these compounds as antimicrobial agents, warranting further investigation [55].



(10)

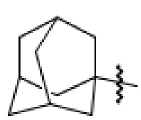
	R	R_1	R_2
10a.	OCH_3	H	H
10b.	Cl	H	H

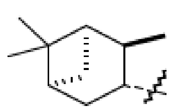
N.D. Franz *et al* (2017) A series of indole-2-carboxamides were synthesized, demonstrating inhibition of MmpL3 and potent activity against various mycobacterial species, including fast and slow-growing types. These compounds showed selectivity for mycobacteria without significant bactericidal effects on other pathogens like S. aureus or P. aeruginosa. Minimal cytotoxicity was observed against human THP-1 cells, indicating good selectivity indices. The promising results suggest these compounds as potential candidates for further preclinical testing as therapeutics against non-tuberculous mycobacteria (NTM) [56].



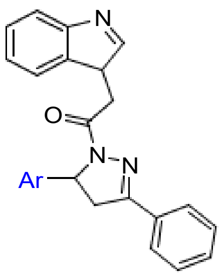
(11)

R

11a. 

11b. 

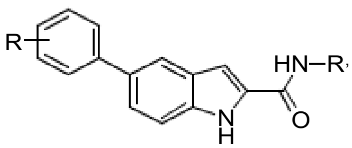
Quazi *et al (2017)*synthesized Series of 1 of 1-[(3,5 diphenyl substituted) -4,5-dihydro-1H-pyrazol-1-yl]-2-(3H-indol-3-yl) ethan-1-one derivatives The synthesized new compounds Show potency against gram positive and gram negative bacteria. All molecules exhibits moderate to average antifungal activity [57].



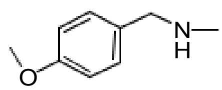
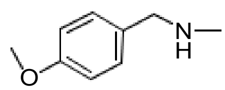
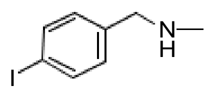
(12)

	Ar
12a	C_6H_5
12b	$C_6H_4OCH_3(4)$
12c	$C_6H_4Cl(4)$
12d	$C_6H_4Cl(2)$
12e	$C_6H_4N(CH_3)2$
12f	$C_6H_4NO_2(4)$

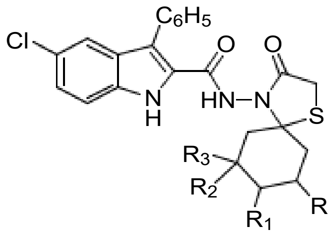
Mane D Y *et al (2016)* *synthesized* A series of novel, bioactive 5-substituted indole-2-carboxamide derivatives. Molecules showed good antibacterial activity against *K. pneumoniae* and *E. coli* [58].



(13)

.	R	R،
13a	4-OMe	
13b	4-F, 3-Me	
13c	4-OMe	

Cihan-Ustundağ*et al* (2019) synthesized series of indole-based spirothiazolidinones and evaluated, in vitro, for their antitubercular, antiviral, antibacterial, and antifungal activities [59].

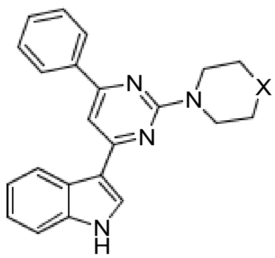


(14)

	R	R_1	R_2	R_3
14a	H	H	H	H
14b	CH_3	H	H	H
14c	H	CH_3	H	H
14d	H	C_3H_7	H	H
14e	H	C_6H_5	H	H

3.1.2.2. Antimalarial Activities:

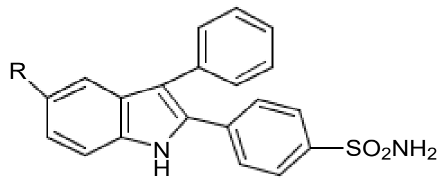
Agarwal et. al. (2005) In this study, a collection of substituted indole analogs were made and assessed for their in vitro antimalarial efficacy against P. falciparum. Among the synthesized compounds, six displayed a MIC of 1 lg/mL, demonstrating remarkable activity. These compounds exhibited significantly higher potency in vitro compared to pyrimethamine, indicating their potential as potent antimalarial agents deserving further investigation [60].



(15)

		X
15a	=	N-Me
15b	=	CH_2
15c	=	O

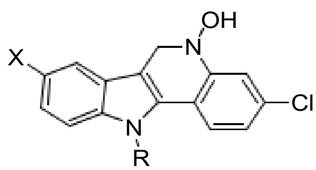
S.Muthu Kumar et al (2005) A series of derivatives, including 2-(4-amino sulfonyl phenyl) 3-phenyl indole substituted amine, 2-(4-amino sulfonyl phenyl) 3-phenyl-5 chloro indole, and 2-(4-amino sulfonyl phenyl) 3-phenyl-5 fluoro indole, were synthesized and their structures confirmed via various analytical techniques. Their antimalarial activities were evaluated against both chloroquine-sensitive (D10) and chloroquine-resistant (RSA11) strains of Plasmodium falciparum in vitro. The 2-(4-amino sulfonyl phenyl) 3-phenyl-5 chloro indole derivatives showed enhanced activity compared to the unsubstituted analogues, indicating potential as antimalarial agents [61].



(16)

	R
16a	F
16b	OCH3
16c	I

LM Werbel et. al. (1993) made a series of antimalarial derivatives. The basic side chain as well as the ring N-oxide are critical for antimalarial although the most active analog in our studies was the 8-nitro compound [62].

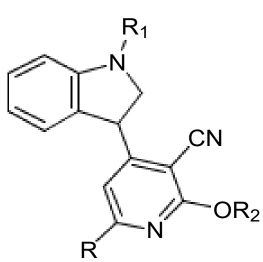


(17)

X	R
Cl(8-NO_2)	$Et_2NCH_2CH_2$

3.1.2.3 Anti-inflammatory Activities:

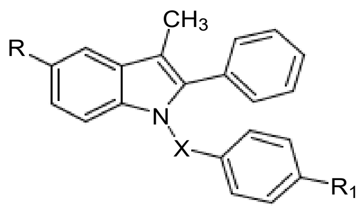
Srour, Panda, Salman et al (2018) Some novel bronchodilatory Indole– pyridine conjugates were synthesized in a facile pathway through reaction of 2-[(1- alkyl-1H-indol-3-yl)methylene]malononitriles 4a,b with the corresponding ketone-containing compounds using of sodium alkoxide. The structures of the made molecules were affirmed via single-crystal X-ray studies. When tested on histamine-precontracted isolated tracheal rings of guinea pigs, compound **18a** exhibited potent bronchodilation properties, approximately twice as potent as the standard bronchodilator, theophylline.Additionally, few of the molecules which were synthesized exhibited good results in reducing interleukin-8 (IL-8) production during lipopolysaccharide-induced airway inflammatory bioassays, indicating potential anti-inflammatory effects [63].



(18)

	R	R_1	R_2
18a	Ph	Et	Et
18b	4-ClC_6H_4	Et	Me
18c	4-ClC_6H_4	Et	Et

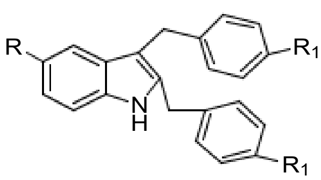
Khaled R. A. Abdellatif et. al. (2015) A series of 3-methyl-2-phenyl-1-substituted-indole derivatives, including analogs of indomethacin, were synthesized through Fisher indole synthesis by reacting propiophenone with various substituted phenylhydrazine hydrochlorides. These molecules were then assessed for their anti-inflammatory and analgesic properties both in vitro and in vivo. Among them, the methanesulphonyl derivatives 19**a, 19b, & 19c** showed the greatest anti-inflammatory and analgesic activities[64].



(19)

	R	**X**	**R_1**
19a	SO2CO3	CO	H
19b	SO2CO3	CO	4-Cl
19c	SO2CH3	CH2	H

Mónica S. Estevão et.al. (2012) In this study, a small library of new indolic compounds with two different substitution patterns on the indole scaffold was synthesized. Evaluation of the synthesized indole library against COX-1 and COX-2 enzymes revealed that compound 15d exhibited significant activity at 50 mM, displaying 70% inhibition of COX-2 and low inhibition of COX-1 (18 ± 9%). Docking studies supported these findings, indicating that compound **20d** likely functions as the most potent selective COX-2 inhibitor in this series, with a binding orientation similar to the known selective inhibitor SC-558 [65].

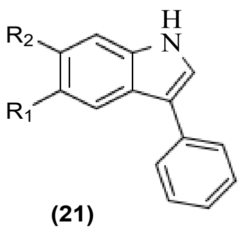


(20)

	R	**R_1**
20a	SO2Me	F
20b	SO2Me	Cl
20c	SO2Me	Br
20d	SO2NH2	F

3.1.2.4 Anti- Alzheimer Activity:

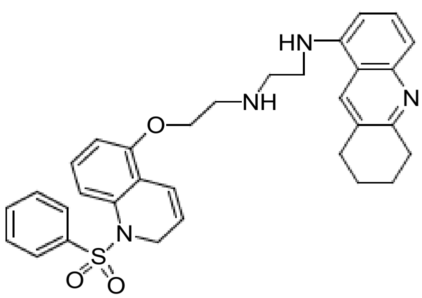
Laura Llorach-Pares. Et al (2018) Alzheimer's disease (AD) is increasingly becoming a significant health and socioeconomic concern today. It is a neurodegenerative disorder without a cure, expected to escalate due to population aging. Current AD treatments offer only modest symptom relief. These studied in silico methods to assess the inhibitory activity of various marine natural compounds and newly designed molecules derived from them against the aforementioned protein kinases. The investigation unveiled potential new inhibitors with therapeutic applications. compounds 21a and 21c could be possible ATP-competitive inhibitors against GSK3β, CK1δ, DYRK1A, and CLK1[66].



(21)

	R1	**R2**
21a	Br	Br
21b	Cl	Cl
21c	Br	Cl

WichurT. et al (2021) A series of compounds aimed at targeting disease-related processes was synthesized, resulting in the identification of two promising candidates, compounds 17 and 35. These compounds act as both 5-HT6R antagonists (with Ki values of 13 nM and 15 nM, respectively) and cholinesterase inhibitors, employing distinct mechanisms of enzyme inhibition. Additionally, they exhibit favourable pharmacological characteristics and possess a promising ADMET profile [67].

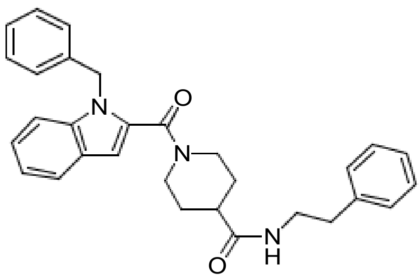


(22)

3.1.2.5 Anti-viral activity:

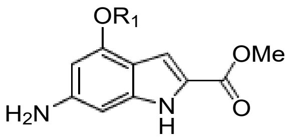
Zhang M. et al (2015) Indole derivatives possess a distinctive capability to mimic peptide structures and bind reversibly to enzymes, offering significant potential for the discovery of novel drugs with diverse mechanisms of action. Notably, seven indole-containing drugs were among the Top-200 Best Selling Drugs by US Retail Sales in 2012, highlighting their commercial importance. Moreover, the market boasts numerous approved indole-containing drugs, along with compounds undergoing various clinical phases or registration statuses, underscoring the ongoing interest and investment in harnessing the therapeutic potential of these compounds [68].

Delekta, P. C.et al (2014)detailed the antiviral effectiveness of the leading third-generation compound, **(23).** Through cell-based assays utilizing western equine encephalitis virus replicons, these compounds exhibited remarkable half-maximal inhibitory concentrations of 1 M and selectivity indices surpassing 100. Additionally, **(23)** demonstrated consistent potency against fully infectious virus in cultured human neuronal cells. Importantly, these compounds displayed wide-ranging inhibitory activity against various RNA viruses in culture, encompassing members of the *Togaviridae, Bunyaviridae, Picornaviridae*, and *Paramyxoviridae* families [69].



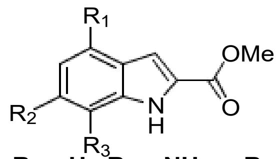
(23)

Xue S. ***et al*****(2014)** A novel set of derivatives based on indole-2-carboxylate was synthesized and assessed for their broad-spectrum antiviral properties in vitro. Some compounds showed significant antiviral effects, notably compound **(24),** which displayed a remarkable selectivity index (SI) of 17.1 against Cox B3 virus. Another compound, **(25),** exhibited potent inhibition against influenza A with an IC50 of 7.53 μmol/L and the highest SI value of 12.1. Analysis of structure-activity relationships (SAR) indicated that the presence of alkyloxy at the 4-position of the indole ring was dispensable for antiviral activity. However, introducing an acetyl substituent at the amino group proved detrimental to antiviral activity against RNA viruses [70].



R_1 = Isobutyl

(24)



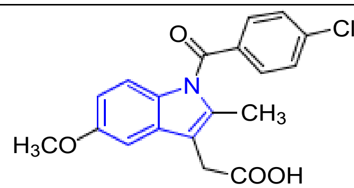
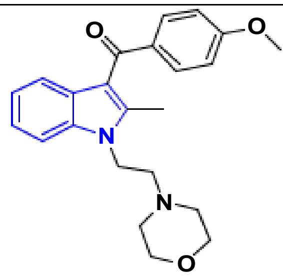
R_1 = H, R_2 = NH_2 , R_3 = H

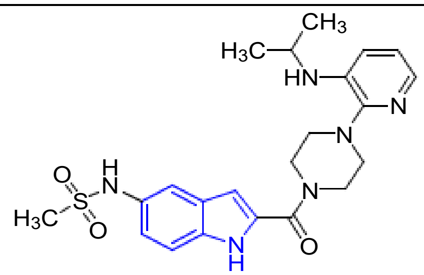
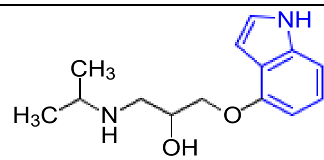
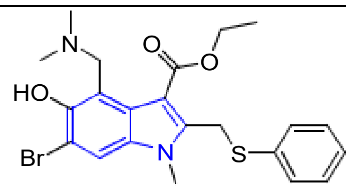
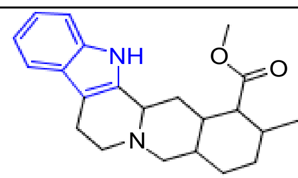
(25)

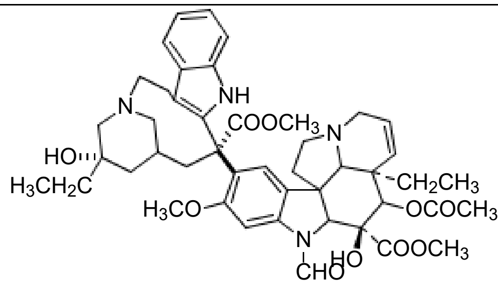
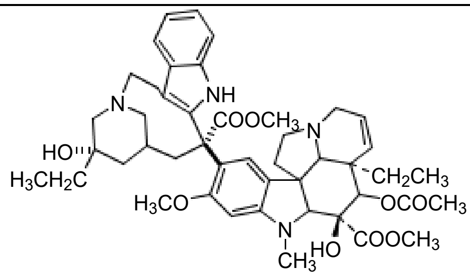
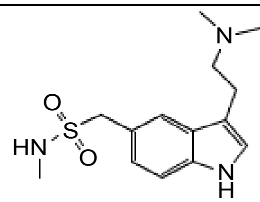
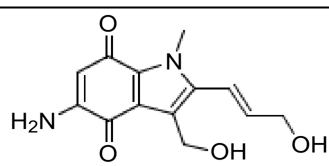
3.1.3 Marketed Preparations of Indole:

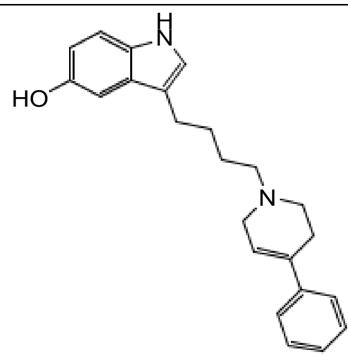
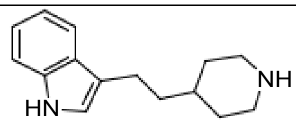
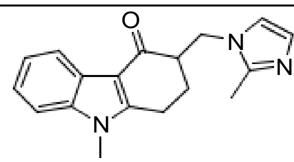
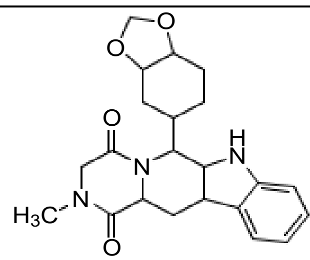
Some successful Indole base drugs available in market presented in table no.

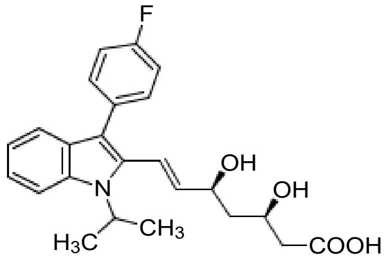
Table 3.2: Some successful Indole base drugs available in clinical therapy [185-192]:

Sr. No.	Name of the Drug	Structure	Applications
1.	Indomethacin	 **2-(1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl)acetic acid**	Anti-inflammatory drug (NSAID)
2.	Pravadoline	 **(4-methoxyphenyl)(2-methyl-1-(2-morpholinoethyl)-1*H*-indol-3-yl)methanone**	Analgesic Drugs

3.	Delavirdine	 ***N*-(2-(4-(3-(isopropylamino)pyridin-2-yl)piperazine-1-carbonyl)-1*H*-indol-5-yl)methanesulfonamide**	Antiretroviral agent
4.	Pindolol	 **1-((1*H*-indol-4-yl)oxy)-3-(isopropylamino)propan-2-ol**	Antihypertensive drugs
5.	Arbidol	 **ethyl 6-bromo-4-((dimethylamino)methyl)-5-hydroxy-1-methyl-2-((phenylthio)methyl)-1*H*-indole-3-carboxylate**	Antiviral drugs
6.	Yohimbine	 **methyl 2-methyl-1,2,3,4,4a,5,7,8,13,13b,14,14a-dodecahydroindolo[2',3':3,4]pyrido[1,2-*b*]isoquinoline-1-carboxylate**	Sexual dysfunction

7.	**Vincristine**	 **methyl (3a*R*,5*S*)-4-acetoxy-3a-ethyl-9-((5*S*,9*S*)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2*H*-3,7-methano[1]azacycloundecino[5,4-*b*]indol-9-yl)-6-formyl-5-hydroxy-8-methoxy-3a,3a^{1},4,5,5a,6,11,12-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate**	Anticancer
8	**vinblastine**	 **methyl (3a*R*,5*S*)-4-acetoxy-3a-ethyl-9-((5*S*,9*S*)-5-ethyl-5-hydroxy-9-(methoxycarbonyl)-1,4,5,6,7,8,9,10-octahydro-2*H*-3,7-methano[1]azacycloundecino[5,4-*b*]indol-9-yl)-5-hydroxy-8-methoxy-6-methyl-3a,3a^{1},4,5,5a,6,11,12-octahydro-1*H*-indolizino[8,1-*cd*]carbazole-5-carboxylate**	Anticancer
9	Sumatriptan	 **1-(3-(2-(dimethylamino)ethyl)-1*H*-indol-5-yl)-*N*-methylmethanesulfonamide**	Antimigraine
10	Apaziquone	 **(*E*)-5-amino-3-(hydroxymethyl)-2-(3-hydroxyprop-1-en-1-yl)-1-methyl-1*H*-indole-4,7-dione**	Anticancer

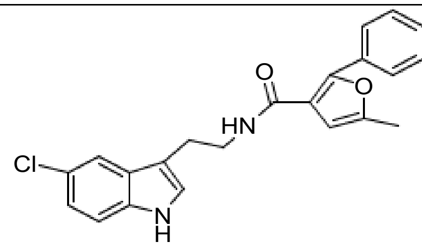
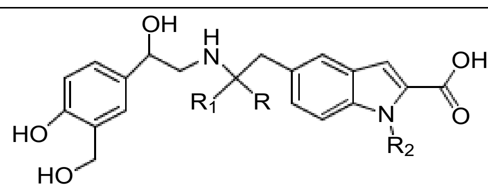
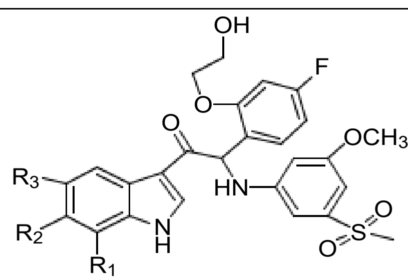
11	Roxindole	 **3-(4-(4-phenyl-3,6-dihydropyridin-1(2*H*)-yl)butyl)-1*H*-indol-5-ol**	Schizophrenia
12	Indalpine	 **3-(2-(piperidin-4-yl)ethyl)-1*H*-indole**	Antidepressant
13	Ondansetron	 **9-methyl-3-((2-methyl-1*H*-imidazol-1-yl)methyl)-1,2,3,9-tetrahydro-4*H*-carbazol-4-one**	Anti-nausea and vomiting
14	Tadalafil	 **6-(hexahydrobenzo[*d*][1,3]dioxol-5-yl)-2-methyl-2,3,6,6a,7,11b,12,12a-octahydropyrazino[1',2':1,6]pyrido[3,4-*b*]indole-1,4-dione**	To improve erectile dysfunction

15	Fluvastatin	 **(3*R*,5*S*,*E*)-7-(3-(4-fluorophenyl)-1-isopropyl-1*H*-indol-2-yl)-3,5-dihydroxyhept-6-enoic acid**	Anti-hyperlipidemia

3.1.4 Recent Patent of Indole

Few patents of Indole have discussed below in **Table 3.8.**

Table 3.3: Recent Patents of Indole [193-200]:

Year	Patent No.	Activity	Lead Compound
2017	EP3190109B1	**Treatment of neurodegenerative disorder**	
2008	Au2005311925a1	**PPAR active compounds**	**Not Mentioned**
2007	**US 7,183.294 B2**	**Treatment of inflammatory, allergic and respiratory diseases**	
2017	**Wo 2017/046258 a**	**Antiviral activity**	

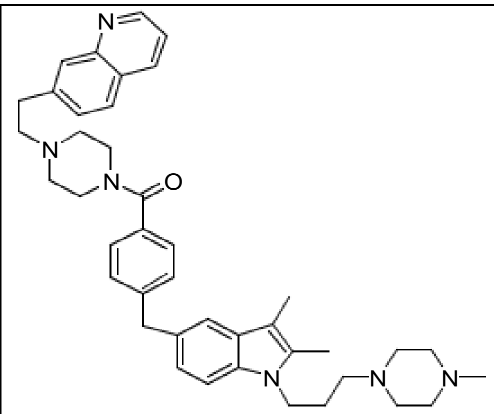
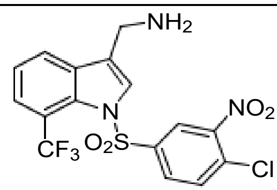
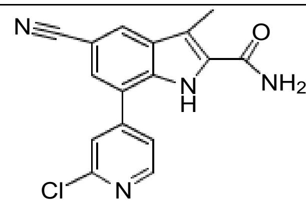
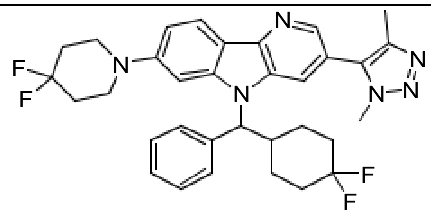
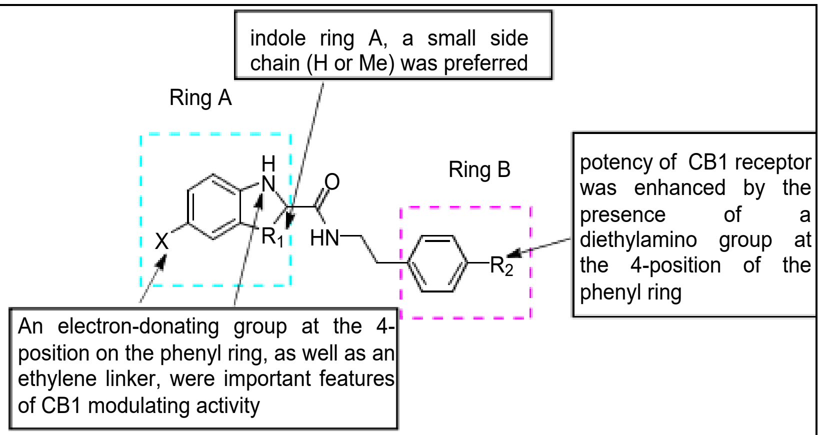
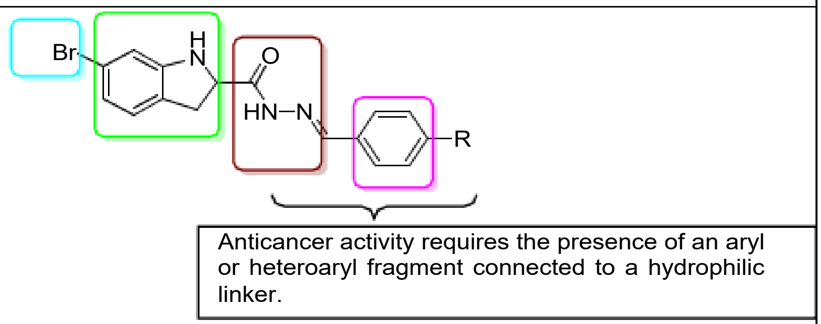
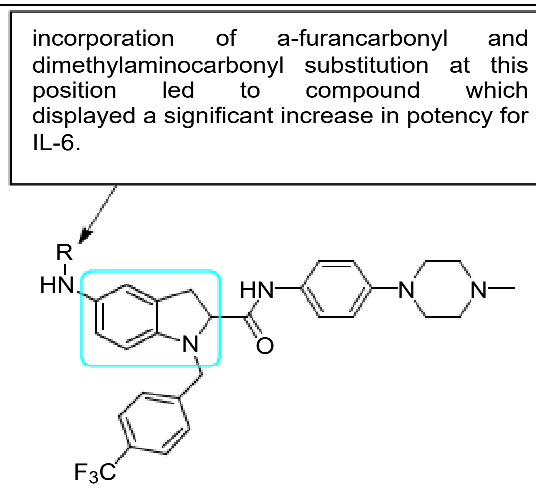
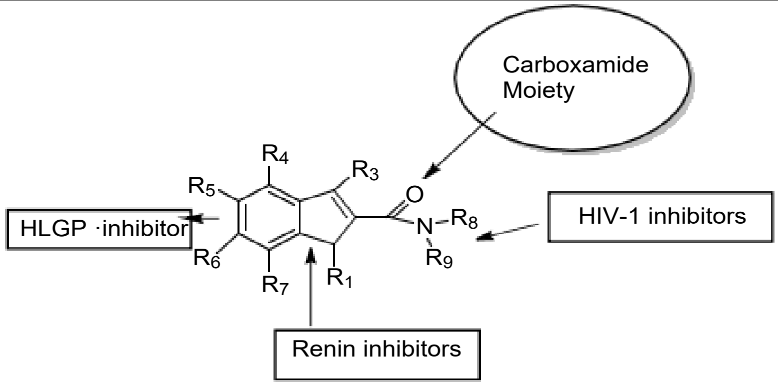
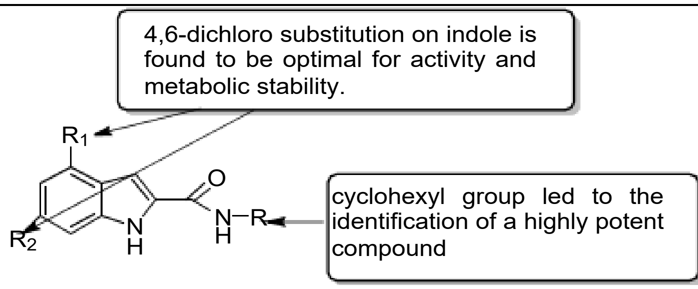
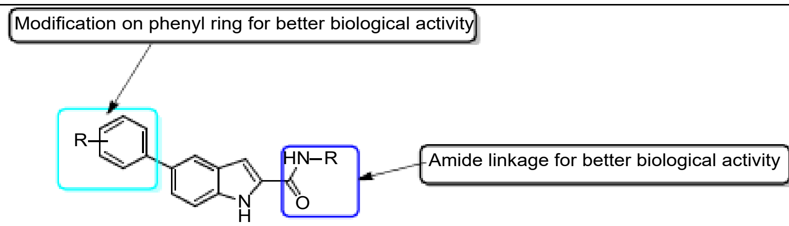
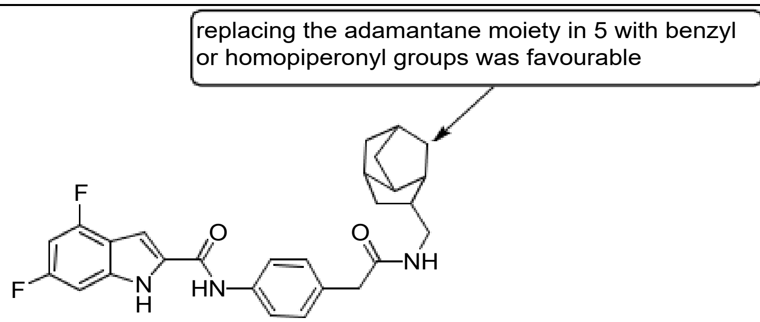
2016	**WO2016008011A1**	**Anticancer drugs**	
2010	**US7807705B2**	**Anti-tumor agent**	
2015	**WO2015036412A1**	**Treatment of Neurogenerative &Neuropsychosis disorder.**	
2016	**WO2016183115A1**	**Anti-Cancer agents**	

Table 3.4: SAR studies of Indole-2- carboxamide derivatives [201-205]:

Sr. No.	**Activity**	**SAR**

<table>
<tr><td>1.</td><td>CB1 receptor allosteric modulators</td><td>
</td></tr>
<tr><td>2.</td><td>Antitumor activity</td><td>
</td></tr>
<tr><td>3.</td><td>Anti-inflammatory activity</td><td>
</td></tr>
</table>

4.	**Enzyme inhibitors**	
5.	**Antitubercular activity**	
6.	**Antimicrobial activity**	
7.	Antitumor Activity	

3.2 RESEARCH GAP:

Literature studies revealed that indole-2-carboxamide are well documented for potential Biological activity. SAR studies performed on this nucleus demonstrated that substitution are mainly tried on pyrrole ring of indole-2-carboxamide, while substitution on the phenyl ring is relatively less explored, confined to mainly halogens.

So, the current proposal, we envisioned to explore the effect of large substitution at phenyl ring on the antimicrobial and anticancer activity.

Secondly, although free amide group preferentially at the second position of indole is found to be crucial for the activity, however only few studies explored the effect of extended amide on activity. So, we are planning to extent the amide by making substitution on nitrogen, and subsequently anti-microbial and anti-cancer will be evaluated.

3.3 RESEARCH HIGHLIGHTS:

Indole containing pharmacophore have been the promising scaffold for the lead compounds in clinical evaluations. This review compiles the recent development on indole derivatives as antimicrobial and anti-cancer agents based on mechanism of action, such as HDAC inhibitors, DNA topoisomerases, SIRT and MDM2 inhibitors, tubulin inhibitors, and aromatase inhibitors. Additionally, the current research has also inferred SAR of some of the well studied class of compounds, eg., HDAC inhibitors. Most of the HDAC inhibitors consist of hydroxamic acid group as ZBG, a cap group, and an aromatic or aliphatic linker. The indole scaffold is either used as the cap group or the aromatic spacer. The selectivity of the active moiety can be increased by optimizing the substituent on the indole scaffold, and hence the potential toxicity (such as fatigue, cardiotoxicity and hematotoxicity) could be significantly reduced. In addition, hybridization of indole with other active pharmacophore would be a judicial approach to design novel and potent anti-microbial and anti-cancer agents.

CHAPTER-4

MATERIALS ANDMETHODS

4.1 Computer Hardware and Software

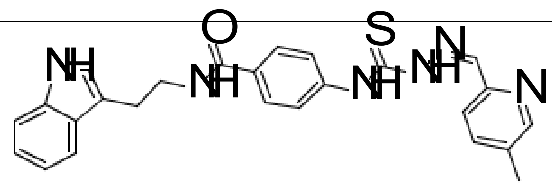
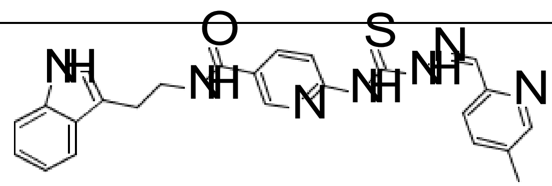
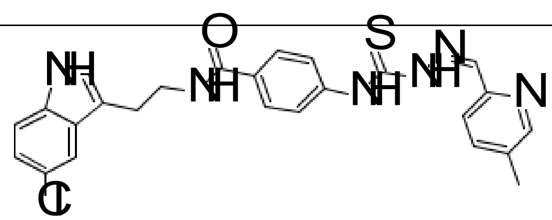
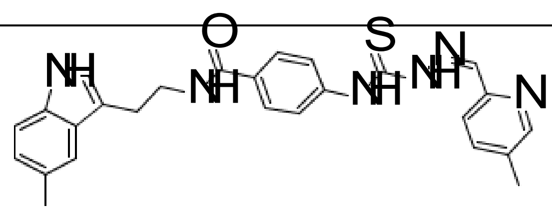
All the CADD work was done by using Lenovo thinkpad system having intel core i5 @ 2.40 GHz, 8 GB RAM and 64-bit operating system. Marvin sketch of ChemAxon has been used in the molecular modeling work including drawing of structures, energy minimization etc. QSARINS software of the University of Insurbia is employed to develop and externally validate the generated QSAR model [206]. AutoDock tools and AutoDock vina of the scripps research institute is employed for all the molecular docking studies [207].

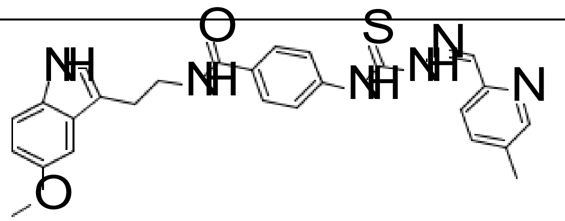
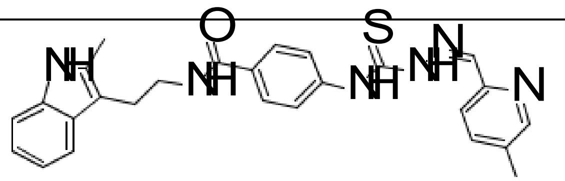
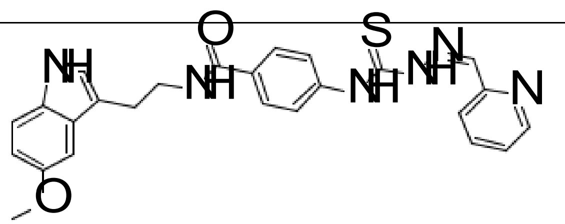
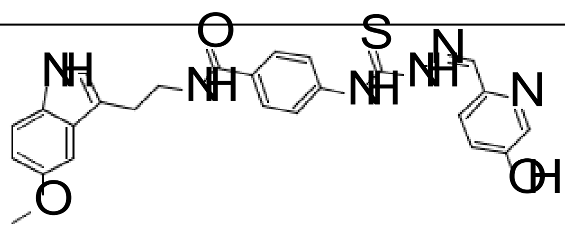
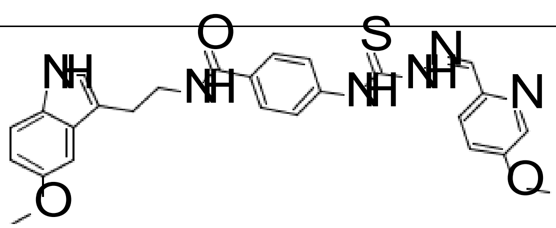
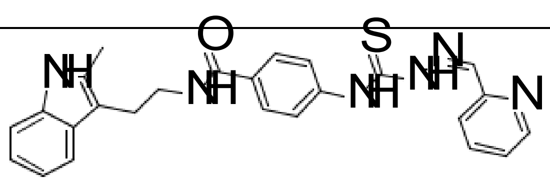
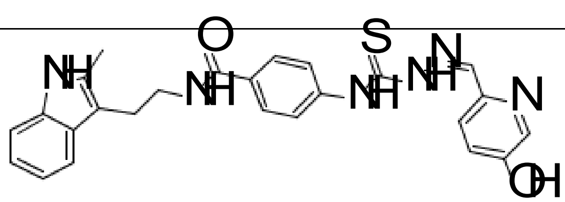
4.2 QSAR analysis

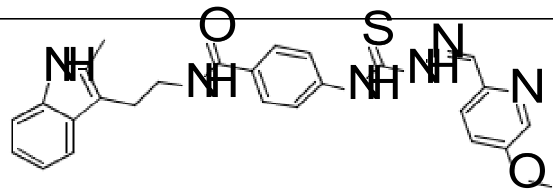
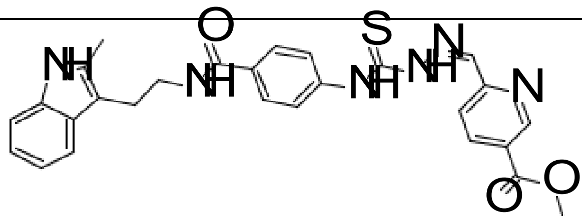
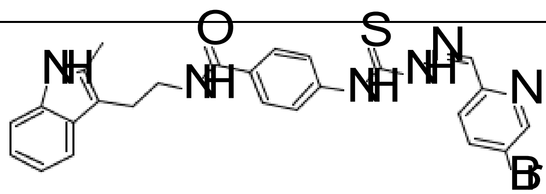
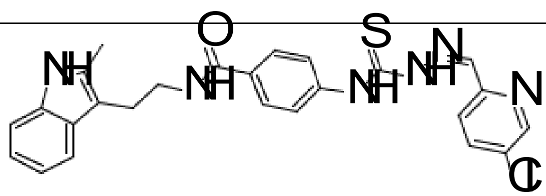
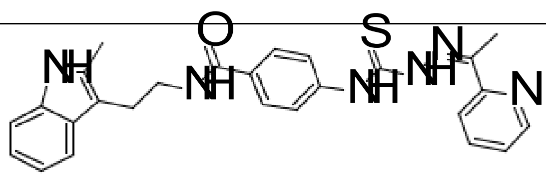
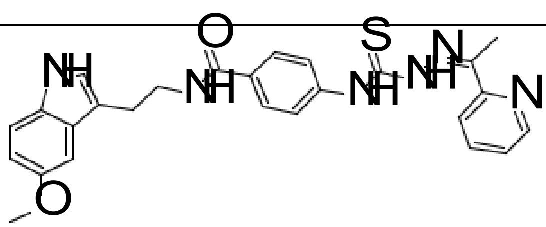
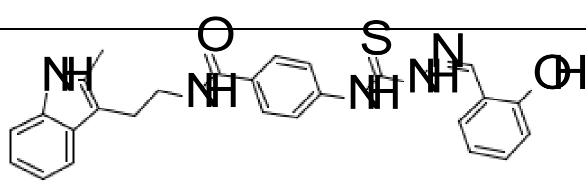
4.2.1 Collection of Dataset and Optimization

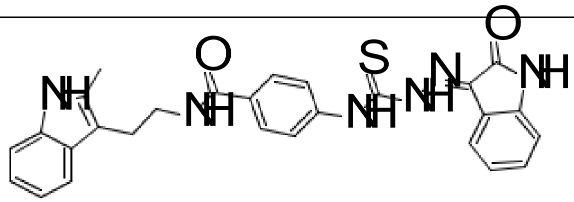
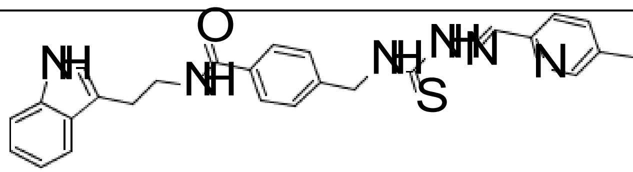
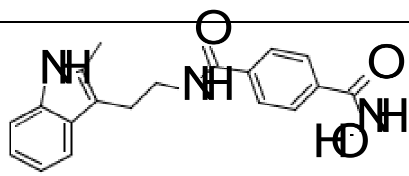
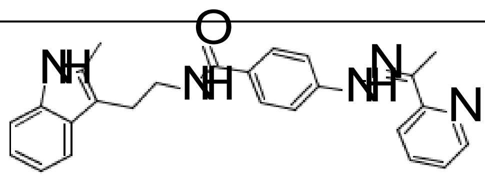
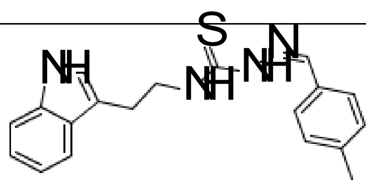
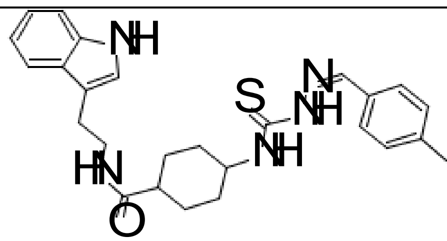
Fifty-One (51) synthesized thiosemicarbazone-indole derivatives taken from the literature were used for making the 2D-QSAR model **[208]**. The inhibitory activity of the reported compounds was found in the micromolar range and exhibits the potential of the moieties to inhibit 50% of the growth of PC3 cell lines (IC_{50}). To remove the skewness in the data, IC_{50} values of these 51 compounds has been changed to negative logarithm values (PIC_{50}) **[209]**. The chemical structures of thiosemicarbazone-indole derivatives and their biological activity are given in the **table 4.1**

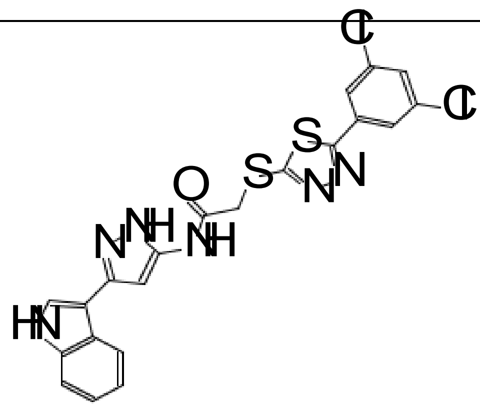
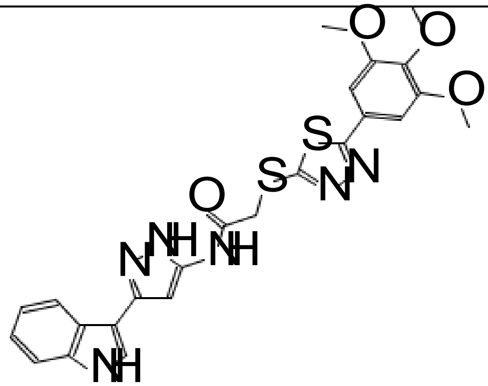
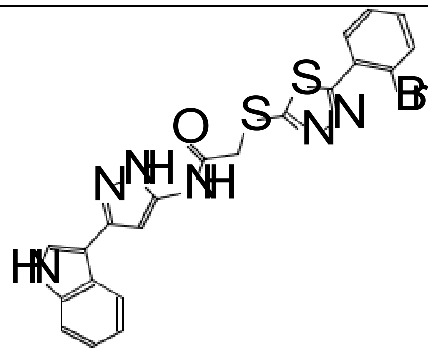
Table 4.1: Structure of the 24 compounds used for the generation along with their IC_{50}& calculated PIC_{50} values

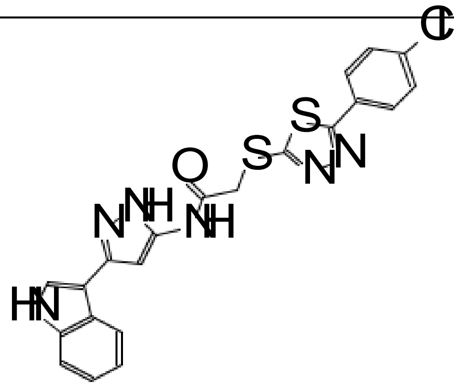
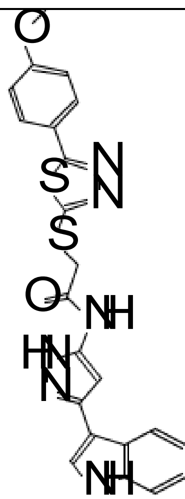
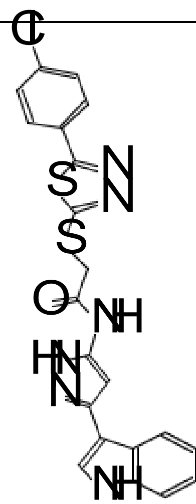
S. No.	Compound Structure	IC_{50} value	PIC_{50} value
1.		0.241±0.050	6.61
2.		0.512±0.120	6.29
3.		0.121±0.032	6.91
4.		0.081±0.012	7.09

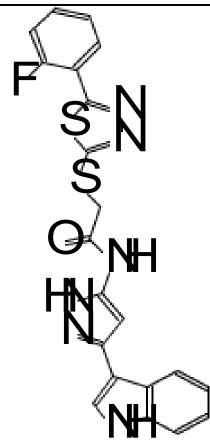
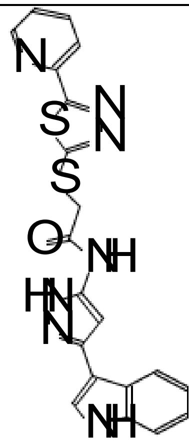
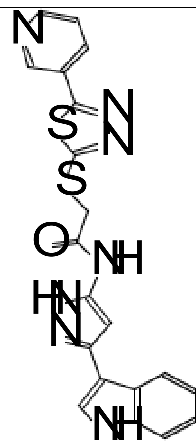
5.		0.061±0.020	7.21
6.		0.054±0.012	7.26
7.		0.133±0.014	6.87
8.		2.485±0.395	5.6
9.		0.093±0.053	7.03
10.		0.091±0.024	7.04
11.		1.501±0.176	5.82

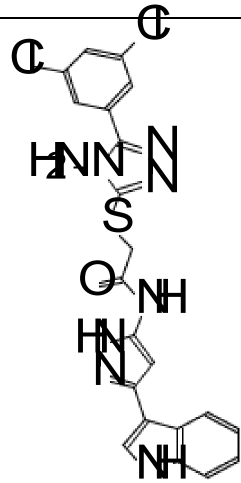
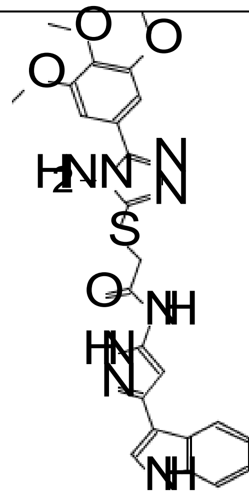
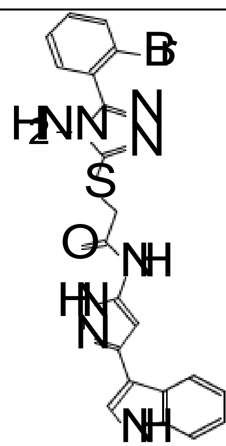
12.		0.084±0.030	7.07
13.		1.601±0.742	5.79
14.		0.322±0.020	6.49
15.		0.454±0.051	6.34
16.		0.707±0.032	6.15
17.		0.947±0.086	6.02
18.		5.321±0.263	5.27

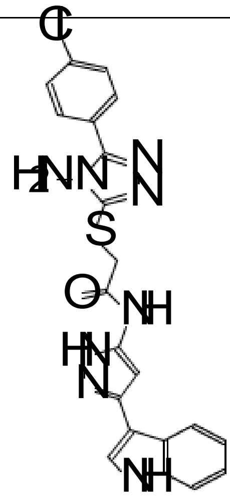
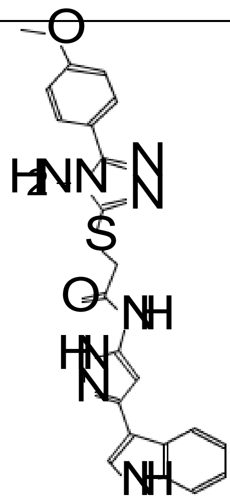
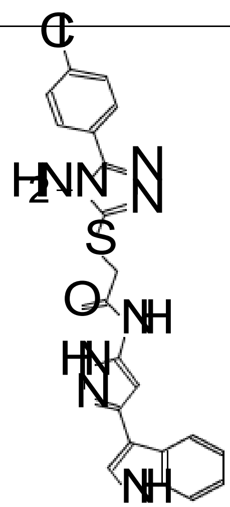
19.		16.987±0.178	4.77
20.		1.424±0.153	5.84
21.		20	4.69
22.		0.406±0.091	6.39
23.		0.601±0.042	6.21
24.		2.223±0.345	5.65

25.		0.433	6.36
26.		0.124	6.9
27.		18.8	4.72

28.		1.28	5.89
29.		0.834	6.07
30.		4.33	5.36

31.		14.2	4.84
32.		7.96	5.09
33.		12.0	4.92

34.		27.3	4.56
35.		29.8	4.52
36.		67.7	4.16

37.		4.79	5.31
38.		21.4	4.66
39.		11.8	4.92

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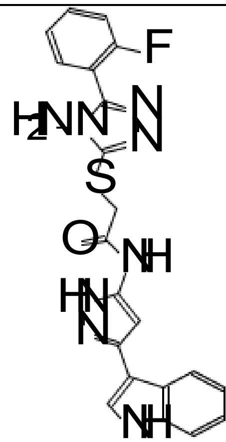
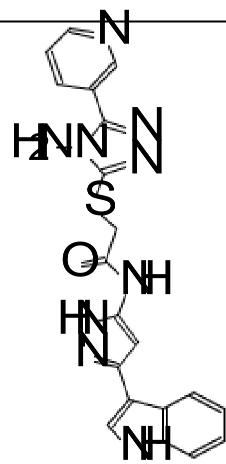
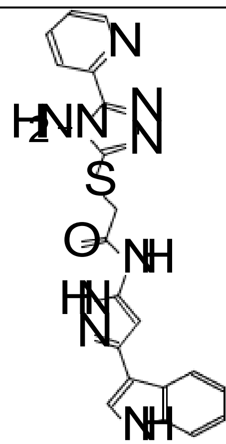
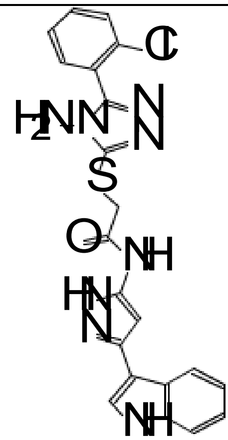
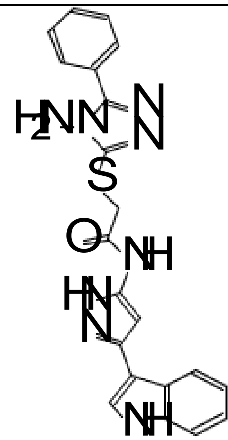
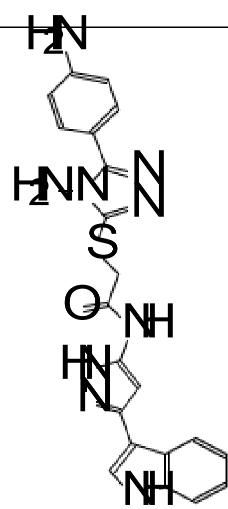
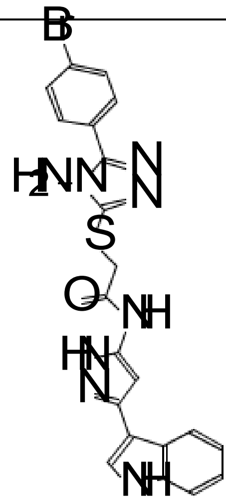
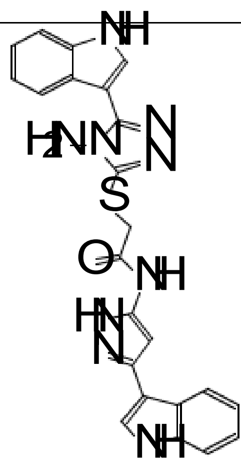
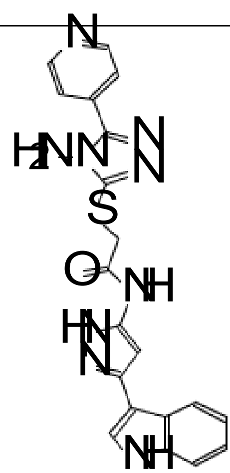
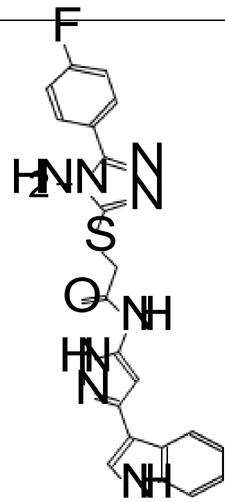
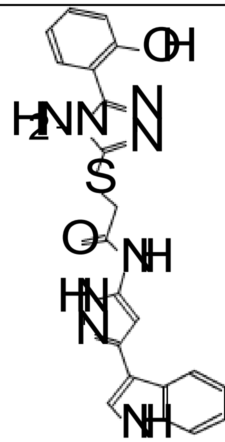
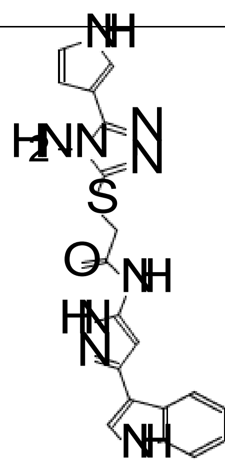
40.		10.1	4.99
41.		1.15	5.93
42.		2.97	5.52

43.		56.8	4.24
44.		23.9	4.62
45.		1.73	5.76

46.		5.81	5.23
47.		31.3	4.5
48.		30.3	4.51

49.		93.9	4.02
50.		4.14	5.38
51.		2.72	5.56

4.2.2 Molecular descriptor calculations

Molecular descriptors of the 51 derivatives were calculated employing the PADEL descriptor software **[210]**. All the structures of the 51 derivatives were drawn in the mol format and then subjected to PADEL which computes a total of more than 1850 descriptors which includes autocorrelation, geometrical, electrostatic, topological, spatial, constitutional and thermodynamic descriptors.

4.2.3 Data pretreatment, dataset division and QSAR model generation

Before the development of the QSAR model, constant and inter correlated descriptors were removed for the development of a robust and reliable equation. For this purpose 80% variance cut-off value is used for removing both constant and inter-correlated descriptors. For the division of training and test dataset, a random approach is used for the division and 70% of the molecules divided into training and remaining 305 were divided into test data set. For generating the QSAR model, a search heuristic approach called as Genetic Algorithm (GA) is used which mimics the techniques of natural selection like inheritance, crossover, mutation, and selection.

4.2.4 Internal Validation

The cross validation approach was employed for the assessing the predictive ability of the generated QSAR model through internal validation. The following equation is used for calculating the cross validated Q^2_{cv}:

$$Q^2_{cv} = 1- [\Sigma(Y-Y_{pred})^2/ \Sigma(Y-Y_{mean})^2]$$

Here, Y represents the observed value (PIC_{50}),Y_{pred} stands for the predicted value of the biological activity by the QSAR model &Y_{mean}stands for the average of Y of the training set compounds.

Another parameter for assessing the quality and reliability through internal validation is squared correlation coefficient R^2 value of the training set. But this value can be biased as its value is not as reliable if we increase the number of descriptors. To overcome this hindrance, a new parameter R^2_{adj} is used which is calculated as follows:

$$R^2_{adj} = R^2\text{-}p(n\text{-}1)/n\text{-}p\text{+}1$$

Where p is the number of the descriptors employed and n is the number of molecules employed in the training set for the development of the QSAR model. There is an acceptable fact that if difference between R^2 and R^2_{adj} is less than 0.3 then we can infer that numbers of descriptors selected are acceptable[211].

4.2.5 External Validation

For assessing a QSAR model for its robustness, Golbraikh and Tropsha has given some statistical parameters **[212]** which are given in table 2. Where R^2_0 is the coefficient of squared correlation among observed and predicted values and R'^2_0 is the same among predicted and observed values of the test set.

Table 4.2: Golbraikh and Tropsha parameters for the validation of the 2D QSAR model

S.No.	Parameter	Threshold value
1	Q^2	Threshold value $Q^2>0.5$
2	R^2_{train}	Threshold value $R^2_{train}>0.6$
3	$\|R^2_0-R'^2_0\|$	Threshold value $\|r_0^2-r'_0{}^2\| < 0.3$
4	k or k'	0.85<k<1.15 & 0.85<k'<1.15
5	$R^2_{test}-R^2_0/R^2_{test}$	Threshold value $R^2-R^2_0/R^2 < 0.1$

4.2.6 Y randomization test

Y randomization test is performed to evaluate that the QSAR model generated is not resulted through by chance instead is a robust model. This test is performed by shuffling the value of biological activity while keeping the values of descriptors constant. This shuffling is done n number of times and robustness of the developed model is assessed through comparing R^2 and Q^2 of Y randomized equations with original QSAR equation and it should be as low as possible **[213]**.

4.2.7 Applicability Domain

Applicability Domain (AD) is the chemical space of the developed QSAR model where all the predictions done by the equation is of the highest accuracy. As per the 3rd principle of Organization for economic Co-operation and development (OECD), it is highly suggested to define the AD of a QSAR model. AD is used for identifying the response outliers as well as influencers in the QSAR model **[214]**.

In the current study, Williams plot and insurbia graph is employed for defining AD of the formed QSAR model [215]. This is a simple approach in which every new chemical is defined whether it will be within the AD or will be an outlier. The leverage h_i of each chemical of training as well prediction dataset is calculated as follows:

$$h_i = x_i^t(X^tX)x_i$$

Where x_i is the descriptor vector of the under consideration data point, Xasthe descriptor matrix and X^tas the transpose of the descriptor matrix. The threshold leverage h^* is calculated as

$h^* = 3(p+1)/n$

Where, p = number of variables

n = the number of compounds in the training set

For every chemical the value of h_i calculated should be less than the threshold value, otherwise it is considered as outside the AD but if it has small standardized residual than it may not be considered as outlier. For standardized residuals a cut-off value of ±3 is measured as inside the AD.

4.2.8. Biological Activity prediction of the designed compounds

Biological activity of all our proposed 51 compounds was predicted from the mathematical equation obtained from our QSAR model developed. Initially, molecular descriptor calculation was performed of these derivatives using PADEL software and then substituting the values of these descriptors in the QSAR equation we obtained our predicted biological activity.

4.3 MOLECULAR DOCKING:

Molecular docking is an essential technique in molecular biology, particularly in structural biology and computer-assisted drug design. It involves predicting the predominant binding model(s) of a ligand with a protein that has a known three-dimensional structure. This process aims to determine the preferred orientation of one molecule relative to another, forming a stable complex.

The method leverages the increasing availability of high-resolution crystal structures of protein receptors, thanks to advances in high-throughput crystallography and genomics. These detailed protein structures are crucial in drug discovery projects. By understanding protein-ligand interactions at a molecular level, researchers can identify potential drug candidates (leads) and refine these leads into effective drugs. This knowledge accelerates the drug development process, making molecular docking a valuable tool in the quest for new therapeutics [215-217].

Molecular docking has many significant applications, like virtual screening for hit identification, drug discovery through lead optimization, predicting biological and ADME activity, and identifying binding sites via blind docking. It also plays an important role in de-orphaning receptors, studying protein-protein or protein-nucleic acid interactions, understanding structure-function relationships, elucidating enzymatic reaction mechanisms, and advancing protein engineering. Within rational drug design, CADD methods are becoming highly important for creating workflows that are faster, more efficient, and cost-effective. A fundamental fact in the drug discovery and the development is interaction between receptors or enzymes and their ligands [218].

Molecular docking involves generating multiple conformations of a ligand within an active site and scoring them to identify those that closely match the bioactive conformation seen in X-ray crystallography. Docking algorithms help identify potential binders from databases and estimate protein-ligand binding affinities. This computational method predicts possible binding modes by mapping the active site with interaction points (a grid) and fitting the ligand through grid or energy searches. Docking can be categorized into rigid docking, where the receptor and ligand are treated as inflexible, and flexible docking, where both can adapt their shapes for a better fit [219-220]

In rigid type of molecular docking, both receptor and ligand are kept rigid. In reality, molecules are supple even in their lowest energy states. Flexible docking accounts for this by considering at least the ligand as flexible, resulting in more accurate binding energy calculations between receptor and ligand. Most current docking programs, such as Molegro Virtual Docker (MVD), AutoDock, DOCK, FlexX, Glide, and GOLD, treat the ligand with full flexibility but often assume the receptor is rigid or allow limited flexibility to side chains. Among these, Autodock and Molegro Virtual Docker are the most widely used for docking studies [221].

Two commonly utilised methods are often used by the molecular docking community. 02 techniqes are available for use: the first matches the protein and ligand as complementary surfaces using a matching technique [222-223] the second simulates the real docking process and calculates the pairwise interaction energies between ligand-protein pairs.[224]

Indole-2-carboxamide derivatives are well known for their anticancer action, as demonstrated in the literature, and require further investigation to improve their pharmacological results. The mechanism of receptor-ligand interactions may potentially be clarified with the use of molecular docking research. Docking studies could be useful in this investigation to clarify the mechanisms of receptor [225].

4.3.1 Tyrosine Kinase Receptor:

Tyrosine Kinase Receptor (**PDB code: 6Z4B) possible target protein for anticancer activity**A subclass of tyrosine kinases known as receptor tyrosine kinases (RTKs) is responsible for mediating cell-to-cell communication and regulating a variety of intricate biological processes, such as cell division, growth, motility, and metabolism [226].

A novel technique to treating cancer is called targeted therapy, which involves the use of medications that specifically target proteins found in cancerous cells. Receptor tyrosine kinase (RTK), which is involved in stimulating the growth and proliferation of cancer cells. By blocking RTKs, cancer may be prevented from progressing further [227].

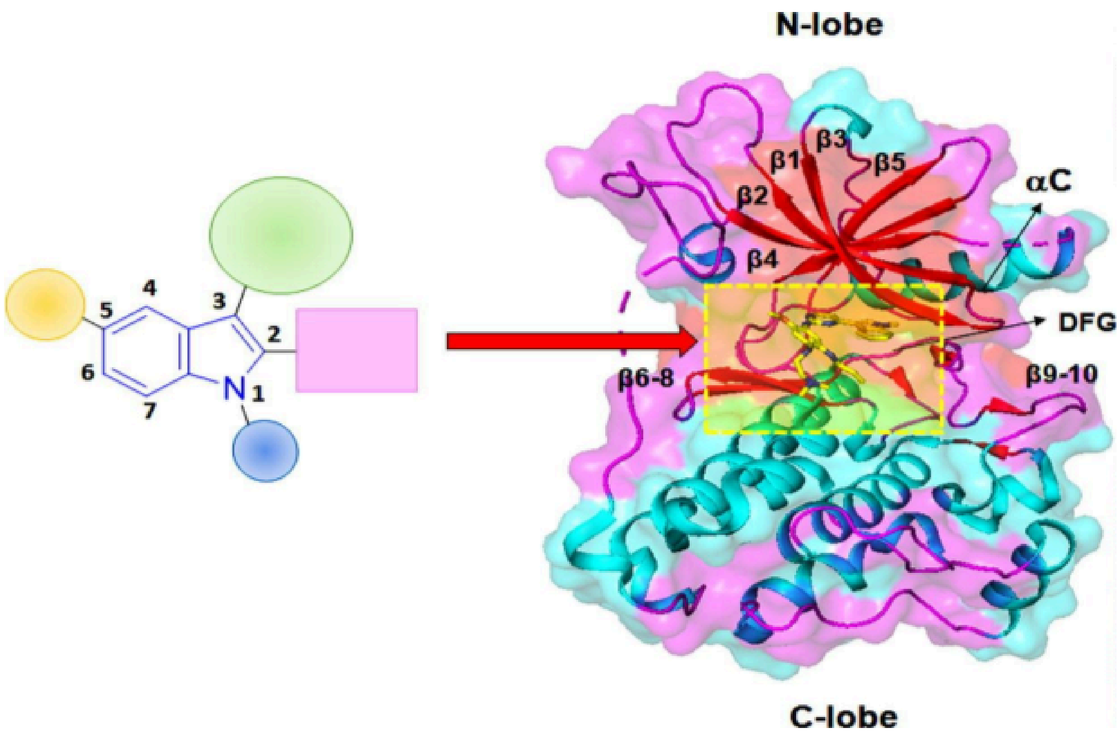


Fig. 4.1: indole derivatives are important in kinase targeted drug design [228]

4.3.2 DNA DNA gyrase, a type II topoisomerase, introduces negative supercoils into DNA utilizing ATP hydrolysis. This enzyme is crucial for all bacteria but is not found in higher eukaryotes, which makes it an appealing target for antibacterial drug development [229].

4.3.3 Indole -2- Carboxamide as Anticancer Agents:

Molecular docking of all our proposed molecules is performed against the tyrosine kinase receptor (PDB ID 6Z4B) and taking Osimertinib as the reference for comparative study.

4.3.4 Indole-2- carboxamide as antimicrobial Agent:

The crystal structures of DNA gyrases from related microorganisms were obtained from the Protein Data Bank (PDB) at http://www.rcsb.org. The PDB IDs **(4CKLand 1EA1)**for the studied microorganisms were used as follows: [230].

4.3.5 Methodology:

Docking is a computer method that is used to forecast possible ligand binding configurations inside the active region of a receptor. To do this, an active site representation is produced, usually in the form of a grid containing interaction points. The ligand is then positioned into the binding site using techniques such as grid or energy searches. The calculation of binding energy takes into account a number of interactions, such as van der Waals, electrostatic, and aromatic interactions [231,232].

Docking studies has been performed with a set of theoretically designed indole derivatives based on literature [233]. The basic structure of analogues is designed as given in Figure 4.2 and Table 4.1-4.3

4.3.5.1 Data-set selection

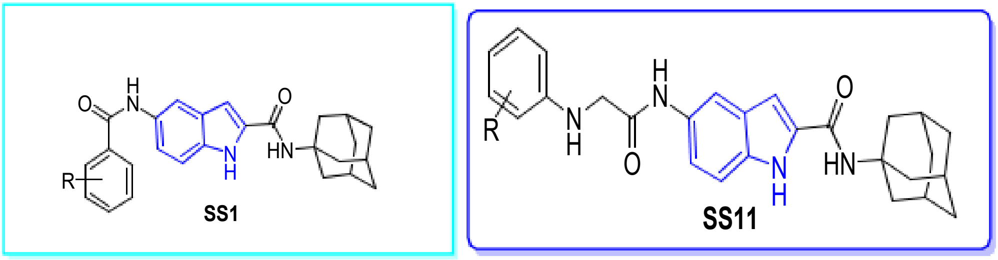


Fig. 4.2: Basic structures of novel designed Indole-2- carboxamide derivatives

4.3.5.2 Ligand preparation: The compounds were prepared using marvin sketch, undergoing a conversion from 2D to 3D through build and optimization methods Following this, the refined 3D structures were saved in (PyMOL) PDB file format. During the molecular preparation within the software, tasks encompassed the assignment of bonds, determination of bond order, hybridization, management of charges, addition of explicit hydrogens, and incorporation of flexible torsion in ligands. Ensure Correct Protonation and Orientation and convert also in PDBQT format.

4.3.5.3 Protein preparation/ Target Preparation: Open PyMOL and load the protein structure (PDB file. Remove Water and Other Heteroatoms. Add Hydrogen Atoms (if not already present), Save the Modified Protein as new PDB file. Convert Files to PDBQT Format Using MGLTools.

4.3.5.4 Analysis of docking results:

- Set Up the Docking Parameters (Define the Grid Box) and run the docking using the following command.
- Adjust the center_x, center_y, center_z, and size_x, size_y, size_z parameters based on the binding site coordinates.
- Analyse the results [234].

4.3.5.6 Molecular Dynamics Simulation: Molecular dynamics (MD) simulations were performed using GROMACS 2022.2, employing the following steps.

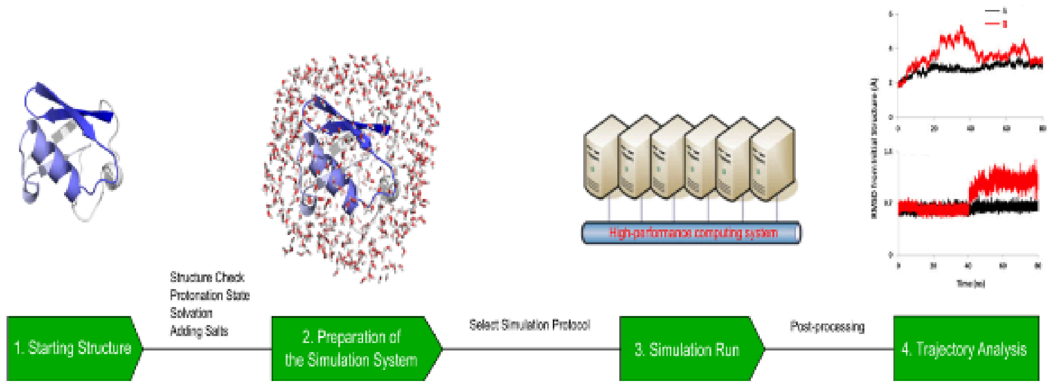


Fig. 4.3: Molecular Dynamics Simulation Process

(a) Preparation of enzyme: Pymol was utilized for exporting the three- dimensional (3D) models of ligand-protein complexes into the pdb format. Molecular dynamics (MD) simulations were then conducted using the GROMACS software package (version 2022.2) to evaluate the dynamic behavior of the complexes [235–237]. The CHARMM27 force field was utilised by pdb2gmx to produce protein topology [238], whereas the SwissParam server was utilised to create ligand topology [239].

(b) Setting up system for simulation: After applying the force field, the complexes were introduced into the system. Utilizing periodic boundary conditions, we employed the TIP3P water model [240] to solvate the complexes within a cubic box, ensuring a distance exceeding one nm from the protein's periphery. Na+ ions were then Incorporated to nullify the system, followed by energy minimization employing the steepest descent method for 50,000 steps. Subsequently, the system underwent equilibration through 100 ps of NVT simulation at 300 K, followed by an additional 100 ps of NPT simulation. In the constant-temperature, constant-pressure (NPT) ensemble, the leapfrog algorithm facilitated independent coupling of various components, including proteins, ligands, water- molecules, and ions [241]. To sustain a consistent environment (300 K temperature and 1 bar pressure), the Berendsen temperature and pressure coupling constants were set at 0.1 and 2, respectively [242]. Ultimately, a molecular dynamics (MD) simulation unfolded in an isothermal and isobaric ensemble at 300 K for100 ns. To maintain a constant pressure of 1 bar, the pressure coupling time-constant was configured to 1 ps, and bond lengths were controlled using the LINCS method [243]. Van der Waals and Coulomb interactions were truncated at 1.2 nm, and the PME algorithm [244], integrated into GROMACS, effectively handled errors resulting from this truncation.

(c) Visualization and analysis of simulation : The trajectory files are observed via VMD (Visual Molecular Dynamics) 1.9.2 [245], and analysis is conducted using the internally developed tool HeroMDAnalysis [246,] in addition to Xmgrace 5.1.25 [247].

‘Drug-likeness’, a qualitative property of chemicals assigned by experts committee vote, is widely integrated into the early stages of lead and drug discovery. Its conceptual evolution paralleled work related to Pfizer's ‘rule of five’ and lead-likeness, and is placed within this framework. The discrimination between ‘drugs’ (represented by a collection of pharmaceutically relevant small molecules, some of which are marketed drugs) and ‘nondrugs’ (typically, chemical reagents) is possible using a wide variety of statistical tools and chemical descriptor systems.

4.4 *Drug Likeliness Studies* ‘Drug-likeness’, a qualitative property of chemicals assigned by experts committee vote, is widely integrated into the early stages of lead and drug discovery. Its conceptual evolution paralleled work related to Pfizer's ‘rule of five’ and lead-likeness, and is placed within this framework. The discrimination between ‘drugs’ (represented by a collection of pharmaceutically relevant small molecules, some of which are marketed drugs) and ‘nondrugs’ (typically, chemical reagents) is possible using a wide variety of statistical tools and chemical descriptor systems [248]
The selected derivatives were loaded into DruLiTO in sdf format and carried out the test for drug likeliness.

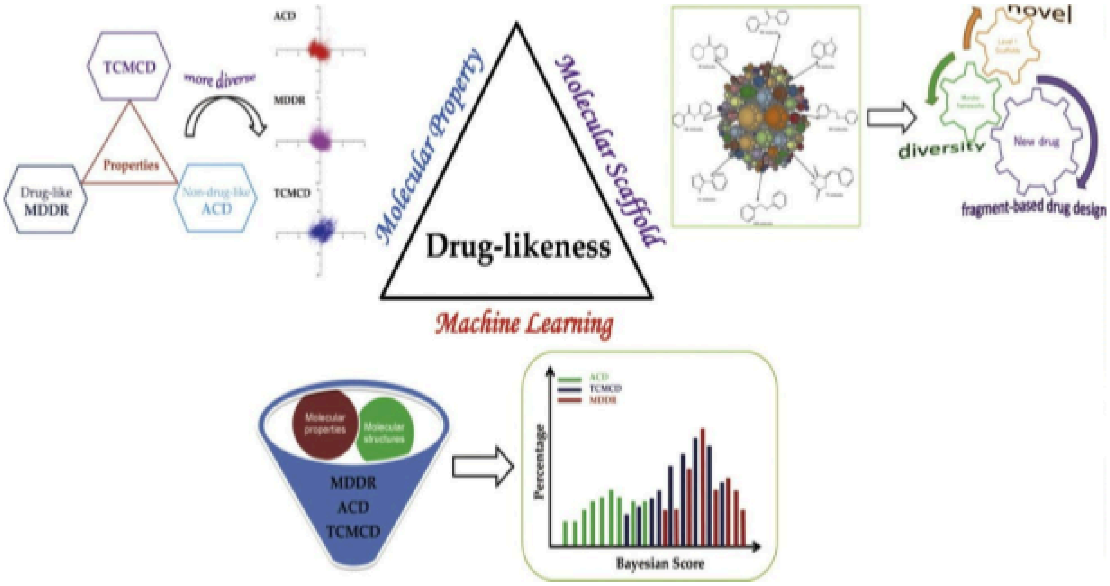


Figure No 4.4: Drug likeliness

4.5 ADME/ Pharmacokinetic Studies :

Docking studies do not offer a thorough evaluation of a drug's effectiveness on their own. SWISS ADME software performs drug-likeness and ADME (absorption, distribution, metabolism, and excretion) assessments to determine a drug's potential biological value. The Swiss Institute of Bioinformatics (SIB) introduced this software. Website of the Swiss ADME [249] serves as a valuable resource for scientists globally.

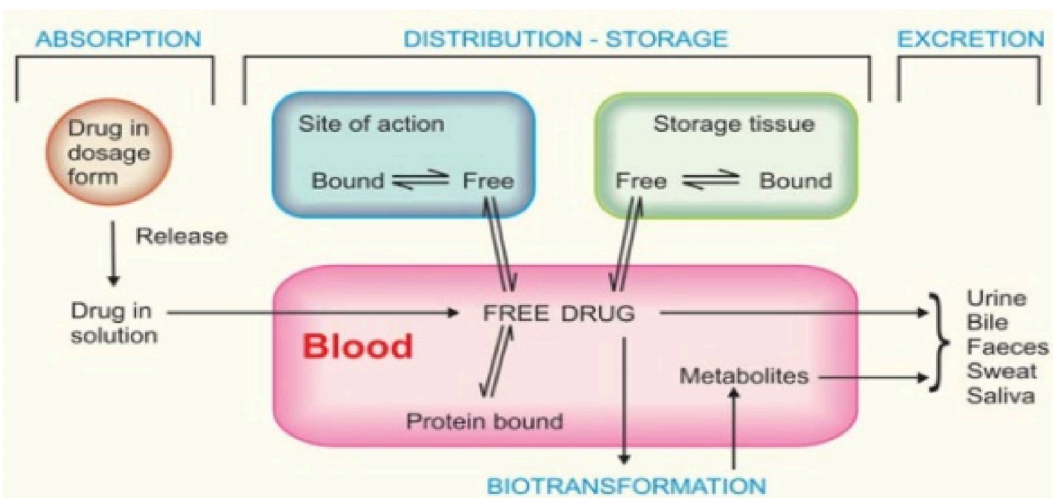


Fig. 4.5: Mechanism of Pharmacokinetics

The software accepts ligands through the SMILES (Simplified Molecular Input Line Entry System) interface in order to generate a pharmacokinetic profile. With Swiss ADME, the ADME profile for chemicals was produced. While the Lipinsky rule of five was developed in 1997 as a standard for determining pharmacological similarities, other principles 24 also play a role in defining drug-likeness boundaries. According to this rule, a medicine that is intended for oral absorption needs to satisfy at least two of the following requirements: it must have a molecular weight (MW) of less than 500 g/mol, an iLOGP (octanol/water partition coefficient) of 5, and nHBD (H-bond donor) and nHBA (H-bond acceptor) in the range of 10 and 5, respectively. From 3.92 to 5.57 in log P values, 354 to 433 in MW values, 117 to 127 in molar refractivity, and 27 to 30 in total atoms are taken into account by the Ghose filter. The rotatable bond count of 10 and the polar surface area (PSA) of 140 are the drug-likeness restrictions, as per the Veber rule. You can classify solubility in water as highly soluble (0), moderately soluble (4), weakly soluble (6), and insoluble (-10).

4.6. Experimental Chemistry

4.6.1. Materials:

Every chemical used came from Sigma Aldrich, Merck, and Hi-Media Pvt. Limited. Thin layer chromatography and laboratory chemical suppliers in Mumbai and CDH were used to verify the purity of the starting materials used in reactions by measuring their melting or boiling points. All the reactions 41 were monitored using thin layer chromatography.

- The appropriate mobile phases (solvent systems) as applicable were developed using ‘silica gel G’ as the stationary phase.
- Melting points were determined in the open capillary tube using the “Precision Melting Point Apparatus” and are uncorrected.
- To ascertain the purity and homogeneity of synthesized compounds primarily, thin-layer chromatography was carried out.
- The compounds' purity was assessed using "Silica Gel G" coated on laboratory microslides made by dipping or pre-coated plates. The eluent was a mixture of various polar and non-polar solvents in different amounts, and detections were carried out by either exposure to iodine fumes or UV light as needed. The completion of the reaction

was guaranteed by 24 the absence of TLC spots for the starting materials and the emergence of a new TLC spot at a different Rf value.

- Detection was done either by observing in UV light or exposure to iodine vapors as required.
- $_{Rf}$ value was calculated for each compound by using following formula.

$$\mathbf{R_f} = \frac{\text{Distance travelled by the solute}}{\text{Distance travelled by the solvent front}}$$

- The products of all the reactions were purified initially by different workup processes to remove unreacted starting materials if any and then by recrystallization using suitable solvents.
- The SHIMADZU Spectrophotometer was used to record FT-IR (KBr Press Pellet) spectra. The synthesised compounds' 1HNMR 12 (400 MHz) and 13CNMR spectra were recorded in CDCl3 and DMSO using a Bruker Spectrophotometer, with TMS serving as the internal standard (chemical shift δ in ppm). For the spin multiplicities, the symbols s (singlet), d (doublet), t (triplet), and m (multiplet) were used. Mass spectra were obtained on the "GCMS- QP2010S" instrument using the direct injection method.
- Thermo Finnegan Flash EA-1112 series Italy CHNS/O Analyzer was used to perform elemental analyses (C, H, and N, O) of compound XVII. The results were found to be within ±0.4% for each element.

4.6.2. Scheme of Synthesis:

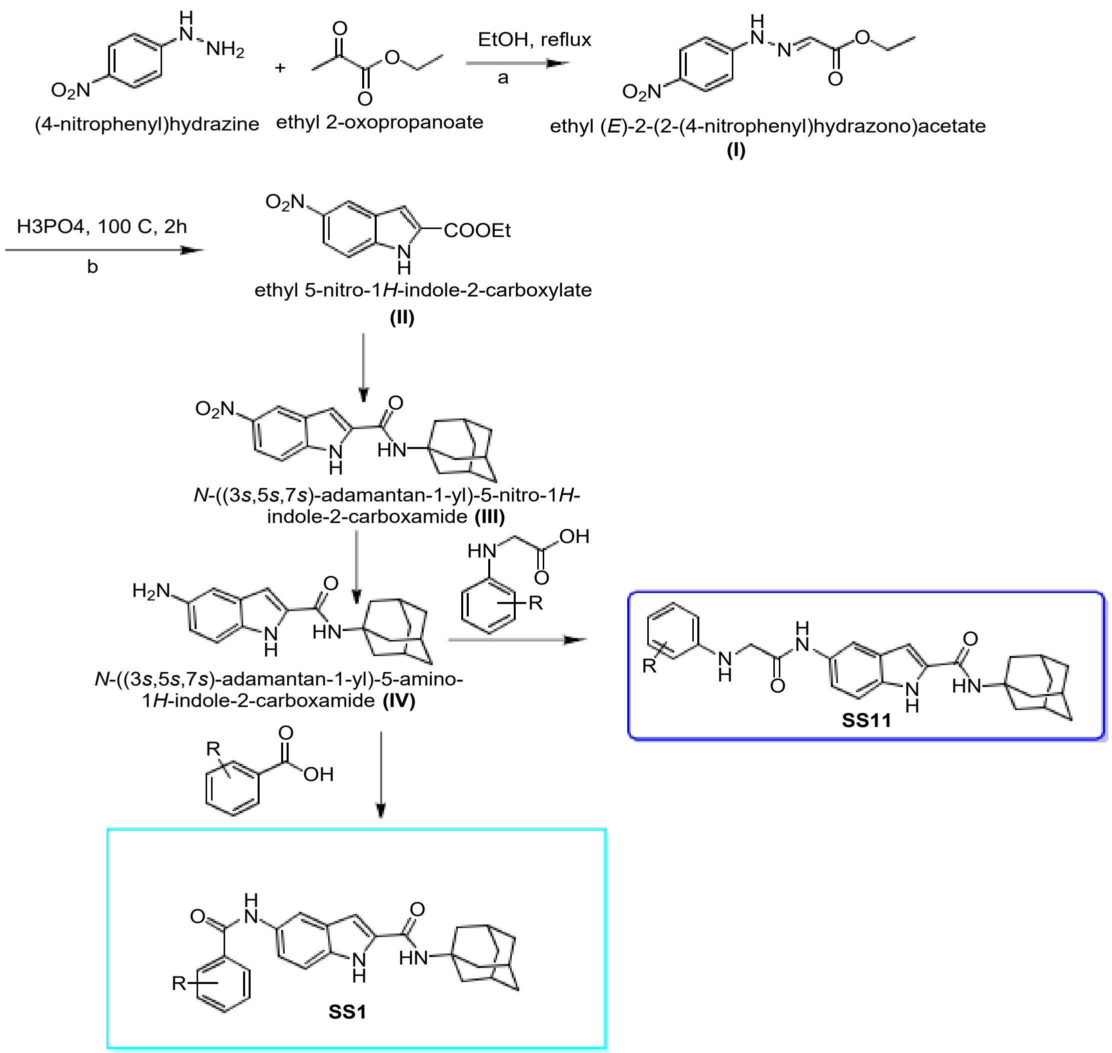


Fig.4.6: Scheme of Chemical Reaction

4.6.3. General procedure for synthesis:

4.6.3.1. *Synthesis of ethyl (2Z)-[2-(4-nitrophenyl) hydrazinylidene] acetate (Compound I)*:

To a mixture of 99% pure (4-nitrophenyl) hydrazine in 15ml of methanol, ethyl 2-oxopropanoate (1.94ml, 0.03mol) was added and refluxed for four hours on the water bath.

The title compound I was obtained by first filtering out the precipitate followed by washing with water and drying under vacuum. 50% aqueous ethanol was used for the recrystallization of the crude product.

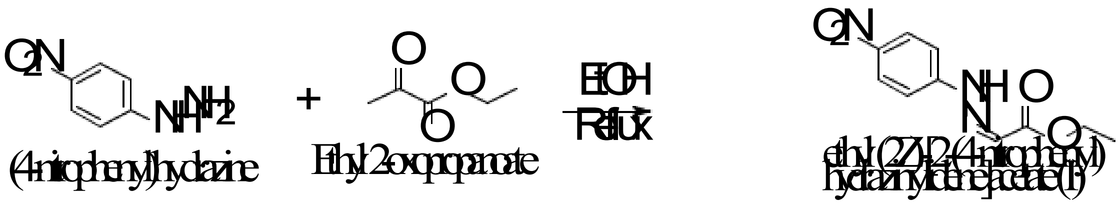


Fig.4.7: ***Synthesis of ethyl (2Z)-[2-(4-nitrophenyl) hydrazinylidene] acetate (Compound I)***

4.6.3.2. ***Synthesis of ethyl 5-nitro-1H-indole-2-carboxylate (II)*****:**

5 gm of Ethyl (2*Z*)-[2-(4-nitrophenyl) hydrazinylidene] acetate (Compound-I) was cooled in an ice bath and then, with continuous stirring, 35 gm of syrupy H_3PO_4 (85% w/v) was added drop wise along with 1 ml con H_2SO_4 as a catalyst. The reaction mixture is kept for refluxing for further 4-5 hours on a water bath with continuous stirring. The deep orange colour is achieved after the completion of reaction. The reaction mixture is then cooled on an ice bath and ice-cold water is added cautiously. The product is obtained by first filtering out the precipitate followed by washing with water and drying under vacuum. 50% aqueous ethanol was used for the recrystallization of the crude product [250].

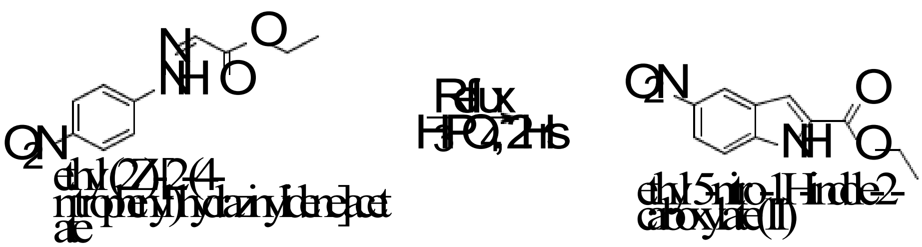


Fig. 4.8:***Synthesis of ethyl 5-nitro-1H-indole-2-carboxylate (II)***

4.6.3.3. ***Synthesis of N-(adamantan-1-yl)-5-nitro-1H-indole-2-carboxamide (Compound-III):***

Ethyl 5-nitro-1H-indole-2-carboxylate (Compound-II) (0.01 mol 4.5gm) were treated with adamantan-1-amine (0.05 mol) in 25 ml of alcohol the reaction mixture refluxed for 8hours with stirring, the termination of reaction was monitored by single spot TLC and It is then cooled to room temperature then filtered off the precipitate.

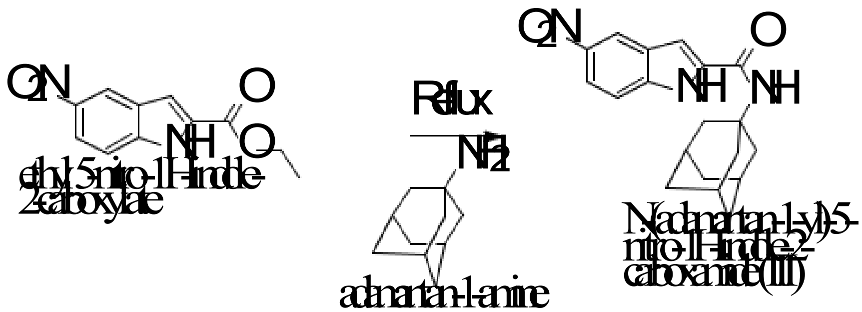


Fig.4.9: ***Synthesis of N-(adamantan-1-yl)-5-nitro-1H-indole-2-carboxamide (Compound-III):***

4.6.3.4. Synthesis of N-(adamantan-1-yl)-5-amino-1H-indole-2-carboxamide (Compound IV):

4 gm of N-(adamantan-1-yl)-5-nitro-1H-indole-2-carboxamide (compound-III) dissolved in ethanol (150ml) and then under goes reduction reaction in presence of 10% Pd/C (300mg) in using hydrogen balloon for 24 hours. The mixture was filtered over Celite, which was washed with methanol. After concentration and dryingunder vacuum, brown powder (91%) was isolated [251].

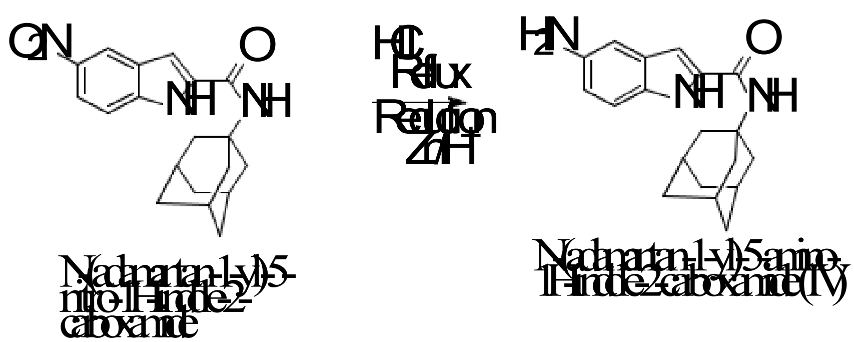


Fig.4.10: ***Synthesis of N-(adamantan-1-yl)-5-amino-1H-indole-2-carboxamide (Compound IV)***

4.6.3.5. ***Synthesis of derivatives of N-(adamantan-1-yl)-5-amino-1H-indole-2-carboxamide (substituted SS-I:***

N-(adamantan-1-yl)-5-amino-1H-indole-2-carboxamide (Compound-IV) is treated with substituted various benzoic acid derivatives and refluxed for 8-10 hours on water bath maintaining constant temperature 60°C It is then cooled at room temperature then filtered off the precipitate and recrystallized from ethanol.

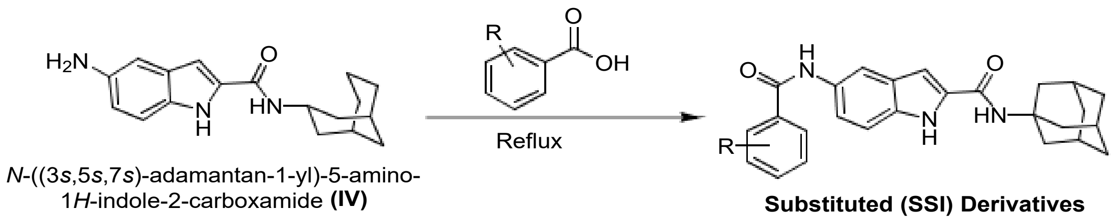


Fig.4.11:*Synthesis of derivatives of N-(adamantan-1-yl)-5-amino-1H-indole-2-carboxamide*

4.6.3.6. Synthesis of derivatives of N-((3s,5s,7s)-adamantan-1-yl)-5-(2-(phenylamino) acetamido)-1H-indole-2-carboxamide (substituted SSII):

0.01 mol of *N*-(adamantan-1-yl)-5-amino-1*H*-indole-2-carboxamide (Compound-IV) is treated with various amino(phenylacetic acid) in presence of (0.01mol)(THF) and pyridine (0.005mol) refluxed for 8-10 hours on water bath maintaining constant temperature 60°C. It is then cooled at room temperature then filtered off the precipitate and recrystallized from ethanol.

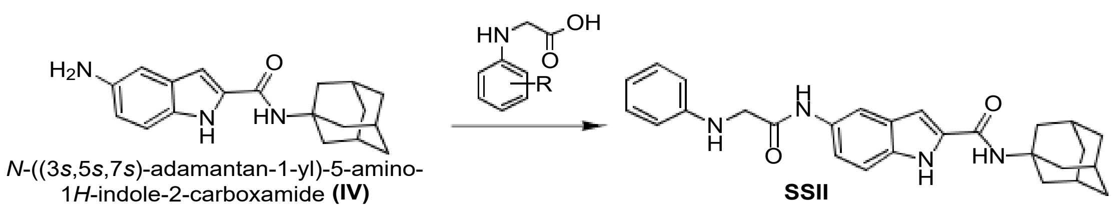


Fig.4.12.: Synthesis of derivatives of N-((3s,5s,7s)-adamantan-1-yl)-5-(2-(phenylamino) acetamido)-1H-indole-2-carboxamide

4.7. Spectral Data [252-254]:

Structural characterization of the synthesized compounds was done by instrumental method of analysis like IR, NMR, and MASS spectroscopy. The spectral data shown in (Appendices No.i-xviii)

Infra Red Spectra (IR):

The IR spectrum gives an idea about probable structure of the compound by predicting thecertain functional groups which absorbs at definite frequencies. IR region ranges between4000-400 cm -1. IR spectra were recorded on SHIMADZU FT-IR spectrometer. Interpretation ispresented under section 5.2 in (Table no.5.4).

NMR Spectra :

NMR spectra is an important method for recording differences in the magnetic properties of different magnetic nuclei available in the molecule and to deduce in the large measure about the position of these nucleiwith in the molecule. We can deduce how many different kinds of environmental are there inthe molecules and also which atoms are present in neighboring groups. Using TMS as an internal standard (chemical shift δ in ppm), the 1HNMR (400 MHz) and 13CNMR spectra of the synthesised compounds were recorded on a Bruker Spectrophotometer in CDCl3 and DMSO. The symbols s (singlet), d (doublet), t (triplet), and m (multiplet) represented the spin multiplicities Interpretation ispresented in section 5.2 in (Table No. 5.5).

Mass Spectra:

Mass spectroscopy is the most accurate method for determining the molecular mass of thecompound and its elemental composition on fragmentation pattern and molecular ion peak(M +). Mass spectra were recorded on 'GCMS-QP2010S' instrument by direct injectionmethod.

Elemental Analysis:

The CHNS(O) Analyzer find utility in determining the percentages of Carbon,Hydrogen, Nitrogen, Sulphur and Oxygen of organic compounds.It works on the basis of the "Dumas method," which entails completely and instantly oxidising the sample through "flash combustion." The thermal conductivity detector (T.C.D.) detects the combustion products after they have been separated by a chromatographic column and provides an output signal corresponding to the concentration of the mixture's constituent parts.

4.8. Pharmacological Screening

Pharmacological or biological activity is the approach which is employed for assessing the beneficial or side effects of any drug molecule in the physiological systems. When the desired drug molecule is a complex chemical entity then the biological activity of the same is shown by the active ingredient or the pharmacophore. Generally the biological activity is considered as the dose dependent matter and as the dose of the substance increases, there are chances of showing the adverse effect by the substance. Antimicrobial and anti-Cancer activities of test compounds were performedas per procedure given below:

4.8.1. Antimicrobial Activity(in-vitro):-

Antimicrobial activities like antibacterial and antifungal were performed by using agar welldiffusion method against Gram-negative bacteria i.e. *E. coli* (MTCC 424), Gram-positive strains i.e. *S. aureus* (MTCC 96)and two fungal strains i.e. *C.albicans* (MTCC 227) and A.niger (MTCC285) by comparisonagainst standard drugs like Ciprofloxacin and ketoconazole respectively [255,256].

Theantimicrobial activity was performed in synthesized compounds, SSI derivatives i.e. SS1F, SS1E, SS1H, SS1N, SS1O, SS1R, SS1S, SS1U, SS1V, SS1X, SS1Y and SS1I derivatives i.e. SS11I, SS11K, SS11U, SS11Y.were evaluated at conc.100µg/ml.

4.8.1.2. Antibacterial activity *(in-vitro)*:-

Nutrient agar media

Nutrient agar media (NAM) had peptone 5g, beef extract 3g, NaCl 5g, nutrient agar 2 % and the final volume of media was adjusted to 1000 mL with double distilled (pH7.0) [257].

Preparation of nutrient broth

All the compounds of the nutrient broth were mixed. The media was sterilized by autoclaving at 121° for 15 minutes. When the temperature of the media lowered to 40-50°C, the broth could be used for the experiment or media could be stored at 0-4°C in refrigerators for further use

Preparation of nutrient agar plates

The flask containing autoclaved media was taken into laminar air flow cabinet. Autoclaved petri dishes were placed in laminar air flow (LAF). When the temperature of the flask containing the media lowered to 40-50˚C, about 40 mL media was poured into each plate. The plates were kept undisturbed for 15-20 minutes. After that media has solidified into the plates, the plates were incubated at 37˚C for 16-24 h. The plates with no growth were used further.Any growth on plates means contamination in the plates and the plates cannot be used further used. Plates without contamination were stored at 4˚C for further use [258].

Procedure:

In-vitro anti-bacterial screening was carried out by agar well diffusion method. A fixed volume i.e. 100 µL of the bacterial inoculum was spread by spreader on a sterilised petri plate containing nutrient agar media. With the help of borer, having 6 mm diameter, 2 wells were bored on each seeded agar plate. 100 µg/mL concentration of each compound were used. Solutions of the compounds were in DMSO and added into the respective two wells of the seeded plate, volume used was 100 µL. For the diffusion of compounds into the agar, plates were kept in LAF for 15 min. Plates were then incubated at 37˚C for 16-20 h in incubator. By measuring the diameter of inhibition zone, anti-bacterial was determined the tests were performed in triplicates (n=3) and mean of the diameter of zone of inhibition were calculated. The results obtained were compared against standard drug (Ciprofloxacin) [259]. Results of zone of inhibition have been summarised in section 5.3.1. in (**Table No.7-Table no.11**).

4.8.1.3. Anti-fungal activity (*in-vitro*):-

Nutrient Sabouraud medium

In sabouraud medium had Enzymatic digest of Casein 5g, Enzymatic digest of Animal Tissue 5g, Dextrose 20g, and the final volume of media was adjusted to 1000 mL with distilled water (pH5.6).The mixture was allowed to boil till itforms a homogeneous solution. The medium wasautoclaved at 121°C for 15 minutes at 15psi [260,261]

Procedure:

The flask containing autoclaved media was taken into laminar air flow cabinet. Autoclaved petri dishes were placed in laminar air flow (LAF). When the temperature of the flask containing the media lowered to 40-50˚C, about 40 mL media was poured into each plate. The plates were kept undisturbed for 15-20 minutes. After that media has solidified into the plates, the plates were incubated at 25˚C for 24 h.A fixed volume i.e. 100 µL of the fungal inoculum was spread by spreader on a sterilised petri plate containing nutrient media. With the help of borer, having 6 mm diameter, 2 wells were bored on each seeded agar plate. 100 µg/mL concentration of each compound were used. Solutions of the compounds were in DMSO and added into the respective two wells of the seeded plate, volume used was 100 µL.

For the diffusion of compounds into the medium, plates were kept in LAF for 15 min. Plates were then incubated at 25˚C for 24h in incubator. By measuring the diameter of inhibition zone, anti-fungal activity was determined. The tests were performed in triplicates (n=3) and mean of the diameter of zone of inhibition were calculated. The results obtained were compared against standard drug (Ketoconazole) [262]. Results of zone of inhibition have been summarized in section 5.3.2. (**Table no. 5.12-Table No.5.14).**

4.8.2. *In-vitro* cytotoxicity study

All the 15 synthesized compounds were checked for their anti-cancer potential against the 8 different human & animal cancer cell lines. The cancer cell lines used for the evaluation include A549 (human alveolar adenocarcinoma cells), MCF-12A cell lines (Michigan Cancer Foundation-12A, both estrogen receptor-positive and progesterone receptor-positive), HeLa (cervical cancer cells),the mouse fibrosarcoma cell line (WEHI-164), mouse nonmalignant cell line (L929), MDA-MB-231 and MCF-7 (human breast adenocarcinoma cells), HEK-293 (normal human embryonic kidney cells)andmouse nonmalignant cell line (L929). The purchasing of the cell lines was done from the National centre for Cell Sciences (NCCS), Pune, India which were maintained in DMEM. The purchasing of the tissue culture medium along with supplements, dyes, Dimethyl Sulfoxide (DMSO) & glycolysis inhibitors, Phosphate buffer saline and foetal bovine serum (FBS) was done from the Sigma-Aldrich Chemical Co (St Louis, USA).The 25 cm^2 tissue culture flask was used for the culturing of the cell lines with the supplementation of the DMEM, 10% FBS, NaHCO3, L-glutamine and solution of the antibiotics containing: penicillin &streptomycin(100 µg/ml both). These culture cell lines were then reserved at 37 °C using a humidified 5% CO_2 incubator (VWR, USA).

4.8.2.1. Microculture tetrazolium (MTT) assay

Sterile 96-well flay bottom culture plates were employed for performing the cytotoxicity assay having seeding density of 105 cells/ml of complete growth medium. Each well of the culture plates was then filled with the 100 µl of cells suspension (*HeLa, MDA-MB-231, MCF-7, A549, HEK-293, WEHI-164, L929, and MCF-12A cell lines*). These plates were then incubated further at 37 °C along with 5% CO_2 kept overnight for the attachment of cells. The synthesized indole derivatives 500 µg/ mL and standard drugs 5-fluro uracil and Doxorubicin500µg/ mL, were supplemented into the suitable wells for every concentration. Cell lines which did not receive any drug were employed as the control in the experiment.

The every concentration of the treated cell lines, control and the blank was executed in triplicate in each plate and the complete experiment is performed thrice for the validation.

To study the treatment effect in a time dependent manner, 72 hours treatment time was selected which was in accordance with the previously performed experiments. 20 µl of MTT solution was added to each well after the 72-h incubation at 37 °C along with 5% CO_2 in incubator. This solution was further incubated for additional 4 hours. By not disturbing the MTT crystals of every well the medium was further aspirated cautiously. For the dissolution of the purple colouredfarmazan crystals, 100 µl of DMSO solution was added to every well. The numerical quantity of the metabolically active cells which survived is proportional to the optical density of formazan at 570 nm measured with the help of the spectrophotometry (Infinite M200 PRO). This whole measurement is done in triplicate for the validation purpose. The IC50 values (minimum concentration of indole derivatives that giving 50% survival of HeLa, MDA-MB-231, MCF-7, A549, HEK-293, WEHI-164, L929, and MCF-12A cells) were then calculated using linear regression interpolation analysis by generating the OD values and the dose-response curves (percentage of cell survivability vs concentration). The GraphPad Prism Software 5.0 was then used for the construction of the histogram for cell survivability. Following equation was used for the calculation of Cell survivability (%)[263].

Cell survivability (%) = [(average OD of treated cell – average OD of blank)/
(average OD of untreated cell-average OD of blank)] X 100

The cytotoxic effect against cancer cell was recorded as IC50 and compared with untreated cells. The percentage of cell survivability values against concentration of respective extracts were plotted in order to determine the IC50 values of each derivative.

CHAPTER-5

RESULTS AND DISCUSSION

5.1 2D-QSAR studies

2D-QSAR model generation is an integral part of the Ligand based drug designing (LBDD) of the CADD. It provides us very useful insights for our designing of the novel biological potent molecules.

5.1.1 QSAR model generation for designing the first series of compounds

The QSAR model was made through employing Genetic Algorithm (GA) to get the multiple linear regression (MLR)model. 3 descriptors were used for generating the QSAR equation. The equation of developed QSAR model is given as follows:

PIC50 = 16.61 – 0.8581ATSC3e -8.8485GATS8v – 0.5174nHBDon_Lipinski (Eq.1)

Where, N_{train}:17, R^2: 0.8622 , R^2_{adj}: 0.8304, Q^2_{loo}: 0.7730, N_{test}: 07, R^2_{test}: 0.7770 & MAE (external): 0.2784. From looking above the QSAR equation, it is evident that the all of the descriptors employed for the generation of the model have contributed negatively in the biological activity. The details of the descriptors employed have been given in the table 3. The graph between the predicted and experimental PIC_{50} values of the molecules employed for generation of the equation is given in the **Figure 5.1**.

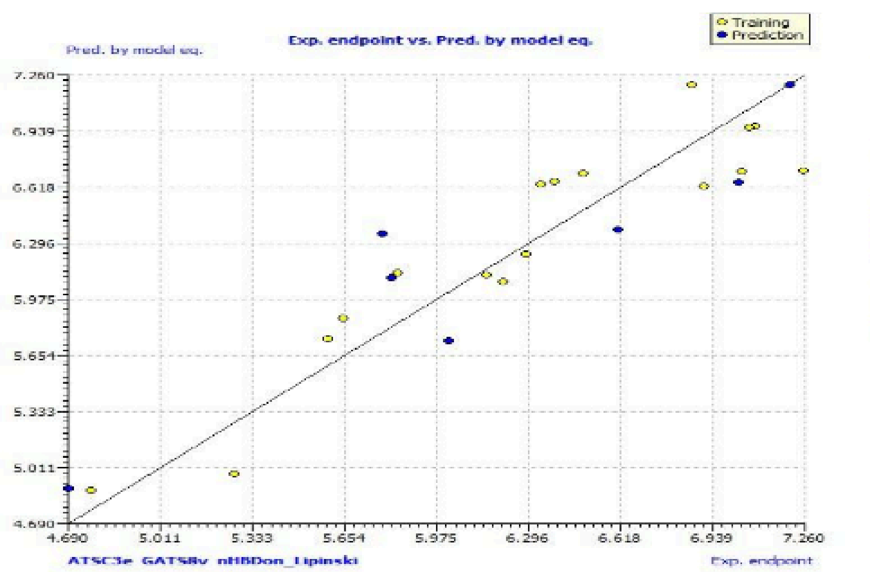


Figure 5.1: The predicted and experimental PIC_{50} values of the compounds employed for the

generation of the 2D QSAR model obtained from the QSARINS software.

Table 5.1: The types of descriptors used for the generation of the 2D QSAR model

S. No.	Name of descriptor	Type	Description	Contribution
1.	ATSC3e	2D	Autocorrelation	Negative
2.	GATS8v	2D	Geary autocorrelation of lag 8 weighted by van der Waals volume	Negative
3.	nHBDon_Lipinski	2D	Number of Hydrogen Bond Donors	Negative

The quality of any QSAR equation developed is assessed both internally and externally. For the validation of the equation internally, our QSAR equation possesses R^2: 0.8622 &R^2_{adj}: 0.8304 values respectively which signifies that predicted biological activity of the developed is well correlated with the experimental values.

Further the robustness of the model and validation that the current model is not developed by fluke is done through Y randomization test. In this, we developed 50 random QSAR models and their values of R^2& Q^2 clearly suggests that they are far behind the values obtained from our original 2D-QSAR equation (**Figure 5.2**).

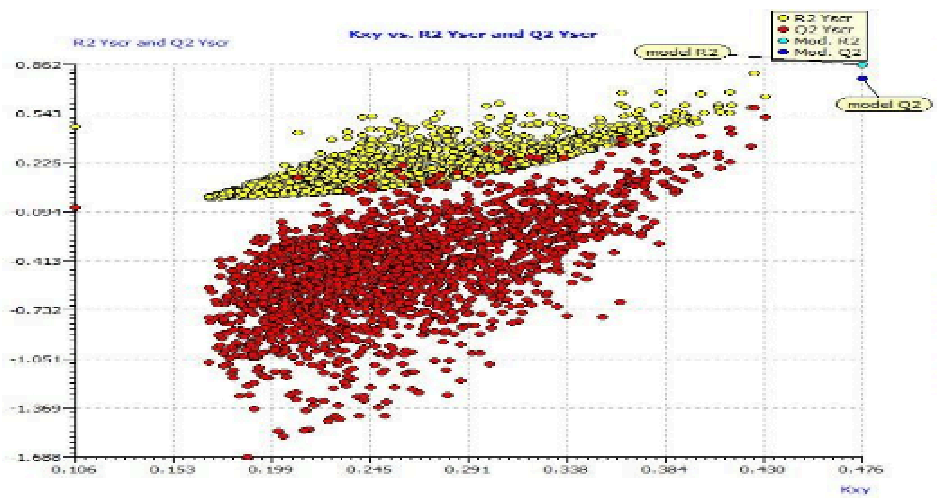


Figure 5.2: Y scrambling plot of generated 2D QSAR modelobtained from the QSARINS software

In defining the Applicability Domain (AD), none of the molecules used for the development of QSAR model falls outside the AD. This clearly suggests that our QSAR model has a great predictability evident through the Williams plot (**Figure 5.3**).

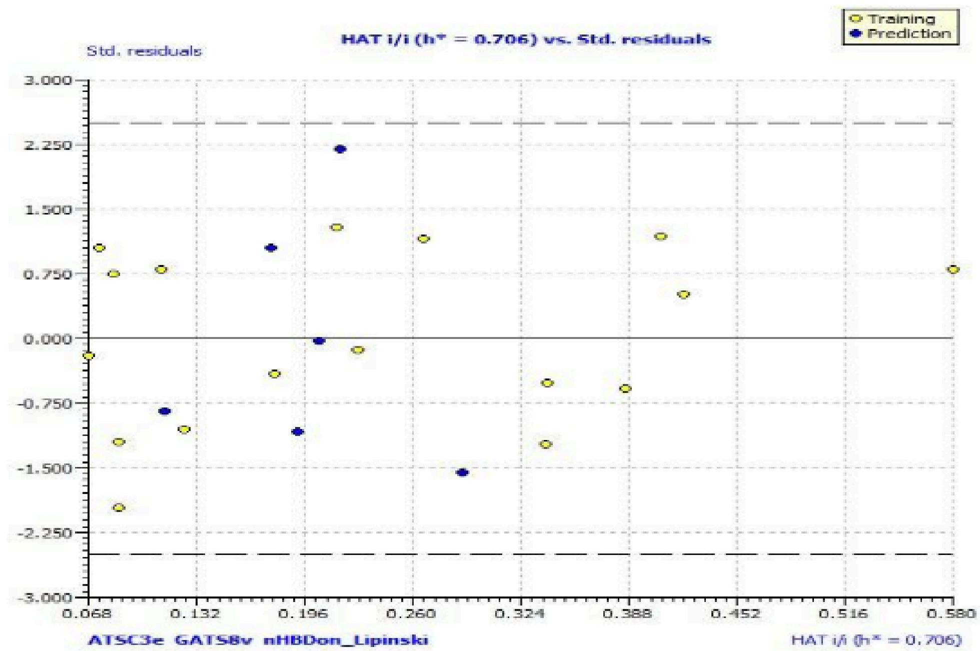


Figure 5.3: Williams plot for AD of the generated 2D QSAR modelobtained from the QSARINS software

The criteria given by the Golbraikh and Tropsha for validating any QSAR model externally are the most acceptable parameters till date. Our model has clearly passes all the criteria set by the Golbraikh and Tropsha for a successful QSAR model (**Table 5.2**)

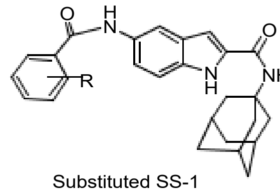
Table 5.2: Golbraikh and Tropsha parameters obtained of the developed QSAR model.

S.No.	Parameter	Threshold value	Model Score
1	Q^2	Threshold value $Q^2>0.5$	0.7730
2	R^2_{test}	Threshold value $R^2_{test}>0.6$	0.8622
3	$\|R^2_0-R'^2_0\|$	Threshold value $\|r_0^2-r'^2_0\| < 0.3$	0.0318
4	k or k'	0.85<k<1.15 & 0.85<k'<1.15	0.9967or 1.0007
5	$R^2_{test}-R^2_0/R^2_{test}$	Threshold value $R^2-R^2_0/R^2 < 0.1$	0.04138

5.1.1.2 Virtual Screening of the designed compounds

The 2D-QSAR model developed in our study is further used for virtual screening through by predicting the PIC_{50} value of our proposed molecules. The predicted PIC_{50} of the proposed compounds is given in the **Table 5.3**. In the virtual screening, all our compounds have shown remarkable predicted biological activity except the compounds 1R & 1U.

Table 5.3: Predicted PIC50 values of synthesized molecules along with values of their descriptors.



Substituted SS-1

S.No.	Name	R	ATSC3e	GATS8v	nHBDon_Lipinski	Predicted activity (PIC_{50})
1.	SS-1D	H	0.01801	1.18328	3	4.575756
2.	SS-1E	4-OH	-0.3156	1.16946	4	4.466878
3.	SS-1H	2,6-di-hydroxy	-0.14666	1.128865	5	4.163588
4.	SS-1N	2-ethyl	0.232791	1.161088	3	4.587754
5.	SS-1O	4-amino	-0.01767	1.124904	5	4.087935
6.	SS-1R	3,5-diamino	-0.1903	1.212957	7	2.422408
7.	SS-1S	3,5-dichloro	-0.35424	1.152108	3	5.170913
8.	SS-1U	4-amino-2-hydroxy	-0.16527	1.116822	6	3.768681
9.	SS-1V	3-methoxy-2-nitroxy	0.440941	1.111587	3	4.846998
10.	SS-1X	3-formyl	0.131693	1.166851	3	4.62353
11.	SS-1Y	4-formyl-3-hydroxy	-0.00632	1.132459	4	4.528773

5.1.2 QSAR model generation for designing the second series of compounds

Statistically Multiple Linear Regression (MLR) equation is generated for our QSAR model using the Genetic Algorithm (GA). 04 descriptors were employed for the generation of our 2D-QSAR model and the equation which came out is as follows:

PIC_{50} = 24.0701 + 4.8883ATSC4e - 12.4816GATS4c - 5.4896GATS8c + 0.0021VR1_Dt

Where, N_{train}:19, R^2: 0.8052, R^2_{adj}: 0.7533, Q^2_{loo}: 0.6461, N_{test}: 08, R^2_{test}: 0.7773 & MAE (external): 0.1784.

From the above equation it is clearly evident that the 02 descriptors (ATSC4e &VR1_Dt) have contributed positively and remaining two descriptors have contributed negatively in the development of our 2D-QSAR model. In Table 5.4, we've outlined the descriptors utilized in model generation. Figure 5.4 illustrates the graphshowing the correlation between the predicted and experimental PIC50 values of the compounds used in model development.

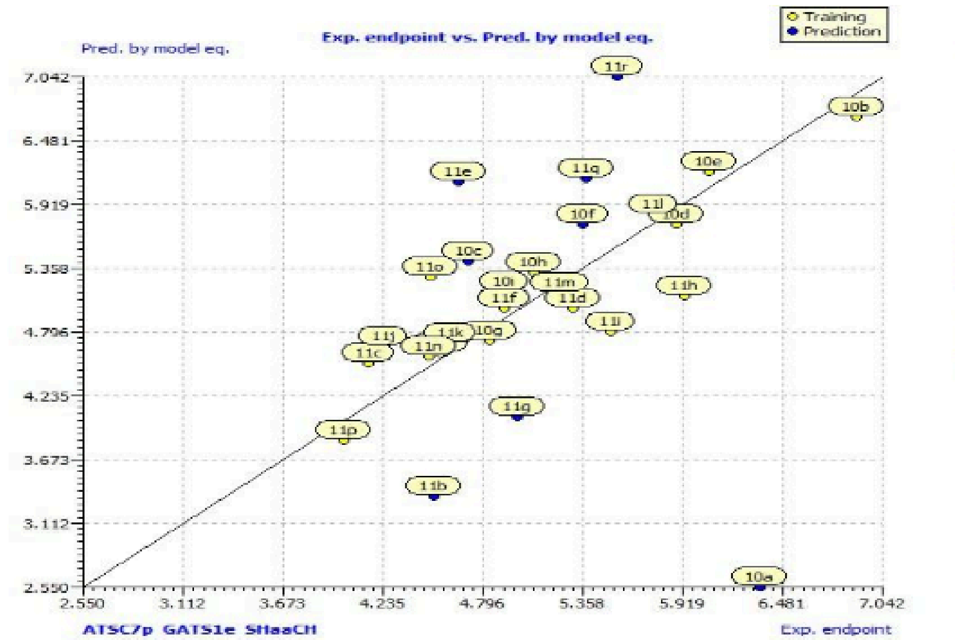


Figure 5.4: The projected and observed PIC_{50} values of the compounds utilized in constructing the 2D QSAR model.

Table 5.4: The types of descriptors used for the generation of the 2D QSAR model

S. No.	Name of descriptor	Type	Description	Contribution
1.	ATSC4e	2D	Autocorrelation	Positive
2.	GATS4c	2D	Geary autocorrelation - lag 4 / weighted by charges	Negative
3.	GATS8c	2D	Geary autocorrelation - lag 8 / weighted by charges	Negative
4.	VR1_Dt	2D	Randic-like eigenvector-based index from detour matrix	Positive

Further to establish that our model is not developed by chance and have sufficient robustness, Y randomization test is performed. We developed 100 random QSAR models and their R^2 & Q^2 clearly suggests that they are very well behind the values of the original QSAR model developed (Figure 5.5).

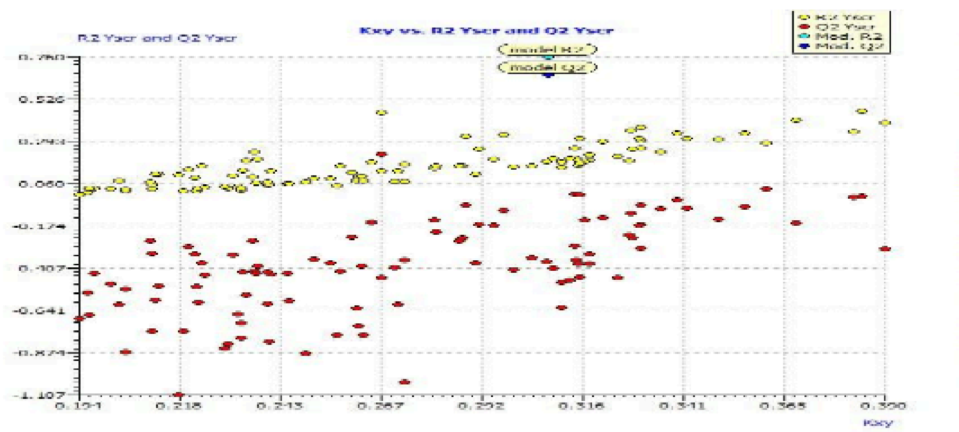


Figure 5.5: The Y scrambling plot of the developed 2D QSAR model

The AD of the developed model is defined through the Williams plot and it clearly shows that all of our compounds falls inside the AD barring the compound 11e and 11r. Both of them are influencer instead of the outliers. This clearly suggests that our QSAR model has a great predictability evident through the Williams plot (Figure 5.6).

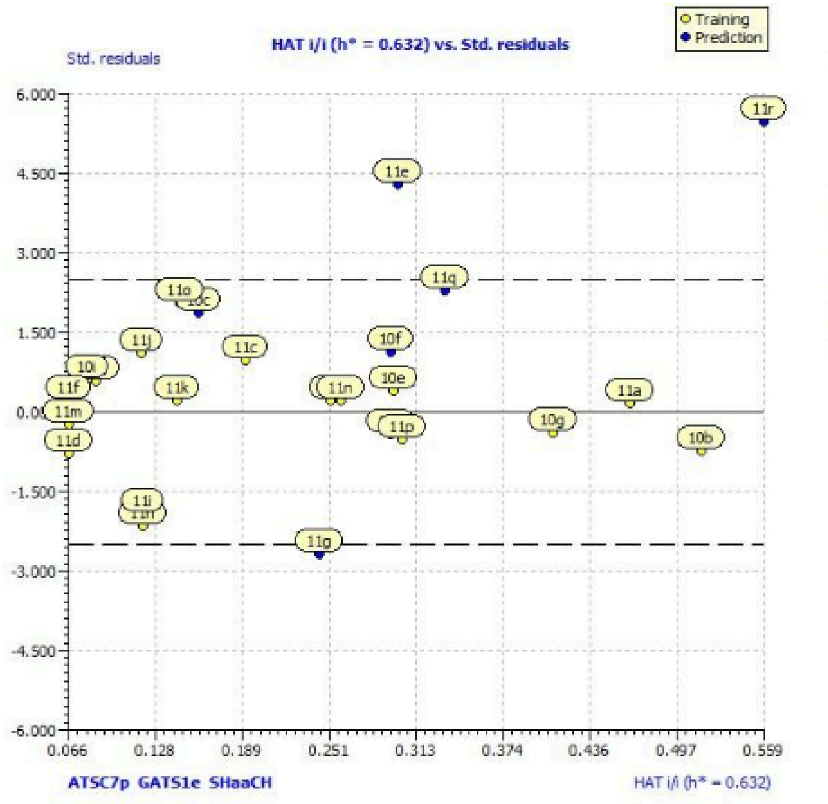


Figure 5.6: The Williams plot for Applicability Domain of the developed 2D QSAR model

The criteria given by the Golbraikh and Tropsha for the external validation are the most acceptable parameters till date for any QSAR model. Our model has clearly passes all the criteria set by the Golbraikh and Tropsha for a successful QSAR model (Table 5.5)

Table 5.5: Golbraikh and Tropsha parameters

S.No.	Parameter	Threshold value	Model Score
1	Q^2	Threshold value $Q^2>0.5$	0.6461
2	R^2_{test}	Threshold value $R^2_{test}>0.6$	0.7773
3	$\lvert R^2_0-R'^2_0 \rvert$	Threshold value $\lvert r_0^2-r'^2_0 \rvert < 0.3$	0.0218
4	k or k'	$0.85<k<1.15$ & $0.85<k'<1.15$	0.9963or 1.0003
5	$R^2_{test}-R^2_0/R^2_{test}$	Threshold value $R^2-R^2_0/R^2 < 0.1$	0.04132

5.1.2.1 Virtual screening of the designed compounds

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Further the 2D-QSAR model generated is employed for the prediction of the biological activity of our proposed 03 compounds. The structure of our three proposed novel indole derivatives were along with their descriptor values and predicted biological activities is given in the table 5.6.

Table 5.6: Structure, descriptor values and predicted biological activity of our proposed compounds

5.2 Molecular docking analysis

Molecular docking is performed to assess the interaction of the designed compounds with the target receptors of anti-cancer, anti-microbial and anti-fungal activity.

5.2.1 Molecular docking for anti-cancer activity series I compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the

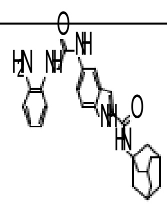
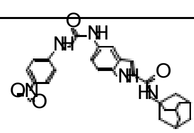
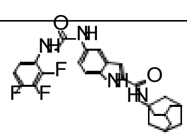
Name of Compound	**Structure**	ATSC4e	GATS4c	GATS8c	VR1_Dt	**Biological Activity predicted (PIC_{50})**
2i		0.1066	1.1097	1.0679	1156.166	6.26
2k		0.1540	1.0579	1.2098	1018.526	5.60
2u		1.1407	1.0876	1.9428	1002.277	7.51

Table 5.7

Table 5.7: The dock score of the synthesized compounds along with their interactions with the different amino acids.

S.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen Bonding	Amino Acids involved in the interaction with ligand
1.	Osimertinib	-9.4	01	LYS745	ILE759, LEU777, MET766, LEU788, LYS745, MET790, LEU718, LEU844, VAL726, ALA743,
2.	SS-1D	-10.7	01	LYS745	LEU777, LEU788, MET766, LEU858, LYS745, ASP855, MET790, LEU844, VAL726, ALA743, CYS797
3.	SS-1E	-10.9	00	NIL	LEU777, LEU788, MET766, PHE856, VAL726, LEU718, LEU797, ALA743, MET790, LYS745

4.	SS-1H	-11.2	01	LYS745	MET790, LEU777, LEU788, MET766, ALA743, VAL726, LEU797, CYS797, LEU858
5.	SS-1N	-10.6	00	NIL	MET790, LEU777, LEU788, LYS745, ALA743, VAL726, LEU844, LEU718, GLY719, CYS797
6.	SS-1O	-10.9	00	NIL	LEU777, LEU788, MET766, MET790, LYS745, ALA743, VAL726, CYS797, LEU718, LEU844
7.	SS-1R	-11.1	01	PHE856	LEU777, LEU788, MET766, MET790, LYS745, ALA743, VAL726, LEU718, LEU844
8.	SS-1S	-11.0	00	NIL	MET790, LYS745, ALA743, VAL726, LEU743, MET793,

					LEU792, LEU718, LEU844, CYS797, ASP855, LEU788, LEU861, LEU862, MET766, LEU861
9.	SS-1U	-11.3	01	LYS745	LEU777, LEU788, MET766, MET790, ASP855, VAL726, LEU743, CYS797, LEU844
10.	SS-1V	-11.8	00	NIL	LEU777, LEU788, MET766, LEU861, LEU862, LEU858, LEU743, VAL726, MET790, LYS745, CYS797, LEU844, LEU718
11.	SS-1X	-10.8	00	NIL	LYS745, VAL726, MET790, LEU844, LEU718, LEU788, LEU743, LEU747, LEU861, LEU862, LEU858, MET766

12.	SS-1Y	-10.8	00	NIL	LEU788, MET766, ASP855, LYS745, LEU777, LEU743, MET790, VAL726, CYS797, LEU718

From the docking analysis, it was interesting to see that all our proposed compounds showed higher dock score when compared to the Osimertinib the reference standard used in the molecular docking analysis. The highest docking store was shown by the compound 1V having the dock score of -11.8 Kcal/mole but this compound didn't show any hydrogen bond interaction (**Figure 5.7**).

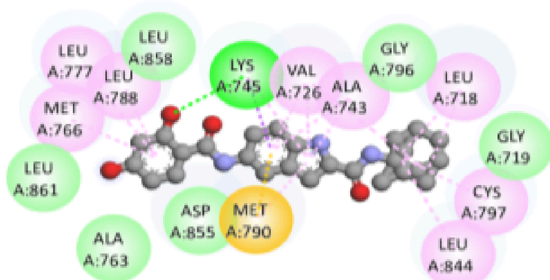


Figure 5.7: Interaction of the compound SS-1H with the target proteinobtained from the Biovia Discovery studio academic visualizer

The standard used Osimertinib has shown one hydrogen bond interaction with the receptor amino acid Lysine745 (**Figure 5.8**). The same type of hydrogen bond interactions are also possessed by the compounds 1D, 1H & 1U with the same amino acids. The compound 1R has also possessed one hydrogen bond interaction with the amino acid Phenyl Alanine 856.

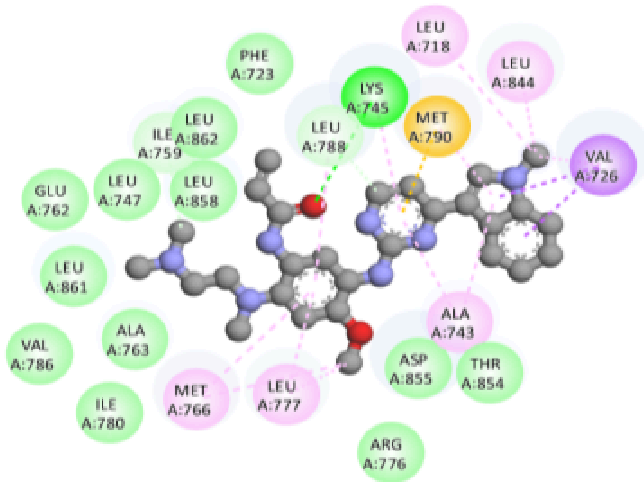


Figure 5.8: Interaction of the Osimertinib with the target protein obtained from the Biovia Discovery studio academic visualizer

5.2.2 Molecular docking for anti-microbial activity of series I compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the **Table 5.8**.

Table 5.8: The dock score of the synthesized compounds along with their interactions with the different amino acids.

S.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen Bonding	Amino Acids involv in the interaction wi ligand
1.	Ciprofloxacin	-8.0	01	ASP115	LEU98, TYR266, VAL90, ARG91, ASP87, GLN94,

					GLY110, SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
2.	SS-1A	-9.9	NIL	NIL	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102
3.	SS-1B	-9.9	NIL	NIL	HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171
4.	SS-1C	-10.1	01	SER97	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114,

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					ASN269, ILE112, VAL268, PHE96
5.	SS-1D	-9.9	01	GLN94	GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
6.	SS-1E	-9.2	NIL	NIL	HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171
7.	SS-1F	-9.1	NIL	NIL	ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
8.	SS-1G	-9.1	01	SER171	ASN 165, ASN 169,

					GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
9.	SS-1H	-10.0	01	SER171	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
10.	SS-1I	-9.8	NIL	NIL	SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
11.	SS-1J	-9.6	NIL	NIL	GLY170, LEU102, SER171, MET92, LEU98, GLN267,

					GLY114, ASN269, ILE112, VAL268, PHE96
12.	SS-1K	-9.2	01	GLY114	SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
13.	SS-1L	-9.4	NIL	NIL	ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
14.	SS-1M	-9.8	NIL	NIL	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112,

					VAL268, PHE96
15.	SS-1N	-10.0	NIL	NIL	SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
16.	SS-1O	-9.5	01	VAL268	ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
17.	SS-1P	-9.6	01	SER172	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171,

					MET92, LEU98
18.	SS-1Q	-9.6	NIL	NIL	SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98
19.	SS-1R	-9.5	NIL	NIL	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
20.	SS-1S	-9.3	01	ASN269	SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267,

					GLY114
21.	SS-1T	-9.8	NIL	NIL	GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
22.	SS-1U	-9.7	NIL	NIL	SER171, MET92, LEU98, GLN267, GLY114, ASN269, ILE112, VAL268, PHE96
23.	SS-1V	-9.0	01	GLY114	GLN94, HIS46, TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92, LEU98, GLN267, GLY114,
24.	SS-1W	-9.5	01	SER171	HIS46, TYR266, SER172, ARG91,

					LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92
25.	SS-1X	-9.7	NIL	NIL	TYR266, SER172, ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92
26.	SS-1Y	-8.6	01	TYR266	ARG91, LEU41, GLY40, ASN 165, ASN 169, GLY170, LEU102, SER171, MET92

From the docking simulations of the synthesized compounds for antimicrobial activity against the series I, it is inferred that all the synthesised compounds has shown better binding affinity with the reference ligand ciprofloxacin (-8.0 Kcal/mole). The reference ligand ciprofloxacin has shown one hydrogen bond interactions with amino acid residue i.e ASP115 (Figure 5.9). Similarly, the most active compound emerged out was compound SS-IC with a docking energy of -10.1 Kcal/mole and one hydrogen bond interaction with the amino acid residue SER97 (figure 5.10).

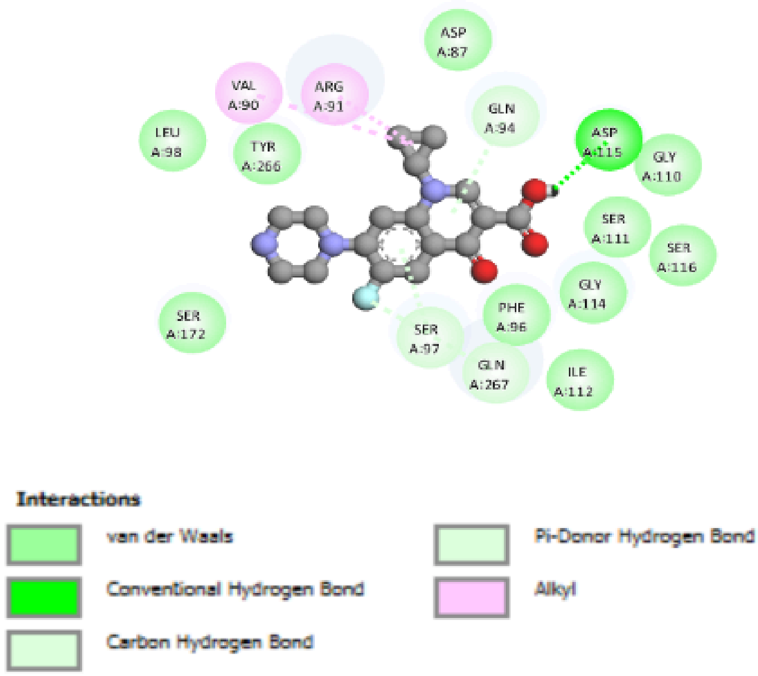

Figure 5.9: Interaction of the Ciprofloxacin with the target protein obtained from the Biovia Discovery studio academic visualize

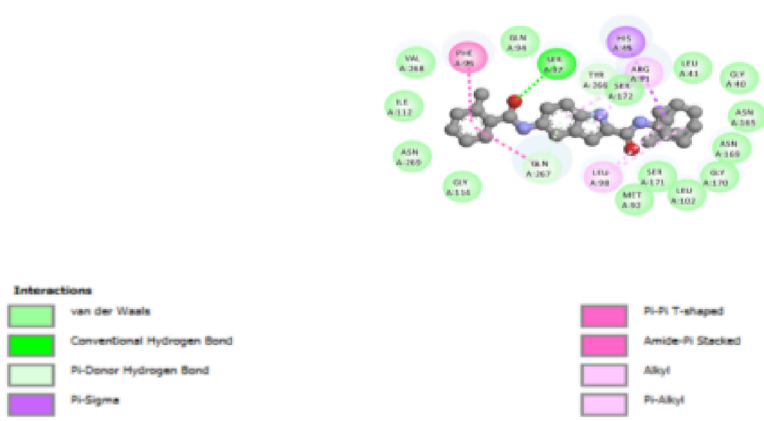

Figure 5.9: Interaction of the SS-IC with the target protein obtained from the Biovia Discovery studio academic visualizer

5.2.3 Molecular docking for anti-fungal activity of series I compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the **Table 5.9**.

Table 5.9: The dock score of the synthesized compounds along with their interactions with the different amino acids.

.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen Bonding	Amino Acids involved the interaction with ligand
1.	Fluconazole	-6.8	02	HIS259, TYR76	MET433, PHE78, LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR7 VAL434
2.	SS-1A	-5.0	NIL	NIl	LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR7 VAL434

3.	SS-1B	-4.8	NIL	NIl	ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR7 VAL434
4.	SS-1C	-4.6	NIL	NIl	MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG9
5.	SS-1D	-5.3	NIL	NIl	PHE78, LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG9 TYR76, VAL434
6.	SS-1E	-5.7	NIL	NIl	LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR7 VAL434
7.	SS-1F	-5.1	NIL	NIl	CYS394, PHE255, ALA73, THR80, PHE8

					MET99, MET79, ARg9 TYR76, HIS392,
8.	SS-1G	-5.2	NIL	NIl	PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392,
9.	SS-1H	-5.0	NIL	NIl	PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG9 TYR76, VAL434
10.	SS-1I	-5.6	NIL	NIl	PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392,
11.	SS-1J	-5.4	NIL	NIl	PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR7 VAL434
12.	SS-1K	-5.7	NIL	NIl	MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG9

13.	SS-1L	-5.8	NIL	NIl	ALA73, THR80, PHE8 MET99, MET79, ARg9 TYR76, HIS392
14.	SS-1M	-5.7	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392
15.	SS-1N	.5.3	NIL	NIl	CYS394, PHE255, ALA73, THR80, PHE8 MET99, MET79, ARg9 TYR76, HIS392
16.	SS-1O	-5.2	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392
17.	SS-1P	-5.0	NIL	NIl	THR260, LEU321, CYS394, PHE255, ALA73, THR80, PHE8 MET99, MET79, ARg9 TYR76, HIS392

18.	SS-1Q	-5.9	NIL	NIl	PHE387, THR260, LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392, LEu324, GLU388
19.	SS-1R	-5.5	NIL	NIl	TYS394, PHE255, ALA73, THR80, PHE8 MET99, MET79, ARg9 TYR76, HIS392, LEu32
20.	SS-1S	-5.5	NIL	NIl	PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392, LEu324
21.	SS-1T	-5.7	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392
22.	SS-1U	-5.1	NIL	NIl	MET79, ALA256, PHE255, PHE88, LEU100, LEU324,

					HIS392, GLN72, ARG9
23.	SS-1V	-4.2	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392
24.	SS-1W	-5.6	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392, LEu324, GLU388
25.	SS-1X	-5.2	NIL	NIl	, CYS394, PHE255, ALA73, THR80, PHE8 MET99, MET79, ARg9 TYR76, HIS392, LEu32 GLU388
26.	SS-1Y	-4.0	NIL	NIl	LEU321, CYS394, PHE255, ALA73, THR80, PHE83, MET9 MET79, ARg96, TYR7 HIS392, LEu324, GLU388

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From the docking simulations of the synthesized compounds for antifungal activity against the series I, it is inferred that all the synthesised compounds has shown lesser binding affinity with the reference ligand Fluconazole (-6.8 Kcal/mole). The reference ligand Fluconazole has shown two hydrogen bond interactions with amino acid residue i.e HIS529 and TYR76 (Figure 5.11). Similarly, the most active compound emerged out was compound SS-IQ with a docking energy of -5.9 Kcal/mole and no hydrogen bond interaction (figure 5.12).

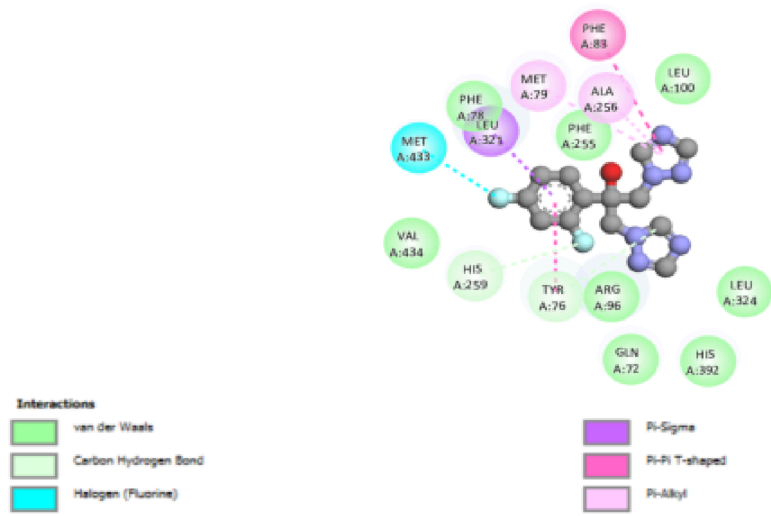


Figure 5.11: Interaction of the Fluconazole with the target protein obtained from the Biovia Discovery studio academic visualize

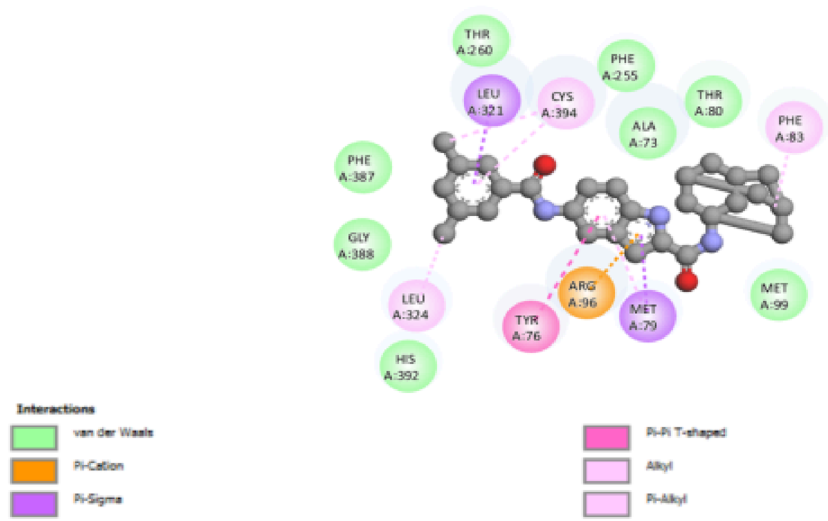


Figure 5.12: Interaction of the SS-1Q with the target protein obtained from the Biovia Discovery studio academic visualizer

5.2.4Molecular docking for anti-cancer activity of series II compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the **Table 5.10**.

Table 5.10: The dock score of the synthesized compounds along with their interactions with the different amino acids.

S.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen Bonding	Amino Acids involved in the interaction with ligand
1.	SS-III	-7.5	02	CYS797, ASP800	ARG803, LEU799, ARG841, VAL726, GLY719, ALA743, THR790, MET766, LYS745, LEU844, ASP855, THR854, LEU718
2.	SS-IIK	-6.6	Nil	Nil	CYS797,ASP800, LEU799, VAL726, PHE723, LYS745, MET766, THR854, THR790, ALA743, ASP855, LEU844, ARG841, GLY719 LEU718
3.	SS-IIU	-7.3	01	ASP800	PHE723, GLY796, ALA743, LEU844, THR790, MET766, THR854, ASP855,

					GLU762, LYS745, LEU788, VAL726, LEU718, GLY719, CYC797, LEU799, ARG841
4.	PD168193 (Internal Ligand)	-7.8	Nil	Nil	THR790, MET766, LEU788, LYS745, PHE723, ASN842, ARG841, CYC797, GLY796, LEU718, LEU844, LEU792, MET793, ALA743, VAL726,

From the docking analysis, one important and interesting postulate which came to the notice is that our 2 proposed compounds have shown hydrogen bonding with the target receptor whereas the reference didn’t show any hydrogen bonding interaction. The dock score of the standard drug PD168193 came out to be -7.8 Kcal/mol which is very much comparable with our two proposed compounds SS-III (-7.5 Kcal/mol) &2U (-7.3 Kcal/mol). The molecular interaction diagram of the internal standard, compounds SS-III & SS-IIU is given in the figure 5.13, 5.14&5.15 respectively.

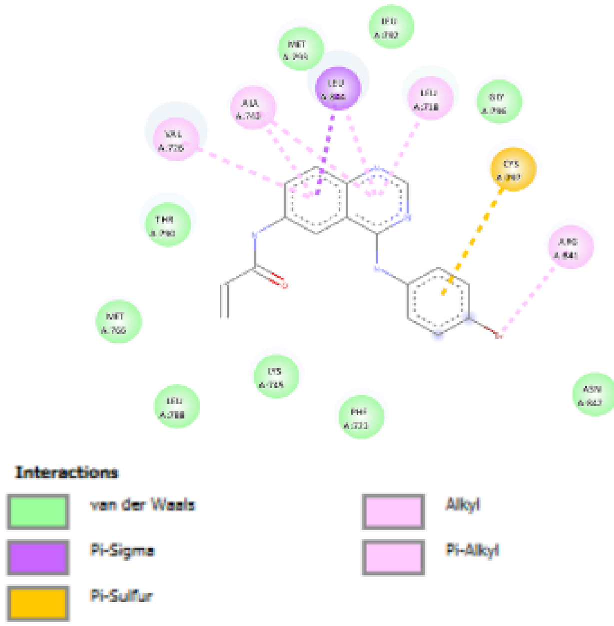


Figure 5.13: Interaction of the internal standard with the target protein

The compound SS-III has shown two hydrogen bond interaction with the amino acid residues ASP800 & CYS797 whereas the compound SS-IIU has shown only one hydrogen bond interaction with the amino acid interaction with the amino acid residue CYS797.

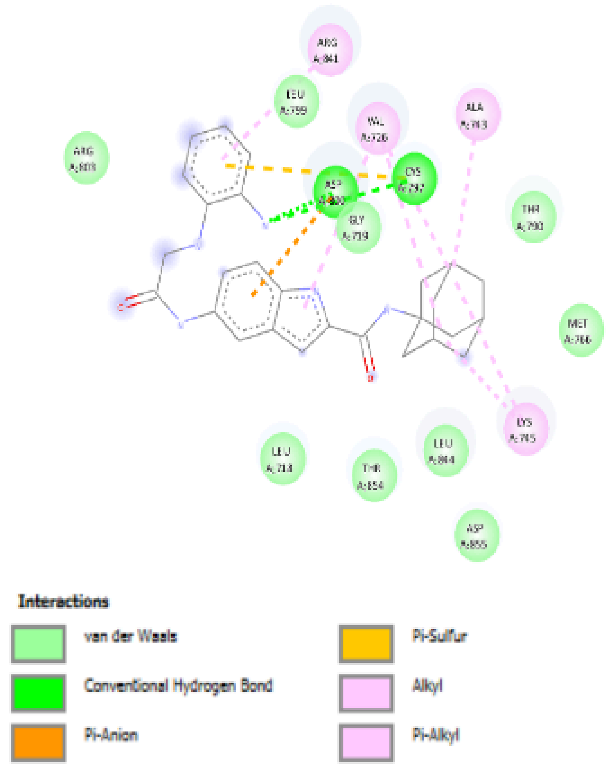


Figure 5.14: Interaction of the SS-III with the target protein

The compound SS-2K (-6.6) Kcal/mol) has shown the least interaction with the target receptor both in terms of dock score and hydrogen bond interactions (nil interaction)

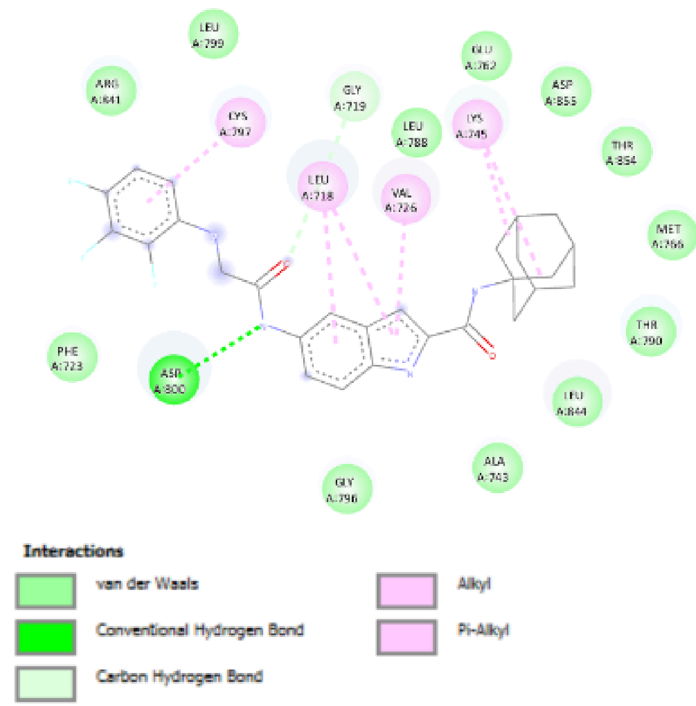


Figure 5.15: Interaction of the SS-IIU with the target protein

5.2.5Molecular docking for antimicrobial activity of series II compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the **Table 5.11**.

Table 5.11: The dock score of the synthesized compounds along with their interactions with the different amino acids.

SS.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen	Amino Acids involved in the interaction with ligand

				Bonding	
1.	Ciprofloxacin	-8.0	01	ASP115	LEU98, TYR266, VAL90, ARG91, ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
2.	SS-IIA	-9.6	NIL	NIL	VAL90, ARG91, ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
3.	SS-IIB	-9.3	01	SER116	SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
4.	SS-IIC	-8.9	01	PHE96	LEU98, TYR266, VAL90, ARG91, ASP87, GLN94, GLY110, SER111, SER116,

					GLY114
5.	SS-IID	-8.8	NIL	NIL	ARG91, ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
6.	SS-IIE	-9.2	NIL	NIL	ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
7.	SS-IIF	-9.1	NIL	NIL	ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96, GLN267, SER97, SER172
8.	SS-IIG	-9.2	NIL	NIL	TYR266, VAL90, ARG91, ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96
9.	SS-IIH	-9.2	01	SER172	GLN94, GLY110, SER111, SER116,

					GLY114, PHE96, GLN267, SER97, SER172
10.	SS-III	-9.3	01	SER111	SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
11.	SS-IIJ	-9.1	NIL	NIL	SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
12.	SS-IIK	-8.9	01	LEU41	TYR266, VAL90, ARG91, ASP87, GLN94, GLY110, SER111, SER116, GLY114, PHE96
13.	SS-IIL	-9.2	NIL	NIL	SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169

14.	SS-IIM	-9.5	NIL	NIL	ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
15.	SS-IIN	-9.0	NIL	NIL	GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
16.	SS-IIO	-9.2	NIL	NIL	ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
17.	SS-IIP	-9.7	02	ASN165, TYR266	GLY170, LEU98, ARG91, SER97, GLN267, VAL268, PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169

18.	SS-IIQ	-9.4	01	GLY40	GLN267, VAL268, PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102
19.	SS-IIR	-9.3	01	SER111	GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
20.	SS-IIS	-9.2	NIL	NIL	PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
21.	SS-IIT	-9.7	NIL	NIL	ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102
22.	SS-IIU	-9.8	01	LEU41	GLN267, VAL268, PHE96, ILE112, ASN269, SER111,

					GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102, ASN 169
23.	SS-IIV	-9.4	01	ASN269	PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45
24.	SS-IIW	-8.8	01	GLY40	VAL268, PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102
25.	SS-IIX	-9.0	NIL	NIL	ASN269, SER111, GLY114, SER172, SER171, LYS42, LEU41, GLY40, HIS45, LEU102
26.	SS-IIY	-9.5	NIL	NIL	VAL268, PHE96, ILE112, ASN269, SER111, GLY114, SER172, SER171,

					LYS42, LEU41, GLY40, HIS45

From the docking simulations of the synthesized compounds for antimicrobial activity against the series II, it is inferred that all the synthesised compounds has shown better binding affinity with the reference ligand ciprofloxacin (-8.0 Kcal/mole). The reference ligand ciprofloxacin has shown one hydrogen bond interactions with amino acid residue i.e ASP115 (Figure 5.9). Similarly, the most active compound emerged out was compound SS-IIP with a docking energy of -9.7 Kcal/mole and two hydrogen bond interactions with the amino acid residue ASN165 and TYR 266 (figure 5.16).

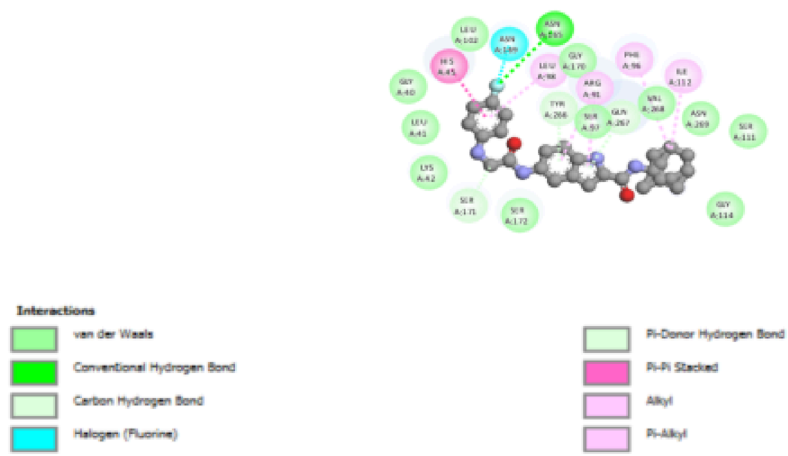


Figure 5.16: Interaction of the SS-IIP with the target protein

5.2.5Molecular docking for antifungal activity of series II compound

The proposed compounds were further evaluated via molecular docking analysis to study their interactivity with the receptor. The results of our docking analysis are given in the **Table 5.12**.

Table 5.12: The dock score of the synthesized compounds along with their interactions with the different amino acids.

SS.No.	Name of compound	Dock Score (KCal/Mole)	No. of H-Bond	Amino acid Residues involved in Hydrogen Bonding	Amino Acids involved in the interaction with ligand
1.	Fluconazole	-6.8	02	HIS259, TYR76	MET433, PHE78, LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR76, VAL434
2.	SS-IIA	-6.5	NIL	NIL	PHE78, LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96
3.	SS-IIB	-6.4	NIL	NIL	LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR76

4.	SS-IIC	-6.1	NIL	NIL	ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR76
5.	SS-IID	-6.4	NIL	NIL	LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96
6.	SS-IIE	-6.4	NIL	NIL	MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96
7.	SS-IIF	-6.6	NIL	NIL	MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR76
8.	SS-IIG	-5.7	NIL	NIL	PHE78, LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96,

					TYR76, VAL434
9.	SS-IIH	-6.0	NIL	NIL	LEU371, MET79, ALA256, PHE255, PHE88, LEU100, LEU324, HIS392, GLN72, ARG96, TYR76, VAL434
10.	SS-III	-6.1	NIL	NIL	PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321
11.	SS-IIJ	-6.2	NIL	NIL	PRO320, PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
12.	SS-IIK	-6.2	NIL	NIL	PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80,

					PHE83, LEU321, CYS394
13.	SS-IIL	-5.9	NIL	NIL	ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394
14.	SS-IIM	-6.6	NIL	NIL	ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394
15.	SS-IIN	-6.9	NIL	NIL	PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321
16.	SS-IIO	-5.6	NIL	NIL	PEO320, PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394

17.	SS-IIP	-6.3	NIL	NIL	PRO386, PEO320, PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99
18.	SS-IIQ	-6.5	NIL	NIL	ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
19.	SS-IIR	-6.6	NIL	NIL	PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
20.	SS-IIS	-6.5	NIL	NIL	PEO320, PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99
21.	SS-IIT	-6.8	NIL	NIL	PEO320, PHE387, ALA400, ALA256, PHE255, TYR76,

					ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321
22.	SS-IIU	-6.9	NIL	NIL	PRO386, PEO320, PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
23.	SS-IIV	-6.6	NIL	NIL	PHE387, ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
24.	SS-IIW	-6.7	NIL	NIL	ALA400, ALA256, PHE255, TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260
25.	SS-IIX	-6.6	NIL	NIL	ALA256, PHE255,

					TYR76, ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394
26.	SS-IIY	-6.3	NIL	NIL	ARG96, MET79, ALA73, MET99, THR80, PHE83, LEU321, CYS394, THR260

From the docking simulations of the synthesized compounds for antifungal activity against the series II, it is inferred that all the synthesised compounds has shown lesser binding affinity with the reference ligand Fluconazole (-6.8 Kcal/mole) except the compounds SS-IIT (-6.8 Kcal/mole) and SS-IIU (-6.9 Kcal/mole). The reference ligand Fluconazole has shown two hydrogen bond interactions with amino acid residue i.e HIS529 and TYR76 (Figure 5.11). Similarly, the most active compound emerged out was compound SS-IQ with a docking energy of -5.9 Kcal/mole and no hydrogen bond interaction (Figure 5.17).

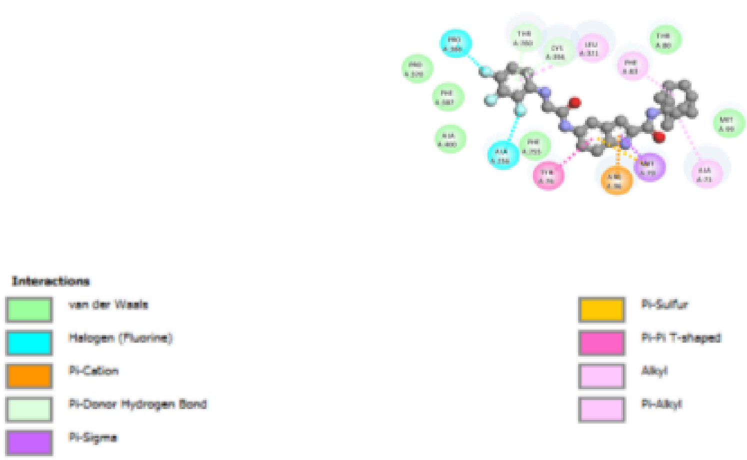


Figure 5.17: Interaction of the SS-IIU with the target protein

5.3 Molecular Dynamics Simulations

5.3.1 Molecular dynamic simulations of EGFR receptor, in complex with compound SS-III, compound SS-IIK, compound SS-IIU, and PD168393

We performed 100 ns molecular dynamics (MD) simulations for four models, compound 2i-EGFR, compound 2k-EGFR, compound 2u-EGFR, and PD168393-EGFR (standard), to evaluate the binding of four compounds, namely, compound SS-III, compound SS-2K, compound SS-IIU, and PD168393 with EGFR receptor (PDB ID: 4LQM) (as illustrated in Figure 5.18). Numerous statistical parameters, such as Root-Mean-Square Deviation (RMSD), Root-Mean-Square Fluctuation (RMSF), hydrogen bond interactions, and their corresponding % occupancies across the simulation period, were used to analyse these simulations.

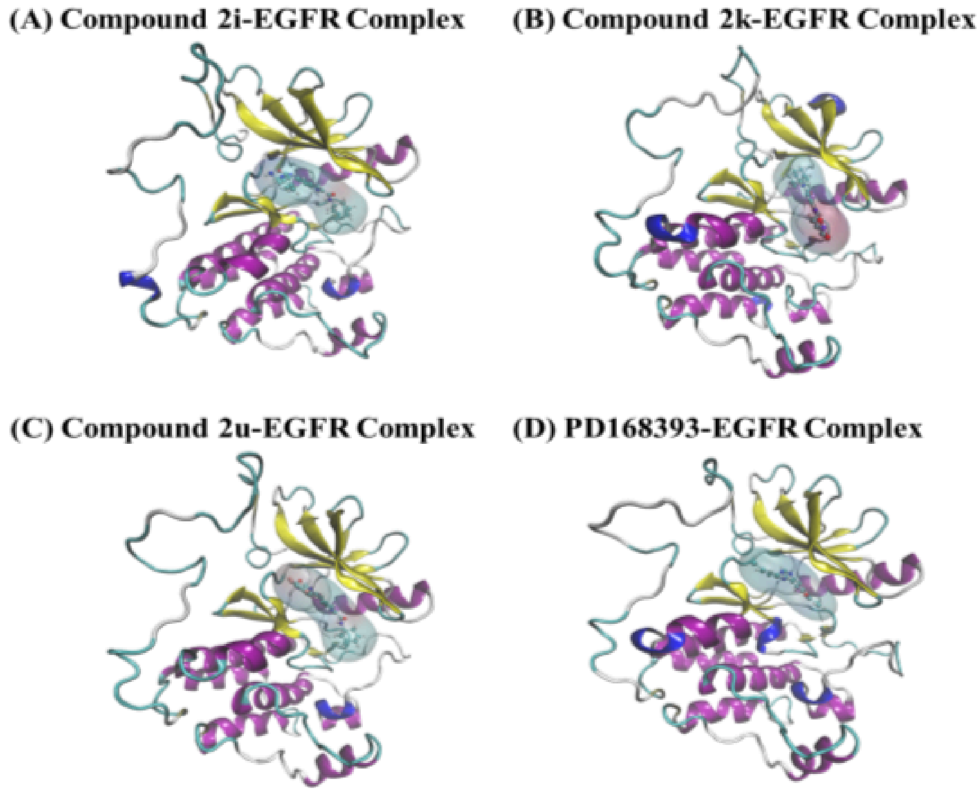


Figure 5.18: Visual depiction of protein-ligand combinations: (A) Compound SS-III-EGFR, (B) Compound SS-IIK-EGFR, (C) Compound SS-IIU-EGFR, and (D) PD168393-EGFR (standard), in which the ligand is depicted with a transparent surface in a CPK representation and the protein is displayed in a cartoon depiction.

5.3.2. RMSD analysis

Analysing the Root-Mean-Square Deviation (RMSD) provides important information about the structural alterations that the ligand and protein go through during the simulation. A multiplot showing the protein's RMSD with time for four different simulations is shown in Figure 5.19. Remarkably, every complex attained a stable phase at some point, as evidenced by RMSD values below 0.3 nm.

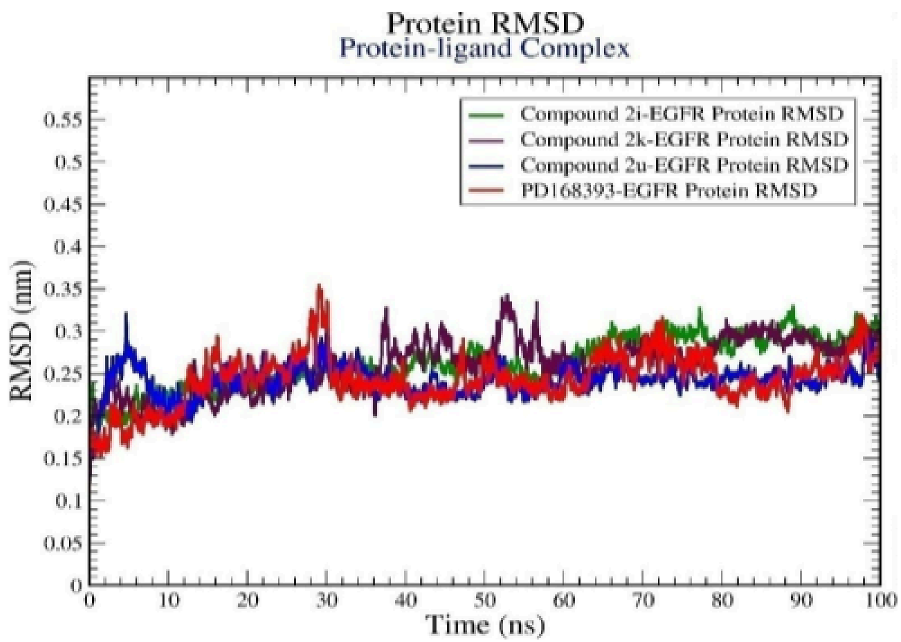


Figure 5.19: Graphical representation of the plots showing ProteinRMSD (nm) versus time (100 ns) for (A) Compound SS-III-EGFR(green in color), (B) Compound SS-IIK-EGFR(maroon in color),(C) Compound SS-IIU-EGFR(red in color), and (D) PD168393-EGFR (blue in color).

The stability of the ligands' binding to the protein can be inferred from their RMSD values. A multiplot showing the ligands' RMSD over time for each simulation is shown in Figure 5.20. Remarkably, RMSD values for all ligands are less than 0.25 nm. It's important to note, nevertheless, that compound SS-III and compound SS-IIU have steady magnitude RMSD values in contrast to the other two. All four ligands have, however, shown RMSD values that are within allowable bounds, suggesting that they can bind to the EGFR receptor efficiently.

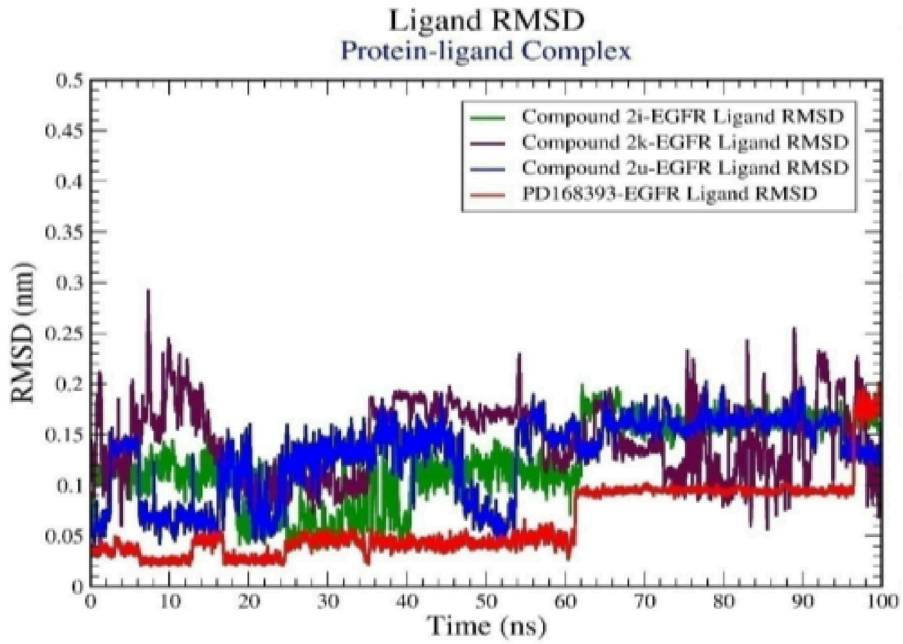


Figure 5.20: Diagrammatic depiction of the plots displaying Ligand RMSD (nm) vs time (100 ns) for Compound SS-III-EGFR (green), Compound SS-IIK-EGFR (maroon), Compound SS-IIU-EGFR (red), and PD168393-EGFR (blue).

5.3.3. RMSF analysis

Protein Root-Mean-Square Fluctuation (RMSF) analysis is a useful method for looking at specific structural alterations in a protein. The protein RMSF (measured in nanometers) is plotted against the residue number index in Figure 5.21. It is noteworthy to highlight that the majority of protein residues in this plot exhibit changes of less than 0.4 nm, indicating that the protein's structure is generally stable.

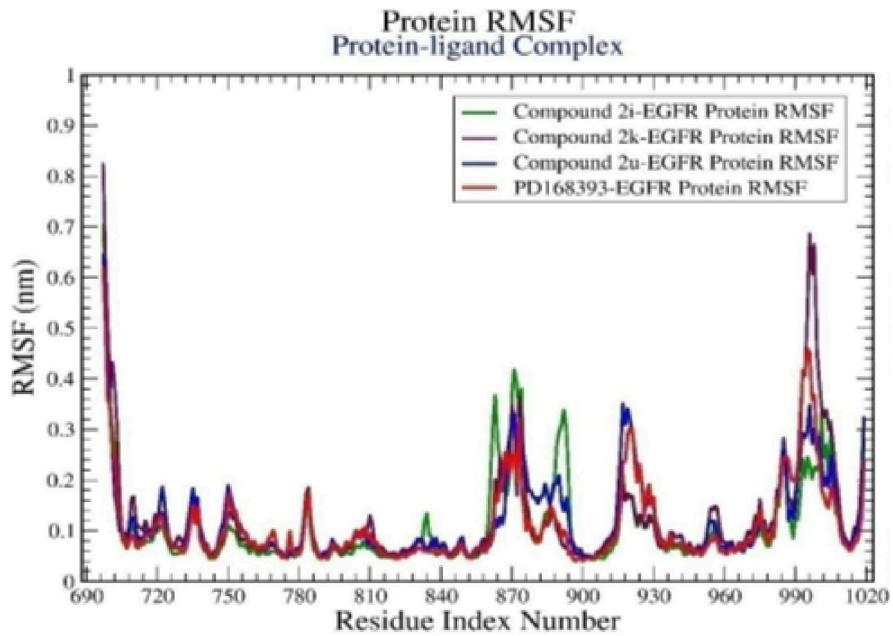


Figure 5.21: Plots for (A) Compound SS-III-EGFR (green), (B) Compound SS-IIK-EGFR (maroon), (C) Compound SS-IIU-EGFR (red), and (D) PD168393-EGFR (blue) that display the protein RMSF (nm) in relation to the residue index number of the protein.

5.3.4. H-bond interaction

Molecular interactions, especially those involving hydrogen bonds (h-bonds), depend on both angle and distance parameters and are dynamically sensitive to perturbations. In our analysis, we examined the h-bond interactions among each complex. Figure 5.22 is a graph that illustrates the quantity of hydrogen bonding over time. Remarkably, the figure revealed that during the simulation, compounds SS-III and SS-IIU, together with the reference molecule PD168393, had stronger and more stable h-bond interactions than the other two compounds.To assess the stability of these contacts and gain further insight, the percentage occupancies of specific residues involved in these h-bond interactions were computed.

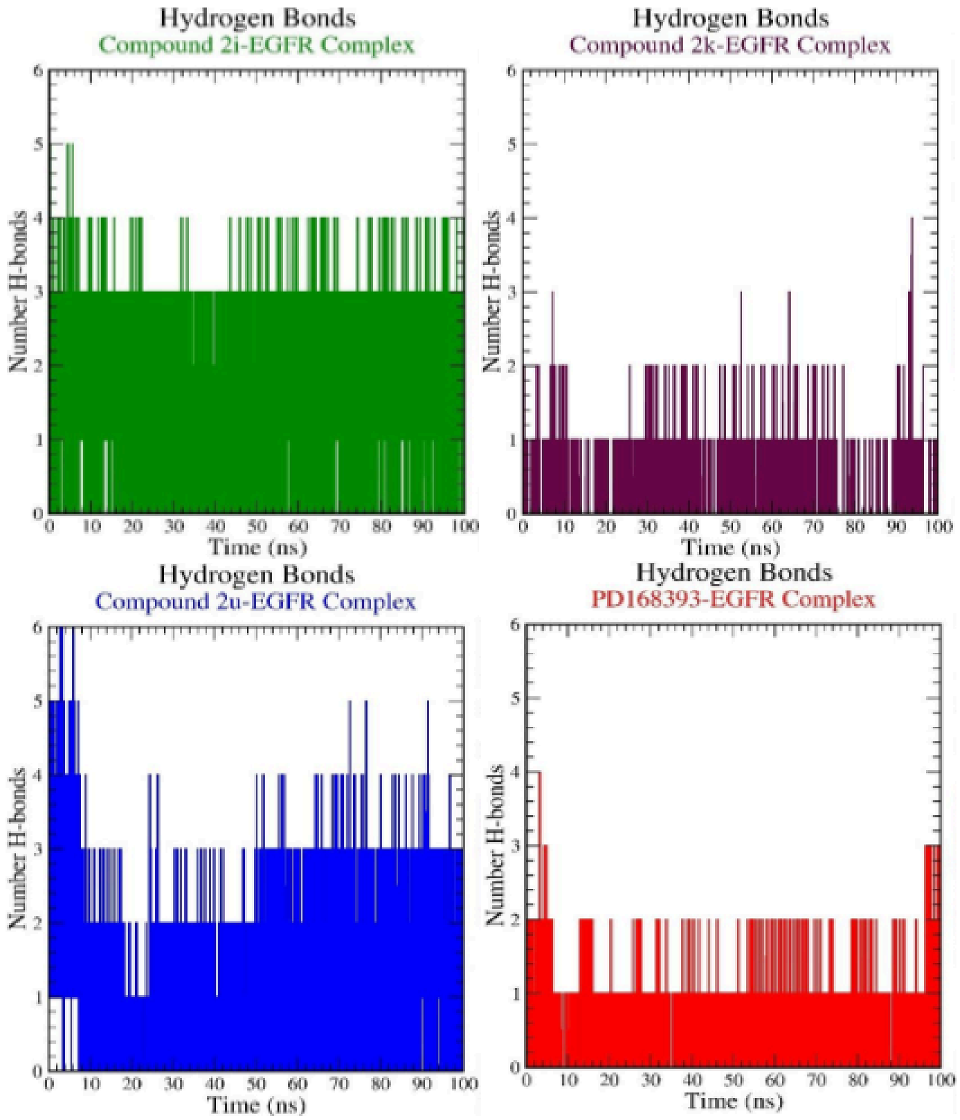
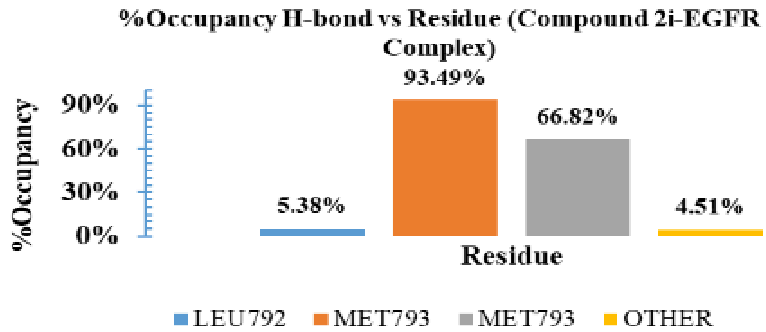
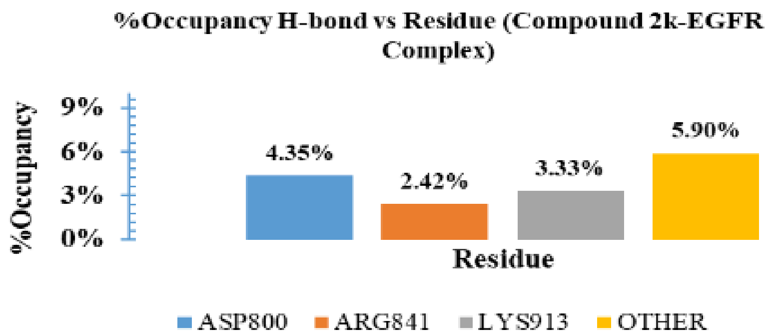
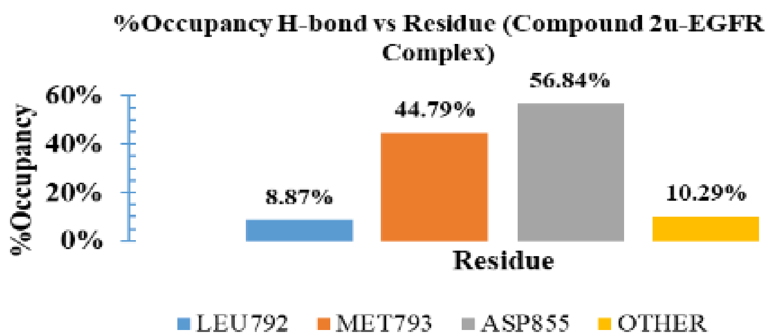


Figure 5.22: Pictorial representation of the number of h-bond contacts formed by ligands,(A) Compound SS-III, (B) Compound SS-IIK, (C) Compound SS-IIU and (C) PD168393in complex withEGFR receptor (PDB ID: 4LQM).

A histogram showing the % occupancies of hydrogen bond connections created by various ligands is shown in Figure 5.23. This graph underscores compound SS-III's capacity to establish multiple interactions with MET793 of EGFR receptor, with an occupancy rate of 93.49 and 66.82%. On the other hand, compound SS-IIU demonstrates stable hydrogen bond interactions with residues ASP855, and MET793, sustained for 56.84%, and 44.79% of the simulation period, respectively. Conversely, compound SS-IIK and PD168393haveless stable hydrogen bond interactions. In summary, these findings suggest that out of four ligands, compound SS-III and compound SS-IIU appear to be the most efficient in binding with EGFR receptor.







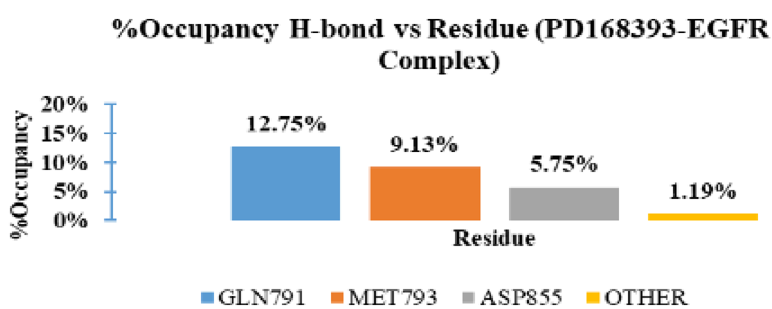


Figure 5.23: Histogram showing %occupancies of the h-bond protein-ligand contacts of(A) Compound SS-III, (B) Compound SS-IIK, (C) Compound SS-IIU and (C) PD168393in complex withEGFR receptor (PDB ID: 4LQM).

5.4 Synthesis of the final compounds

Characterization of the synthesized compounds was done through the traditional spectroscopic techniques which include IR, NMR, Mass spectrometry and the CHN analysis.

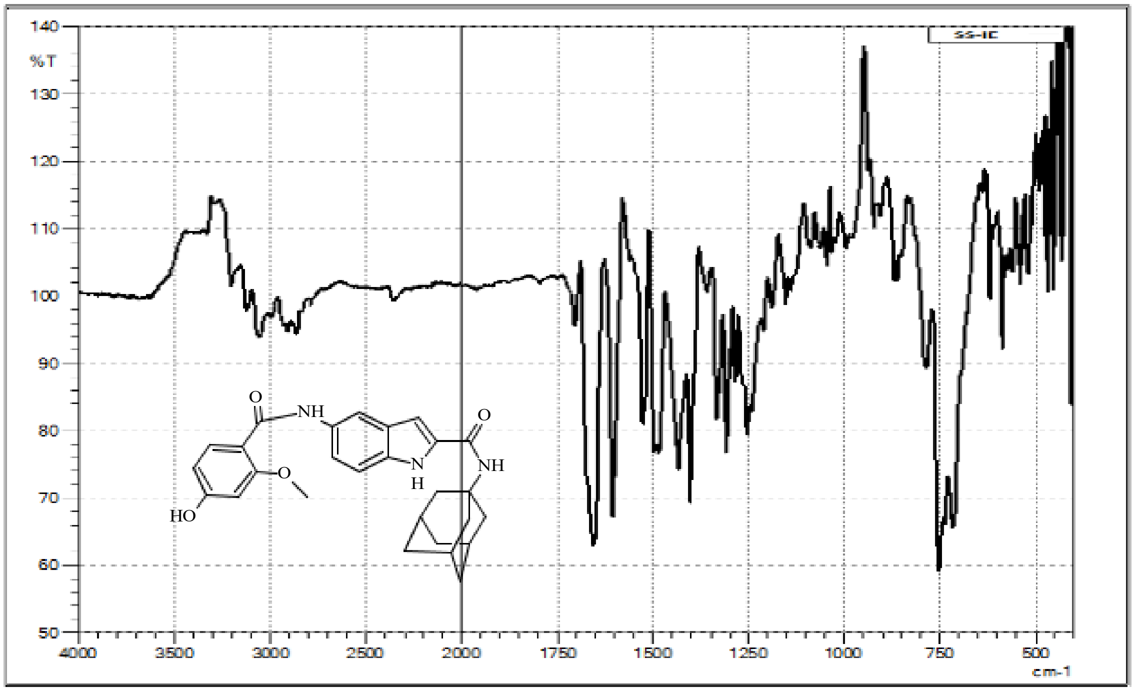


Figure 5.24 FT-IR spectrum of compound SS-IE

Table 5.13: FT-IR of the compound SS-IIE

Sr.No	Wave number (cm^{-1})	Functional group assigned
1	3250	-OH Stretching
2	3100	N-H Stretch of 1^0 amine
3	2940	Aromatic C-H Stretch
4	2710	Aliphatic C-H Stretch

5	1600	C = O Stretch
6	1660	$-OCH_3$ stretch
7	750-850	$-CH_2$, -CHStretch

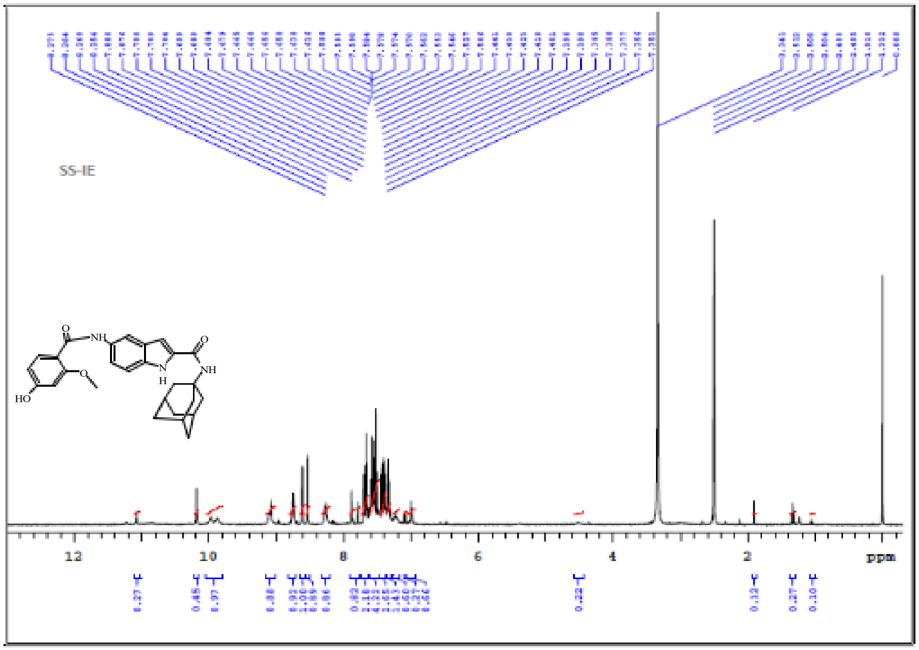


Figure 5.25: H^1 NMR spectrum of compound SS-IE

Table 5.14: H^1 NMR spectrum data of SS-IE

Sl. No	δ Value (ppm)	Peak assigned (Multiplicity)
1	1.0-2.6	-NH (3H)
2	1.9-3.9	$-(CH_3)$ $-(CH_2)_6$, -3CH (18H)
3	6.3-8.8	Ar-H(multiplate)
4	10.1-11.2	-OH (H)

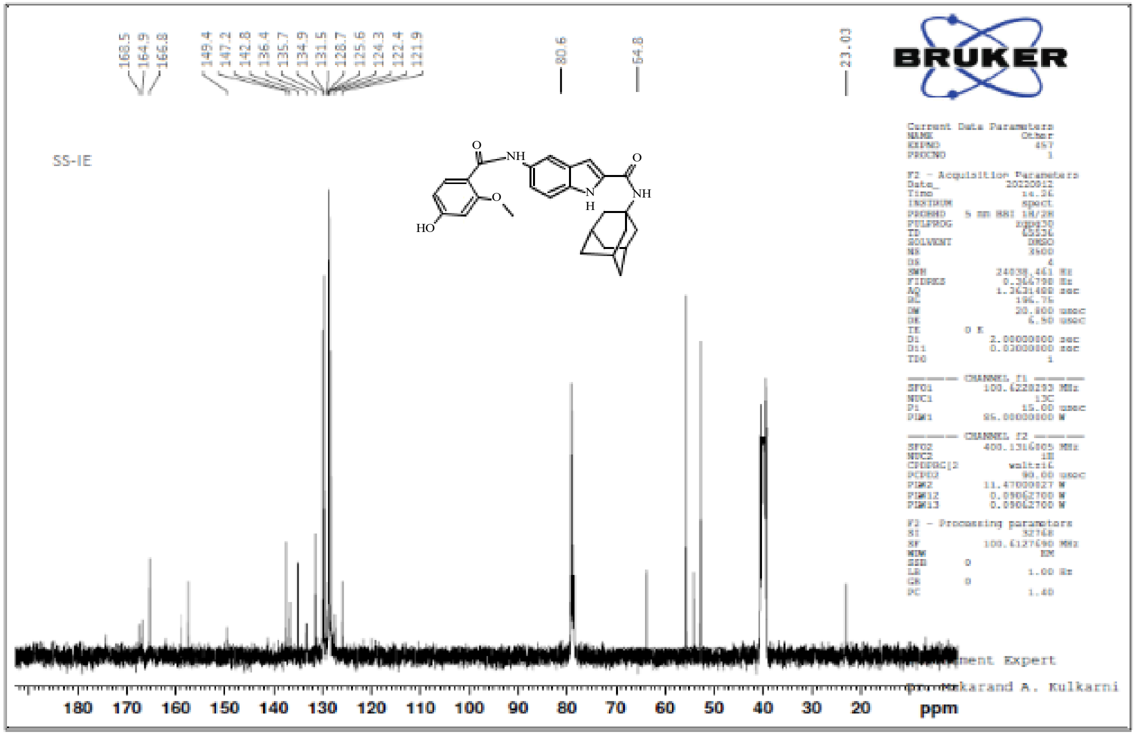


Figure 5.26:^{13}C NMR spectrum of compound SS-IE

Table No 5.15: ^{13}CNMR spectrum data of SS-IE

Sl. No	Carbon's	δ Value (ppm)
1	1C $-CH_3$	21-40
2	10C $-CH_2$, -CH	41-80
3	14C from Aromatic ring	110-148
4	2C from C=O	151-172

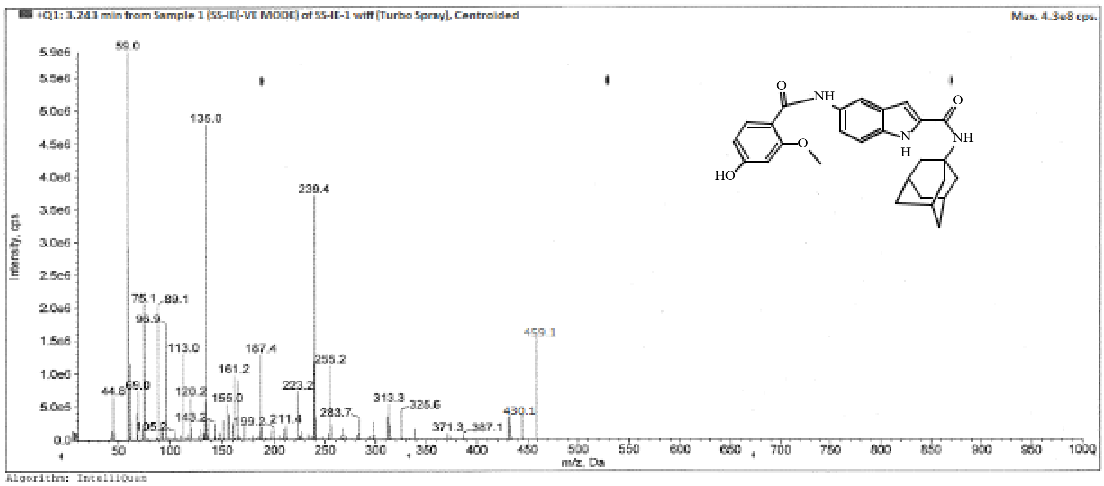


Figure No. 5.27: Mass spectrum of SS-IE

- **M+ Peaks (Mass Peak)at m/z 459 and Base Peak is 430**
- Molecular weight of compound SS-IE is **459.**

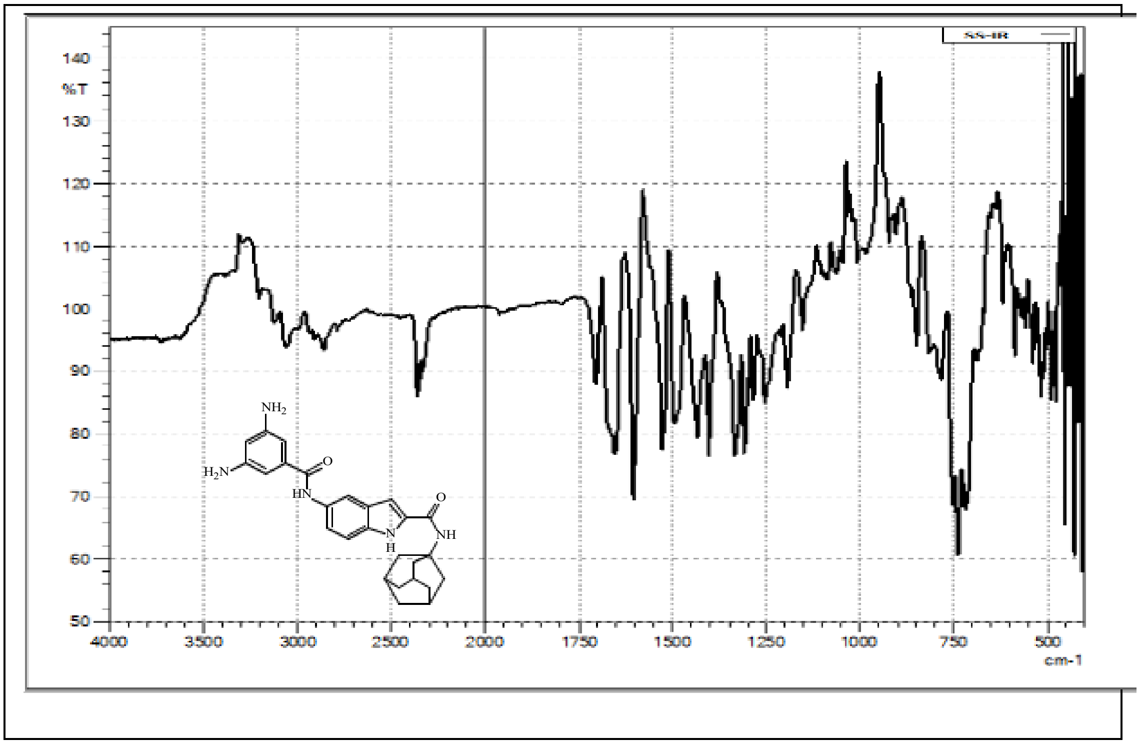


Figure No. 5.28 FT-IR spectrum of compound SS-IR

Table No. 5.16: FT-IR spectrum data of compound SS-IR

Sr.No	Wave number (cm-1)	Functional group assigned
1	3050-3250	N-H Stretch of amine
2	2910	Aromatic C-H Stretch
3	2805	Aliphatic C-H Stretch
4	1545	C = O Stretch
5	735	-CH2, -CH Stretch

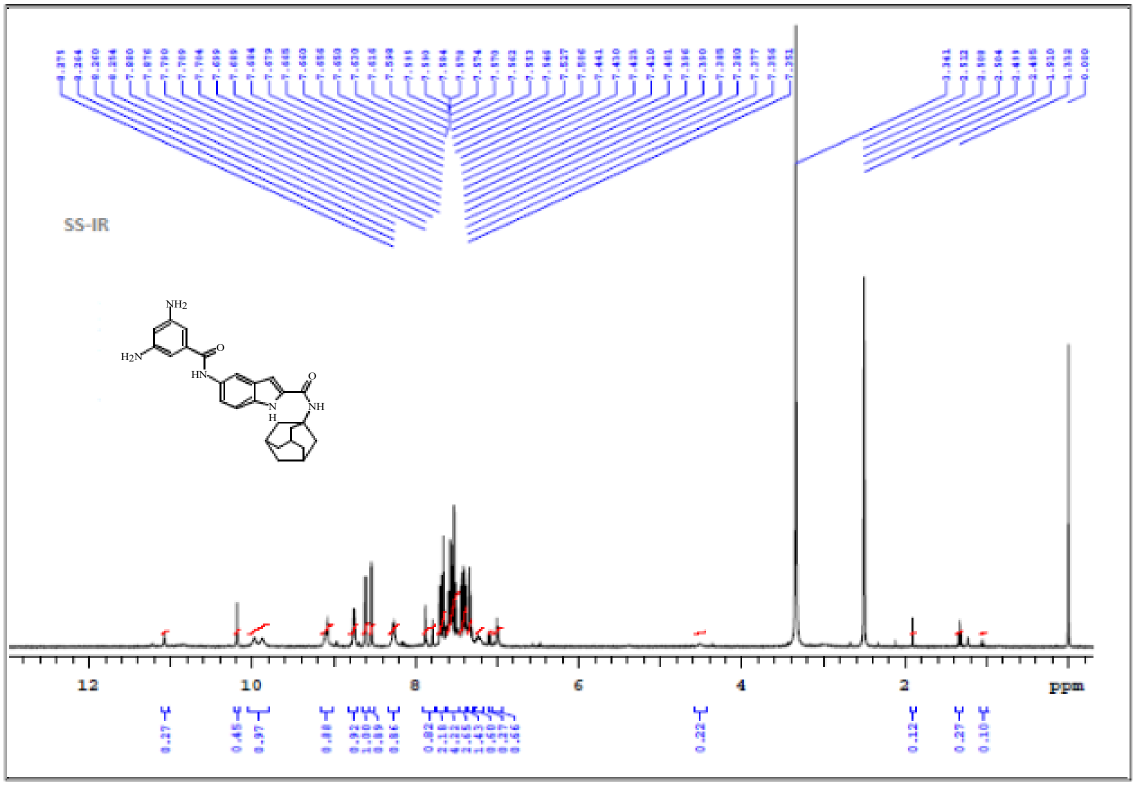


Figure No. 5.29:H[1] NMR spectrum of compound SS-IR

Table No. 5.17: H[1] NMR spectrum data of SS-IR

Sl. No	δ Value (ppm)	Peak assigned (Multiplicity)
1	0.3-1.7	$-(NH_2)_2$ -3NH, (7H)
2	6.9-9.9	-Ar-H(multiplate)
3	1.9-4.8	$-(CH_2)_6$, -3CH(15H)

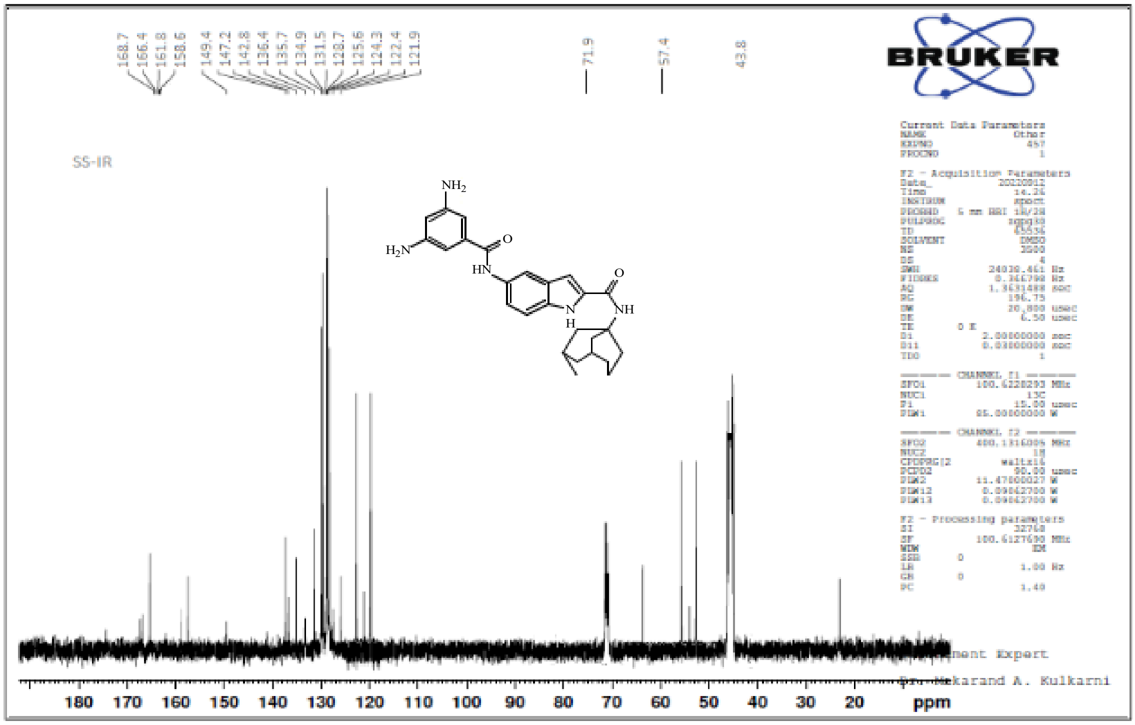


Figure No. 5.30[13]C NMR spectrum of compound SS-IR

Table No. 5.18[13]C NMR spectrum data of compound SS-IR

Sl. No	Carbon's	δ Value (ppm)
1	10C -CH_2, -CH	19-71
3	14C from Aromatic ring	105-140
4	2C from C=O	160-172

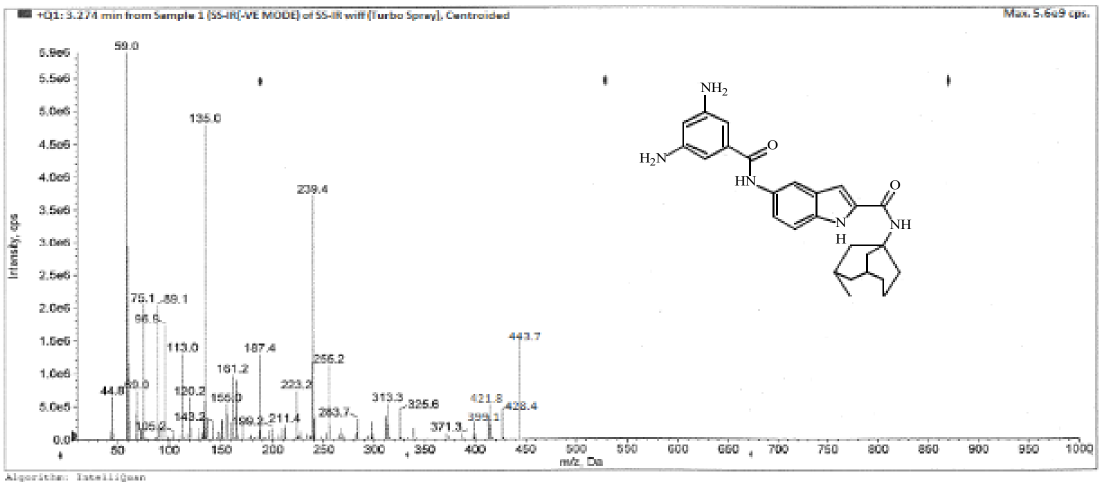


Figure No. 5.31 Mass spectrum of SS-IR

- **M+ Peaks (Mass Peak) at m/z 443.7 and Base Peak is 421.8**
- Molecular weight of compound SS-IRis 443.7.

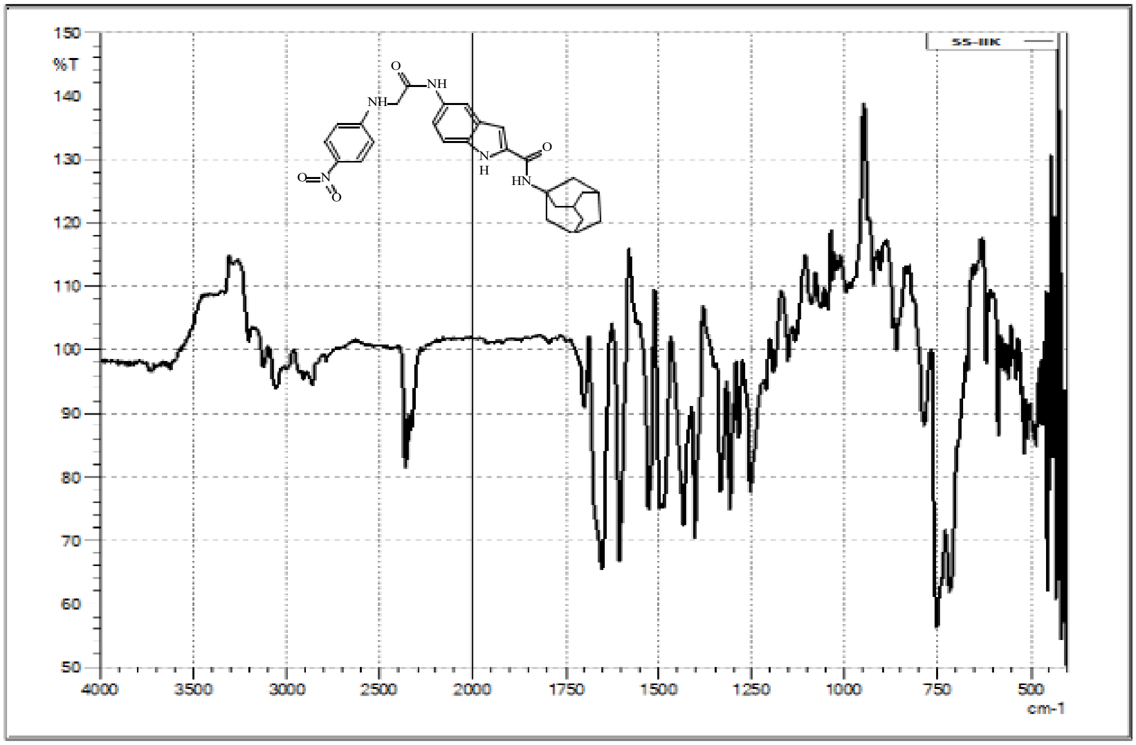


Figure No. 5.32 FT-IR spectrum of compound SS-IIK

Table No. 5.19: FT-IR spectrum data of compound SS-IIK

Sr.No	Wave number (cm^{-1})	Functional group assigned
1	3010-3280	N-H Stretch of amine
2	2850-3000	Aromatic C-H Stretch
3	2810	Aliphatic C-H Stretch
4	1595	C = O Stretch
5	1400	$-NO_2$ stretch
6	750	-CH2, -CH stretch

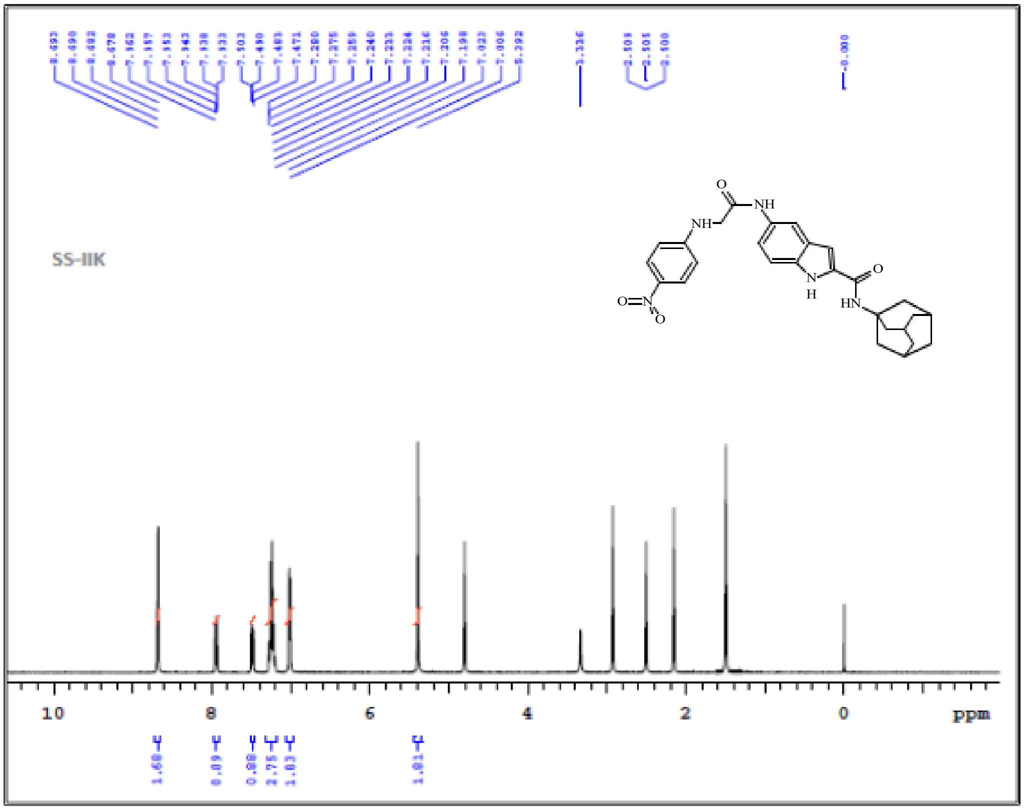


Figure No. 5.33:H[1] NMR spectrum of compound SS-IIK

Table No. 5.20: H[1] NMR spectrum data of SS-IIK

Sl. No	**δ Value (ppm)**	**Peak assigned (Multiplicity)**
1	0.3-2.6 and 4.0-6.0	-NH, (4H)
2	6.9-9.4	-Ar-H(multiplate) (10H)
3	1.9-3.8	$-(CH_2)_6$, .3CH(15H)

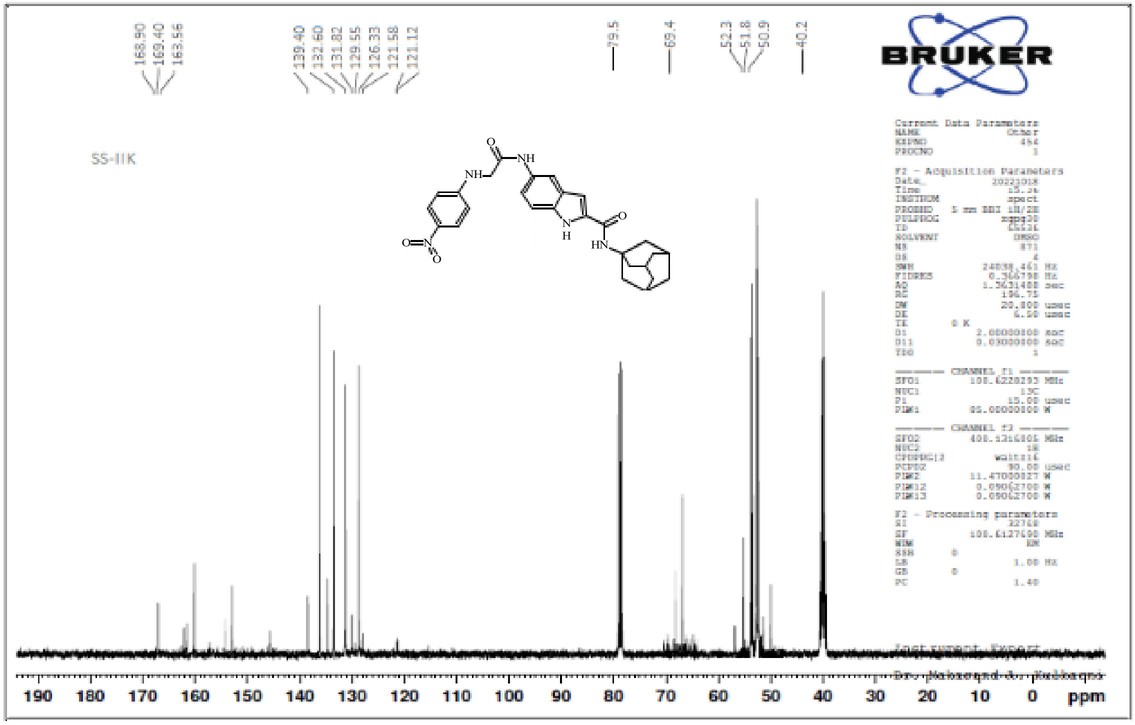


Figure No. 5.34 ^{13}C NMR spectrum of compound SS-IIK

Table No. 5.21 ^{13}C NMR spectrum data of compound SS-IIK

Sl. No	Carbon's	δ Value (ppm)
1	11C -CH_2, -CH	19-79
3	14C from Aromatic ring	115-150
4	2C from C=O	160-172

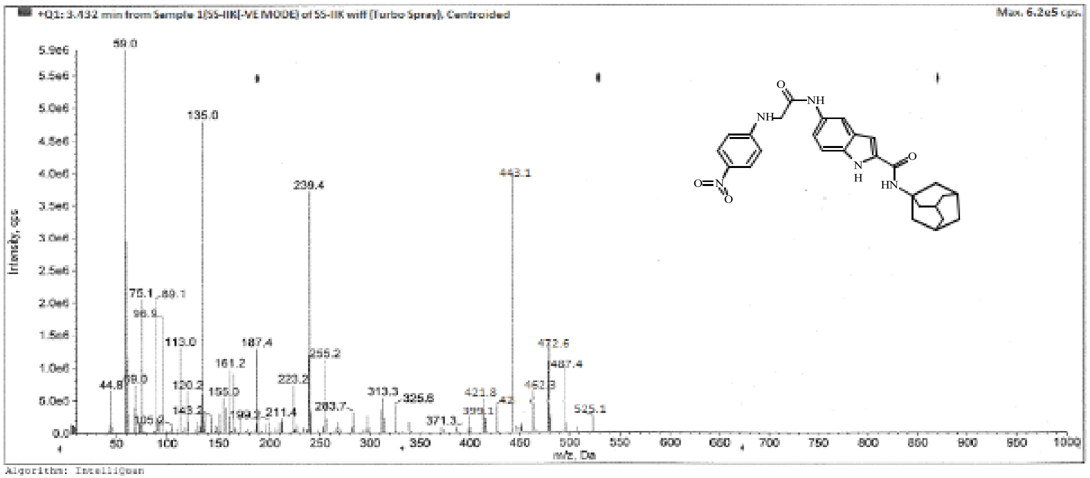


Figure No. 5.35 Mass spectrum of SS-IIK

- **M^+ Peaks (Mass Peak) at m/z 487.4 and Base Peak is 443.1**
- Molecular weight of compound SS-IIKis 487.4.

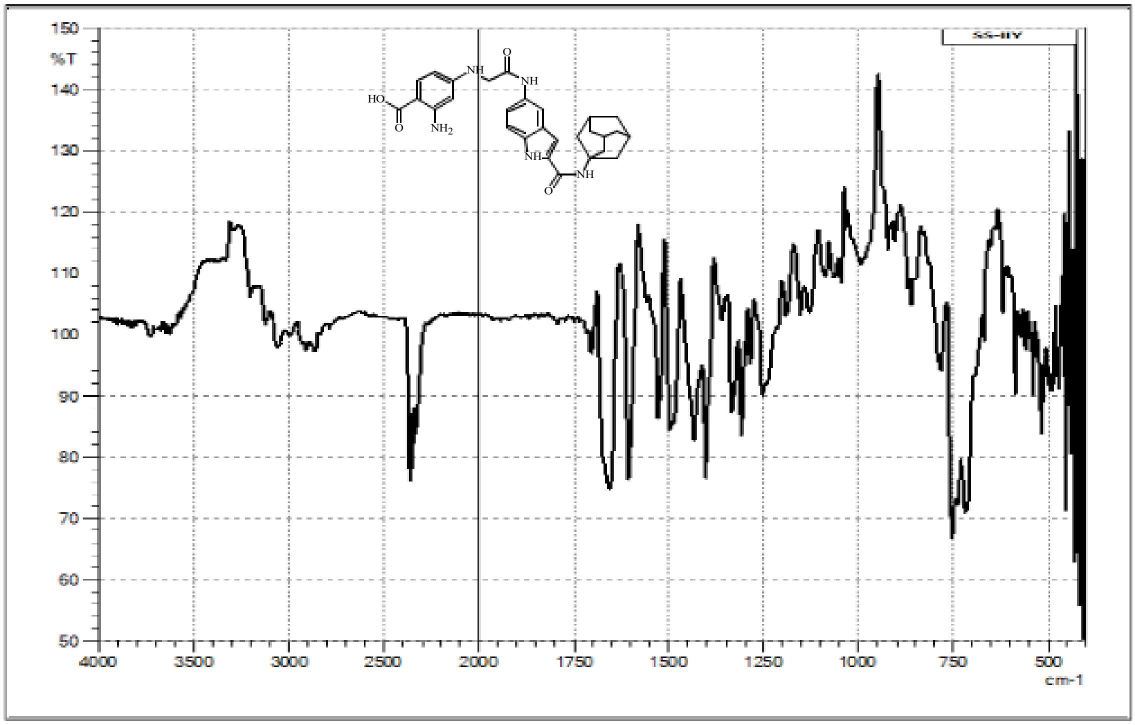


Figure No. 5.36 FT-IR spectrum of compound SS-IIY

Table No. 5.22: FT-IR spectrum data of compound SS-IIY

Sr.No	**Wave number (cm^{-1})**	**Functional group assigned**
1	3010-3100	N-H Stretch of amine
2	2850-3000	Aromatic C-H Stretch
3	2350	Aliphatic C-H Stretch
4	1580	C=O Stretch
5	1675	-COOH stretch
6	750	-CH2, -CH Stretch

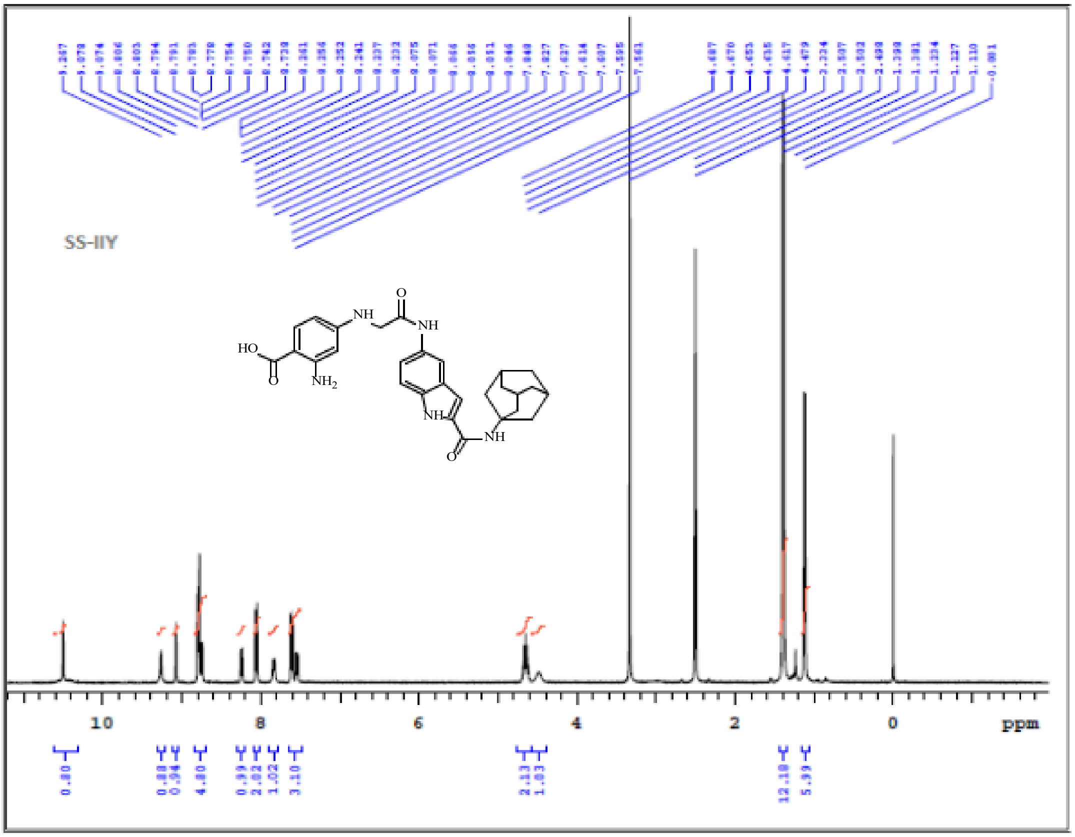


Figure No. 5.37H[1] NMR spectrum of compound SS-IIY

Table No. 5.23 : H[1] NMR spectrum data of SS-IIY

Sl. No	δ Value (ppm)	Peak assigned (Multiplicity)
1	0.3-2.6 and 4.0-6.0	-NH, & NH_2(6H)
2	6.9-9.4	-Ar-H(multiplate) (7H)
3	0.1-2.8	-$(CH_2)_7$, .3CH(17H)
4	10.4	-OH (1H)

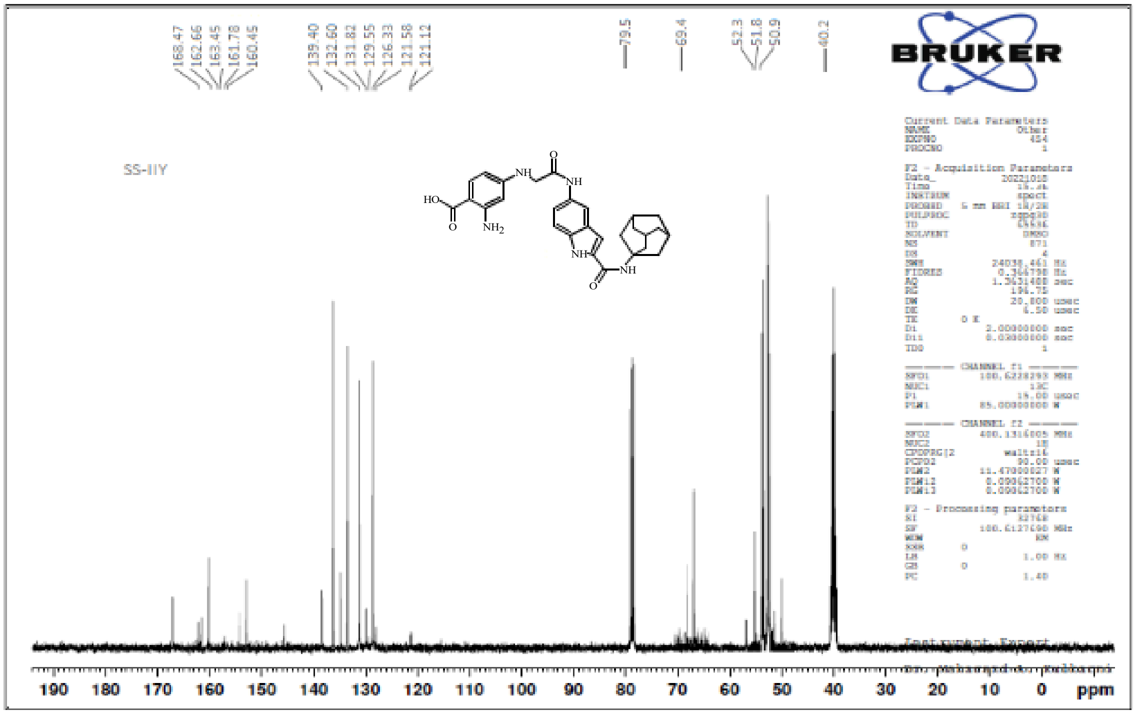


Figure No. 5.38[13]C NMR spectrum of compound SS-IIY

Table No. 5.24[13]C NMR spectrum data of compound SS-IIY

Sl. No	Carbon's	δ Value (ppm)
1	11C $-CH_2$, -CH	19-79
3	14C from Aromatic ring	115-150
4	3C from C=O	160-175

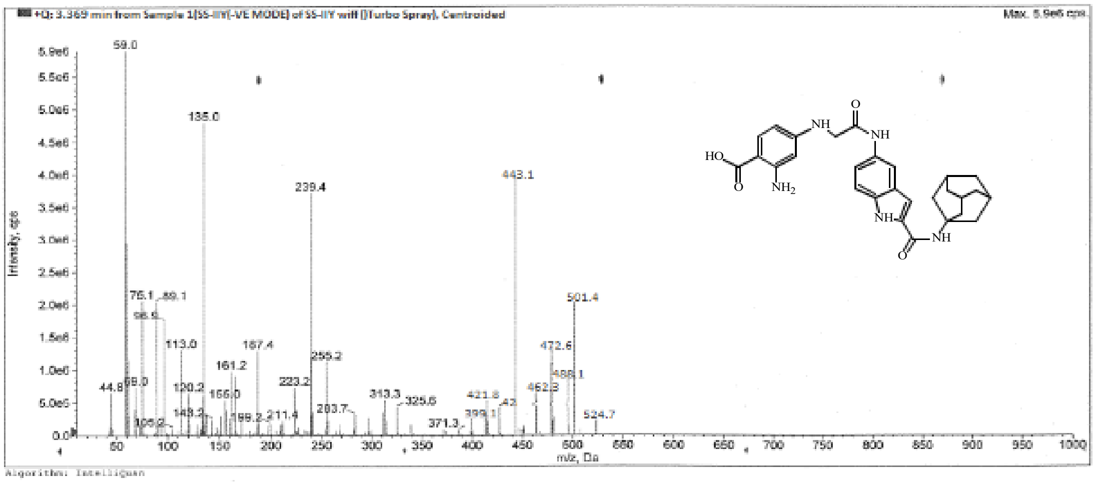


Figure No. 5.39 Mass spectrum of SS-IIY

- **M$^+$ Peaks (Mass Peak) at m/z 501.4 and Base Peak is 443.1**
- Molecular weight of compound SS-IIYis 501.4.

5.5 Drug Likeliness Studies

‘Drug-likeness’, a qualitative property of chemicals assigned by experts committee vote, is widely integrated into the early stages of lead and drug discovery. Its conceptual evolution paralleled work related to Pfizer's ‘rule of five’ and lead-likeness, and is placed within this framework. The discrimination between ‘drugs’ (represented by a collection of pharmaceutically relevant small molecules, some of which are marketed drugs) and ‘nondrugs’ (typically, chemical reagents) is possible using a wide variety of statistical tools and chemical descriptor systems.

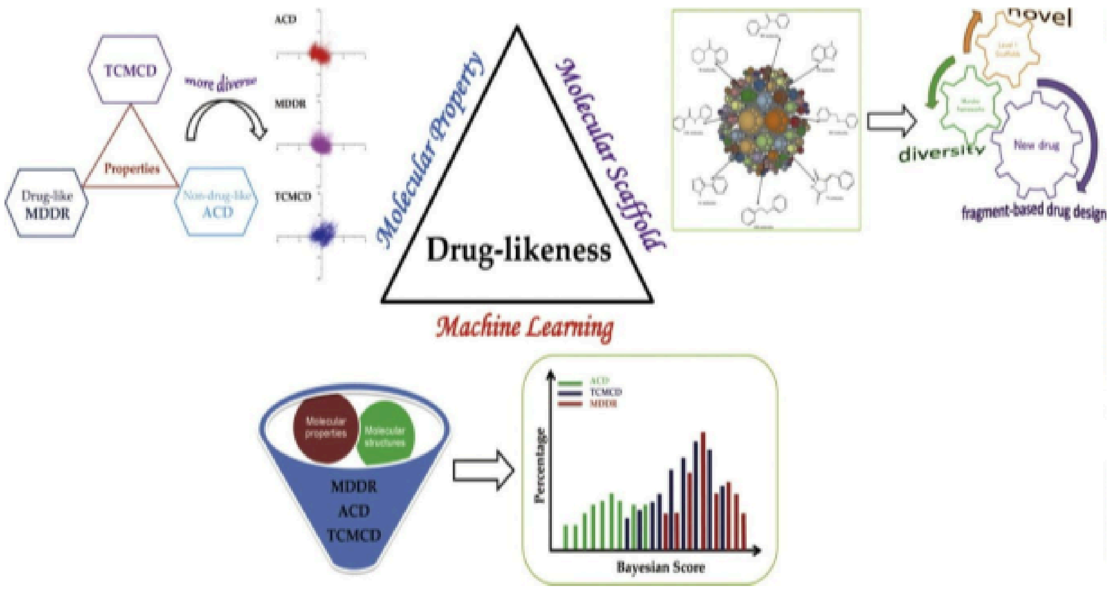


Figure No 5.40: Drug likeliness

Table No 5.25: Drug Likeness Studies

Compounds	Mol_Weight	Logp	Rotatable Bonds	H Bond Acceptors	H Bond Donors	Lipinki's Violations
SS-IA	429.52	4.8244	4	3	4	0
SS-IB	428.536	4.701	4	3	4	0
SS-IC	427.548	5.42722	4	2	3	0
SS-ID	443.547	5.1274	5	3	3	0
SS-IE	459.546	4.833	5	4	4	0
SS-IF	445.519	4.53	4	4	5	0
SS-IG	429.52	4.8244	4	3	4	0
SS-IH	445.51	4.53	4	4	5	0
SS-II	445.51	4.53	4	4	5	0
SS-IJ	443.54	5.1274	5	3	3	0
SS-IK	473.57	5.136	6	4	3	0
SS-IL	458.51	5.027	5	4	3	0

SS-IM	439.55	5.7618	5	2	3	0
SS-IN	441.57	5.6812	5	2	3	0
SS-IO	428.53	4.701	4	3	4	0
SS-IP	458.51	5.027	5	4	3	0
SS-IQ	441.57	5.7356	4	2	3	0
SS-IR	443.55	4.2832	4	4	5	0
SS-IS	482.41	6.4256	4	2	3	0
SS-IT	455.60	6.0713	6	2	3	0
SS-IU	444.53	4.4066	4	4	5	0
SS-IV	488.54	5.0356	6	5	3	0
SS-IW	457.53	4.817	5	3	4	0
SS-IX	441.53	4.9313	5	3	3	0
SS-IY	457.53	4.6369	5	4	4	0
SS-IIA	456.59	5.22552	6	3	4	0
SS-IIB	472.589	4.93112	6	4	5	0
SS-IIC	458.562	4.6227	6	4	5	0
SS-IID	472.589	4.9257	7	4	4	0
SS-IIE	486.616	5.23412	7	4	4	0
SS-IIF	507.034	5.5791	7	4	4	0
SS-IIG	458.562	4.6227	6	4	5	0
SS-IIH	537.458	5.3852	6	4	5	0
SS-III	457.57	4.4993	6	4	5	0
SS-IIJ	457.57	4.4993	6	4	5	0
SS-IIK	487.56	4.8253	7	5	4	0
SS-IIL	487.56	4.8253	7	5	4	0
SS-IIM	472.59	4.0815	6	5	6	0

SS-IIN	532.55	4.7335	8	7	4	1
SS-IIO	468.60	5.5601	7	3	4	0
SS-IIP	460.55	5.0562	6	3	4	0
SS-IIQ	484.6	5.2657	7	4	5	0
SS-IIR	478.54	5.1953	6	3	4	0
SS-IIS	502.61	4.9343	8	5	4	1
SS-IIT	573.89	6.4721	6	3	4	1
SS-IIU	496.53	5.3344	6	3	4	0
SS-IIV	486.57	4.6153	7	4	5	0
SS-IIW	470.57	4.7296	7	4	4	0
SS-IIX	486.57	4.4352	7	5	5	0
SS-IIY	501.58	4.1975	7	5	6	1
5-FU	**325.923**	**6.070**	**4**	**3**	**1**	**0**

5.6 Pharmacokinetic Studies

Pharmacokinetics, derived from the Greek words *pharmakon* (drug) and *kinetikos* (movement), is used to describe the absorption, distribution, metabolism, and excretion of a compound.

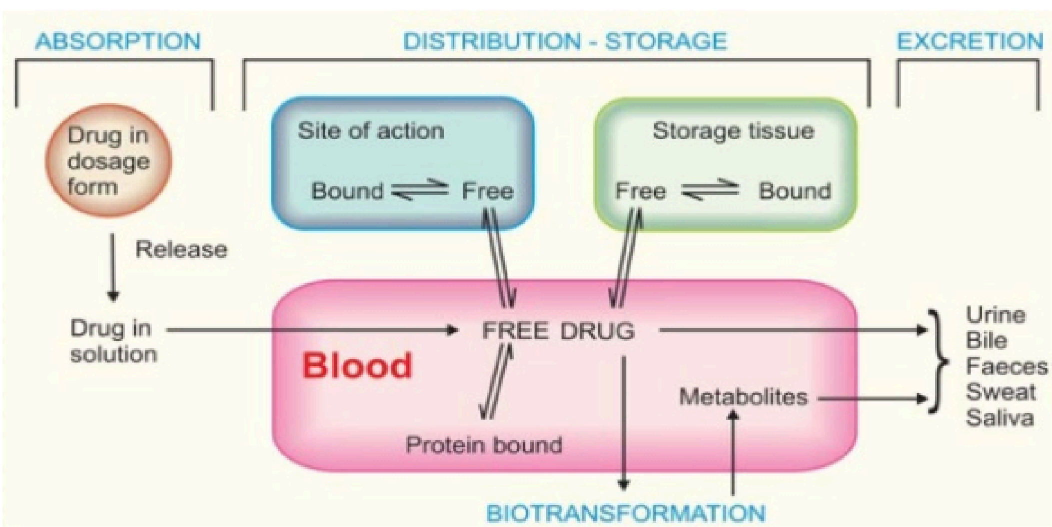


Figure 5.41: Mechanism of Pharmacokinetics

5.6.1 Absorption

When a xenobiotic takes entry inside the bloodstream of the body then this process is termed as the the absorption. Among the all route of administration of a drug, intravenous and oral route is considered as the most accepted one. Intravenous administration of a drug results in the skipping of the absorption directly but in most of the cases oral route is preferred as it is highly desirable for self administration. When a drug is taken orally, first it enters to in the gastrointestinal tract and then goes to the liver through portal circulation and from there it finally enters in the systemic circulation. It is from the systemic circulation from where the drug is travelled to the desired site of action.

Table No 5.26: Drug Absorption properties

Compounds	SURFACE AREA	Water solubility	Caco2 permeability	Intestinal absorption (human)	Skin Permeability	P-glycoprotein substrate	P-glycoprotein I inhibitor	P-glycoprotein II inhibitor
SS-IA	185.95	-3.187	0.898	100	-2.735	Yes	Yes	Yes
SS-IB	186.50	-3.178	0.863	100	-2.735	Yes	Yes	Yes
SS-IC	187.52	-3.751	0.862	92.706	-2.741	Yes	Yes	Yes
SS-ID	192.64	-3.711	0.905	92.856	-2.74	Yes	Yes	Yes
SS-IE	197.43	-3.259	1.018	95.281	-2.736	Yes	Yes	Yes
SS-IF	190.75	-3.002	0.741	90.832	-2.735	Yes	Yes	Yes
SS-IG	185.95	-3.271	1.124	100	-2.736	Yes	Yes	Yes
SS-IH	190.8	-3.57	0.83	96.55	-2.74	Yes	Yes	Yes
SS-II	190.8	-3.58	0.70	96.32	-2.74	Yes	Yes	Yes
SS-IJ	192.6	-4.33	0.77	89.82	-2.74	Yes	Yes	Yes
SS-IK	204.1	-4.46	1.02	100.00	-2.74	Yes	Yes	Yes
SS-IL	195.8	-4.22	0.69	100.00	-2.74	Yes	Yes	Yes
SS-IM	193.2	-4.38	0.66	89.72	-2.75	Yes	Yes	Yes

SS-IN	193.9	-4.37	0.67	89.94	-2.75	Yes	Yes	Yes
SS-IO	186.5	-4.07	0.90	100.00	-2.74	Yes	Yes	Yes
SS-IP	195.8	-4.20	0.67	100.00	-2.74	Yes	Yes	Yes
SS-IQ	193.9	-4.33	0.73	90.25	-2.75	Yes	Yes	Yes
SS-IR	191.8	-3.48	0.68	96.49	-2.74	Yes	Yes	Yes
SS-IS	201.8	-4.38	0.63	87.34	-2.75	Yes	Yes	Yes
SS-IT	200.3	-4.44	0.63	89.61	-2.74	Yes	Yes	Yes
SS-IU	191.3	-3.54	0.79	95.55	-2.74	Yes	Yes	Yes
SS-IV	207.3	-4.42	0.72	100.00	-2.74	Yes	Yes	Yes
SS-IW	196.5	-3.74	1.18	83.43	-2.74	Yes	No	Yes
SS-IX	191.7	-4.22	0.74	89.81	-2.75	Yes	Yes	Yes
SS-IY	196.5	-3.55	0.66	99.99	-2.74	Yes	Yes	Yes
SS-IIA	199.44	-3.279	1.084	92.563	-2.735	Yes	Yes	Yes
SS-IIB	204.23	-3.036	1.121	94.594	-2.735	Yes	Yes	Yes
SS-IIC	197.87	-3.024	1.049	94.124	-2.735	Yes	Yes	Yes
SS-IID	204.55	-3.283	1.199	98.715	-2.736	Yes	Yes	Yes
SS-IIE	210.92	-3.29	1.3	99.183	-2.736	Yes	Yes	Yes
SS-IIF	214.86	-3.287	1.188	99.891	-2.735	Yes	Yes	Yes
SS-IIG	197.87	-2.991	0.954	93.904	-2.735	Yes	Yes	Yes
SS-IIH	211.74	-3.01	0.807	94.913	-2.735	Yes	Yes	Yes
SS-III	198.4	-3.60	0.81	96.65	-2.74	Yes	Yes	Yes
SS-IIJ	198.4	-3.65	0.79	96.58	-2.74	Yes	Yes	Yes
SS-IIK	207.7	-3.75	0.56	100.00	-2.74	Yes	Yes	Yes
SS-IIL	207.7	-3.70	0.58	100.00	-2.74	Yes	Yes	Yes
SS-IIM	203.8	-3.24	0.38	89.47	-2.74	Yes	Yes	Yes
SS-IIN	222.4	-3.78	0.24	97.79	-2.74	Yes	Yes	Yes

SS-IIO	205.1	-3.75	0.86	86.70	-2.74	Yes	Yes	Yes
SS-IIP	197.2	-3.77	0.74	86.35	-2.74	Yes	Yes	Yes
SS-IIQ	209.9	-3.76	1.07	98.68	-2.74	Yes	Yes	Yes
SS-IIR	201.4	-3.89	0.89	86.12	-2.74	Yes	Yes	Yes
SS-IIS	216.0	-3.95	0.98	100.00	-2.74	Yes	Yes	Yes
SS-IIT	221.4	-3.88	0.80	83.67	-2.74	Yes	Yes	Yes
SS-IIU	205.6	-3.89	0.90	85.37	-2.74	Yes	Yes	Yes
SS-IIV	208.4	-3.43	1.03	81.53	-2.74	Yes	No	No
SS-IIW	203.6	-3.72	0.87	100.00	-2.74	Yes	Yes	Yes
SS-IIX	208.4	-3.35	0.59	98.24	-2.74	Yes	Yes	Yes
SS-IIY	213.7	-3.13	0.32	71.54	-2.74	Yes	No	No
5-FU	**171.3**	**-4.97**	**1.23**	**90.15**	**-2.78**	**Yes**	**No**	**No**

5.6.2 Distribution

The travel of the drug molecule from one location or organ to another inside the body is termed as the distribution.

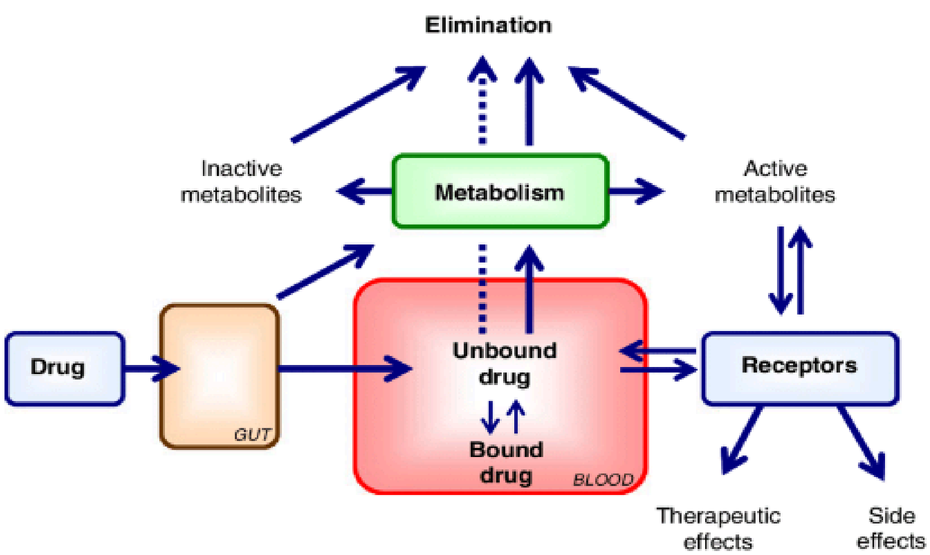


Figure No 5.42: Mechanism of Drug Distribution

Table No 5.27: Drug Distribution Properties

Compounds	VDss (human)	Fraction unbound (human)	BBB permeability	CNS permeability
SS-IA	0.436	0.132	-1.021	-1.894
SS-IB	0.428	0.139	-0.909	-1.864
SS-IC	0.573	0.063	-0.846	-1.627
SS-ID	0.524	0.069	-1.02	-1.869
SS-IE	0.662	0.112	-1.234	-2.044
SS-IF	0.451	0.159	-1.32	-2.138
SS-IG	0.613	0.112	-1.035	-1.888
SS-IH	0.141	0.017	-1.031	-2.134
SS-II	0.144	0.017	-0.944	-2.128
SS-IJ	0.205	0	-0.765	-1.932
SS-IK	0.267	0	-0.947	-2.131
SS-IL	-0.026	0	-0.8	-1.948
SS-IM	0.313	0	-0.61	-1.676
SS-IN	0.313	0	-0.6	-1.693
SS-IO	0.204	0	-0.638	-1.901
SS-IP	0.005	0	-0.806	-1.939
SS-IQ	0.398	0	-0.61	-1.584
SS-IR	0.208	0.042	-0.708	-2.056
SS-IS	0.326	0	-0.917	-1.503
SS-IT	0.32	0	-0.631	-1.706
SS-IU	0.212	0.008	-0.916	-2.119
SS-IV	0	0	-1	-2.168
SS-IW	0.016	0.027	-0.973	-2.094

SS-IX	0.164	0	-0.764	-1.939
SS-IY	0.141	0.002	-0.945	-2.144
SS-IIA	0.584	0.157	-1.088	-1.852
SS-IIB	0.78	0.193	-1.278	-2.04
SS-IIC	0.689	0.195	-1.273	-2.11
SS-IID	0.714	0.126	-1.275	-2.103
SS-IIE	0.712	0.121	-1.287	-2.024
SS-IIF	0.663	0.112	-1.44	-1.983
SS-IIG	0.463	0.251	-1.408	-2.099
SS-IIH	0.434	0.227	-1.605	-1.968
SS-III	0.344	0.033	-0.704	-2.147
SS-IIJ	0.398	0.027	-0.698	-2.161
SS-IIK	0.138	0	-0.868	-2.201
SS-IIL	0.092	0	-0.873	-2.185
SS-IIM	0.352	0.105	-0.91	-2.392
SS-IIN	-0.303	0	-1.086	-2.462
SS-IIO	0.445	0.002	-0.686	-1.918
SS-IIP	0.341	0.011	-0.849	-2.025
SS-IIQ	0.207	0.061	-0.829	-2.078
SS-IIR	0.204	0	-1.032	-2.035
SS-IIS	0.493	0	-0.906	-2.363
SS-IIT	0.221	0	-1.179	-1.751
SS-IIU	0.143	0	-1.235	-2.063
SS-IIV	0.012	0.035	-1.128	-2.431
SS-IIW	0.374	0.019	-0.829	-2.198
SS-IIX	0.205	0.068	-1.087	-2.462

SS-IIY	-0.092	0.049	-1.435	-2.66
5-FU	**0.064**	**0.064**	**0.433**	**-2.797**

5.6.3 Metabolism

The process of making a drug molecule more hydrophilic in nature from its lipophilic profile so that it can be eliminated easily from the body is termed as the metabolism. The process of metabolism or biotransformation is assisted through several enzymes so that it can be easily eliminated. Although metabolism results in the inactive metabolites most of the time, but in certain cases some active metabolites also do produces which contributes to the overall pharmacodynamic profile of the drug.

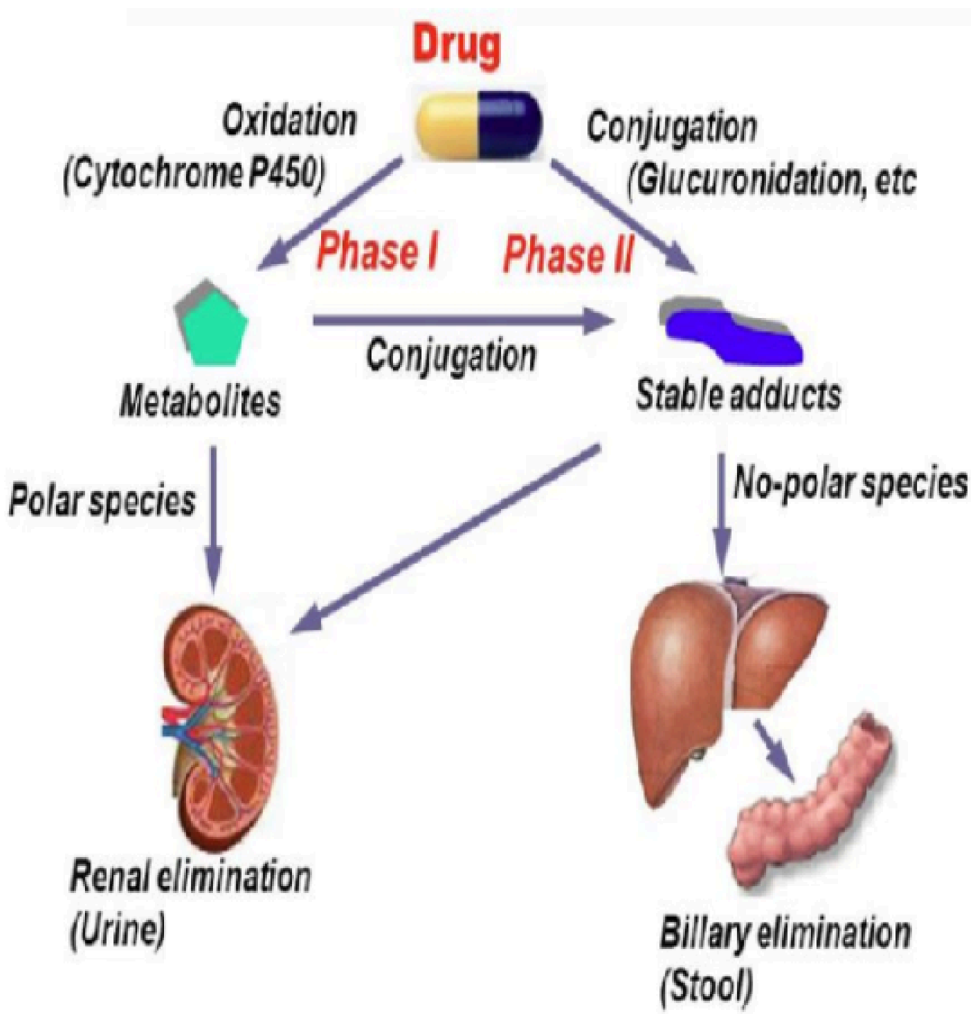


Figure No 5.43: Mechanism of Drug metabolism

Table No 5.28: Drug Metabolism Properties

Compounds	CYP2D6 substrate	CYP3A4 substrate	CYP1A2 inhibitior	CYP2C19 inhibitior	CYP2C9 inhibitior	CYP3A4 inhibitior
SS-IA	Yes	Yes	Yes	Yes	Yes	No
SS-IB	Yes	Yes	Yes	Yes	Yes	No
SS-IC	Yes	Yes	Yes	Yes	Yes	No
SS-ID	Yes	Yes	Yes	Yes	Yes	No
SS-IE	Yes	Yes	Yes	Yes	Yes	No
SS-IF	Yes	Yes	Yes	Yes	Yes	No
SS-IG	Yes	Yes	Yes	Yes	Yes	No
SS-IH	No	Yes	Yes	Yes	Yes	Yes
SS-II	No	Yes	Yes	Yes	Yes	No
SS-IJ	Yes	Yes	Yes	Yes	Yes	Yes
SS-IK	No	Yes	No	Yes	Yes	Yes
SS-IL	No	Yes	Yes	Yes	Yes	Yes
SS-IM	Yes	Yes	Yes	Yes	Yes	Yes
SS-IN	Yes	Yes	Yes	Yes	Yes	Yes
SS-IO	Yes	Yes	Yes	Yes	Yes	Yes
SS-IP	No	Yes	Yes	Yes	Yes	Yes
SS-IQ	Yes	Yes	Yes	Yes	Yes	Yes
SS-IR	No	Yes	Yes	Yes	Yes	Yes
SS-IS	Yes	Yes	Yes	Yes	Yes	Yes
SS-IT	Yes	Yes	No	Yes	Yes	Yes
SS-IU	No	Yes	Yes	Yes	Yes	Yes
SS-IV	No	Yes	No	Yes	Yes	Yes
SS-IW	Yes	Yes	Yes	No	Yes	No

SS-IX	Yes	Yes	Yes	Yes	Yes	Yes
SS-IY	No	Yes	Yes	Yes	Yes	Yes
SS-IIA	Yes	Yes	Yes	Yes	Yes	No
SS-IIB	Yes	Yes	No	Yes	Yes	No
SS-IIC	Yes	Yes	No	Yes	Yes	No
SS-IID	Yes	Yes	No	Yes	Yes	No
SS-IIE	Yes	Yes	No	Yes	Yes	No
SS-IIF	Yes	Yes	No	Yes	Yes	No
SS-IIG	Yes	Yes	No	Yes	Yes	No
SS-IIH	Yes	Yes	No	Yes	Yes	No
SS-III	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIJ	Yes	Yes	No	Yes	Yes	Yes
SS-IIK	No	Yes	No	Yes	Yes	Yes
SS-IIL	No	Yes	Yes	Yes	Yes	Yes
SS-IIM	Yes	Yes	No	Yes	Yes	Yes
SS-IIN	No	Yes	Yes	Yes	Yes	Yes
SS-IIO	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIP	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIQ	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIR	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIS	No	Yes	No	Yes	Yes	Yes
SS-IIT	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIU	Yes	Yes	Yes	Yes	Yes	Yes
SS-IIV	Yes	Yes	No	No	Yes	No
SS-IIW	Yes	Yes	No	Yes	Yes	Yes
SS-IIX	Yes	Yes	No	Yes	Yes	Yes

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SS-IIY	Yes	Yes	No	No	Yes	No
5-FU	**No**	**No**	**No**	**No**	**No**	**No**

5.6.4 Excretion

When any xenobiotic is eliminated completely from the body it is called as the process of excretion. Excretion or elimination of any drug molecule or its metabolite is the ultimate fate of the drug after administration. Knowing the excretion route of any drug molecule is an important factor for knowing the pharmacodynamic of the xenobiotic. Although kidney and liver are two most important sites of drug elimination but it can also be eliminated through the skin, sweat, tear or breath.

Table No 5.29: Drug Excretion Properties

Compounds	Total Clearance (log mL/min/kg)	Renal OCT2 substrate
SS-IA	-0.228	No
SS-IB	-0.27	No
SS-IC	-0.143	No
SS-ID	-0.13	No
SS-IE	-0.273	No
SS-IF	-0.368	No
SS-IG	-0.214	No
SS-IH	-0.336	No
SS-II	-0.368	No
SS-IJ	-0.213	No
SS-IK	-0.238	No
SS-IL	-0.307	No
SS-IM	-0.203	No
SS-IN	-0.149	No
SS-IO	-0.28	No
SS-IP	-0.303	No

SS-IQ	-0.273	No
SS-IR	-0.455	No
SS-IS	-0.747	No
SS-IT	-0.154	No
SS-IU	-0.413	No
SS-IV	-0.38	No
SS-IW	-0.313	No
SS-IX	-0.232	No
SS-IY	-0.362	No
SS-IIA	-0.21	Yes
SS-IIB	-0.336	No
SS-IIC	-0.258	No
SS-IID	-0.167	No
SS-IIE	-0.241	No
SS-IIF	-0.25	No
SS-IIG	-0.271	No
SS-IIH	-0.555	No
SS-III	-0.319	No
SS-IIJ	-0.328	No
SS-IIK	-0.352	No
SS-IIL	-0.356	No
SS-IIM	-0.504	No
SS-IIN	-0.505	No
SS-IIO	-0.252	No
SS-IIP	-0.309	No
SS-IIQ	-0.328	No

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SS-IIR	-0.407	No
SS-IIS	-0.28	No
SS-IIT	-0.582	No
SS-IIU	-0.557	No
SS-IIV	-0.36	No
SS-IIW	-0.258	No
SS-IIX	-0.407	No
SS-IIY	-0.527	No
5-FU	**-0.162**	**No**

5.6.5 Toxicity Studies

Toxicity study is the investigation of either short or long-term toxic effects of a drug or chemical on animals. The toxicity is dose-dependent as asserted by Paracelsus over 500 years ago. However, short-term toxic effect is determined using median lethal dose (LD50) first introduced by Trevan in 1927 and revised many times. Toxicology studies are used to characterize the toxicity profile of a drug by identifying its impact on organ structure and / or functionality. This includes assessment of the severity and reversibility of toxicity, as well as dose ranges and their relationship to exposure.

Table No 5.30: Drug Toxicity Studies

Compounds	**AMES toxicity**	**Max. tolerated dose (human)**	**hERG I inhibitor**	**hERG II inhibitor**	**Oral Rat Acute Toxicity (LD50)**	**Oral Rat Chronic Toxicity (LOAEL)**	**Hepatotoxicity**	**Skin Sensitisation**	**<i>T.Pyriformis</i> toxicity**	**Minnow toxicity**
SS-IA	No	0.09	No	Yes	2.564	1.628	Yes	No	0.287	0.63
SS-IB	No	0.106	No	Yes	2.418	1.715	Yes	No	0.286	0.833
SS-IC	No	-0.192	No	Yes	2.62	1.296	Yes	No	0.296	0.504
SS-ID	No	-0.256	No	Yes	2.662	1.192	Yes	No	0.294	0.227
SS-IE	No	-0.071	No	Yes	2.374	1.12	Yes	No	0.287	0.871

SS-IF	No	0.38	No	Yes	2.41	1.616	Yes	No	0.286	1.274
SS-IG	No	-0.065	No	Yes	2.349	1.505	Yes	No	0.288	1.283
SS-IH	No	0.155	No	Yes	2.429	1.797	Yes	No	0.287	-0.931
SS-II	No	0.121	No	Yes	2.431	1.865	Yes	No	0.287	-0.437
SS-IJ	No	-0.143	No	Yes	2.21	1.649	Yes	No	0.289	-1.666
SS-IK	No	-0.216	No	Yes	2.274	1.419	Yes	No	0.288	-1.944
SS-IL	Yes	-0.204	No	Yes	2.789	2.426	Yes	No	0.287	-1.502
SS-IM	No	-0.089	No	Yes	2.254	1.752	Yes	No	0.29	-1.677
SS-IN	No	-0.092	No	Yes	2.254	1.764	Yes	No	0.29	-1.68
SS-IO	Yes	-0.1	No	Yes	2.523	2.166	Yes	No	0.287	-0.868
SS-IP	Yes	-0.204	No	Yes	2.805	2.606	Yes	No	0.287	-1.507
SS-IQ	No	-0.085	No	Yes	2.288	1.688	Yes	No	0.291	-1.55
SS-IR	Yes	0.143	No	Yes	2.437	2.109	Yes	No	0.286	-0.165
SS-IS	No	-0.047	No	Yes	2.25	1.781	Yes	No	0.291	-1.985
SS-IT	No	-0.09	No	Yes	2.262	1.75	Yes	No	0.289	-1.914
SS-IU	No	0.154	No	Yes	2.4	1.993	Yes	No	0.286	-0.802
SS-IV	No	-0.283	No	Yes	2.776	2.341	Yes	No	0.286	-1.815
SS-IW	No	0.314	No	Yes	2.024	1.878	Yes	No	0.286	-0.659
SS-IX	No	-0.105	No	Yes	2.211	1.84	Yes	No	0.291	-1.113
SS-IY	No	-0.041	No	Yes	2.549	1.87	Yes	No	0.287	-0.584
SS-IIA	No	-0.047	No	Yes	2.434	1.53	Yes	No	0.288	-0.052
SS-IIB	No	0.067	No	Yes	2.245	1.753	Yes	No	0.286	0.233
SS-IIC	No	0.083	No	Yes	2.178	1.857	Yes	No	0.285	0.941
SS-IID	No	-0.157	No	Yes	2.398	1.462	Yes	No	0.287	0.212
SS-IIE	No	-0.144	No	Yes	2.387	1.342	Yes	No	0.287	0.399
SS-IIF	No	-0.119	No	Yes	2.37	1.389	Yes	No	0.287	0.181
SS-IIG	No	0.197	No	Yes	2.422	1.927	Yes	No	0.285	0.815
SS-IIH	No	0.193	No	Yes	2.42	1.844	Yes	No	0.285	0.426
SS-III	No	-0.166	No	Yes	2.498	2.404	Yes	No	0.286	-0.364
SS-IIJ	No	-0.185	No	Yes	2.499	2.258	Yes	No	0.286	0.096
SS-IIK	Yes	-0.196	No	Yes	3.218	2.696	Yes	No	0.286	-0.413
SS-IIL	Yes	-0.175	No	Yes	3.163	2.844	Yes	No	0.286	-1.003
SS-IIM	No	0.187	No	Yes	2.523	2.438	Yes	No	0.285	1.455
SS-IIN	Yes	-0.073	No	Yes	2.735	3.129	Yes	No	0.285	-0.498
SS-IIO	No	-0.194	No	Yes	2.493	2.175	Yes	No	0.287	-1.052
SS-IIP	No	-0.216	No	Yes	2.44	2.157	Yes	No	0.289	-0.242
SS-IIQ	No	-0.08	No	Yes	2.318	1.915	Yes	No	0.286	0.033
SS-IIR	No	-0.235	No	Yes	2.354	1.756	Yes	No	0.287	-0.535
SS-IIS	No	-0.152	No	Yes	2.384	1.998	Yes	No	0.286	-1.07
SS-IIT	No	-0.209	No	Yes	2.391	1.59	No	No	0.287	-1.337
SS-IIU	No	-0.213	No	Yes	2.344	1.523	Yes	No	0.287	-0.504
SS-IIV	No	0.274	No	Yes	2.201	2.334	Yes	No	0.286	0.797
SS-IIW	No	-0.223	No	Yes	2.442	2.119	Yes	No	0.288	-0.227

SS-IIX	No	0.12	No	Yes	2.71	2.241	Yes	No	0.286	0.876
SS-IIY	No	0.541	No	Yes	2.426	2.425	Yes	No	0.285	2.066
5-FU	No	0.275	No	No	2.08	2.043	Yes	No	0.279	1.226

However, the study showed that all the compounds synthesized are potential for theanticancer activity and can be selected based on further *in-vitro* and *in-vivo* activitystudies.

5.7 Biological evaluation

The synthesized indole derivatives were further evaluated for their biological potential against the antimicrobial and anti-cancer activities.

5.7.1 Antibaterial activity

The antibacterial activity results of the synthesized compounds are given in the table 5.27.

Table 5.31: The zone of inhibition antibacterial activity of Indole derivatives (Against Bacteria)Note: -Standard(S) = CiprofloxacinControl (C) = DMF Note: - 0-15 mm poor activity, 15-25 mm moderate activity, 25above good.

CompoundCode	***Escherichia coli*(gram-ve)**			***Staphylococcus Aureus* (gram+ve)**		
	Concentrationofderivatives (µg/ml)			**Concentrationofderivatives (µg/ml)**		
	250	**500**	**750**	**250**	**500**	**750**
	MeanzoneofInhibition(mm)					
SS-ID	13	15	16	12	14	15
SS-IE	12	15	16	11	15	16
SS-IH	**15**	**16**	**19**	**14**	**19**	**21**

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SS-IN 12 16 18 13 15 16
SS-IO 11 17 18 11 13 15
SS-IR 13 16 20 13 18 21
SS-IS 10 15 16 10 13 15
SS-IU 12 15 16 09 12 14
SS-IV 10 15 15 10 13 16
SS-IX 11 16 17 11 14 15
SS-IY 12 14 15 13 13 13
SS-III 13 17 20 14 18 22
SS-IIK 12 14 16 12 15 16
SS-IIU 14 15 16 13 15 15
SS-IIY 12 15 17 11 14 15
Chloramphenicol
(100mcg/ml)
25 26

Fig No. 5.44: Zone of inhibition of antibacterial activity of Indole derivatives against

bacteria.

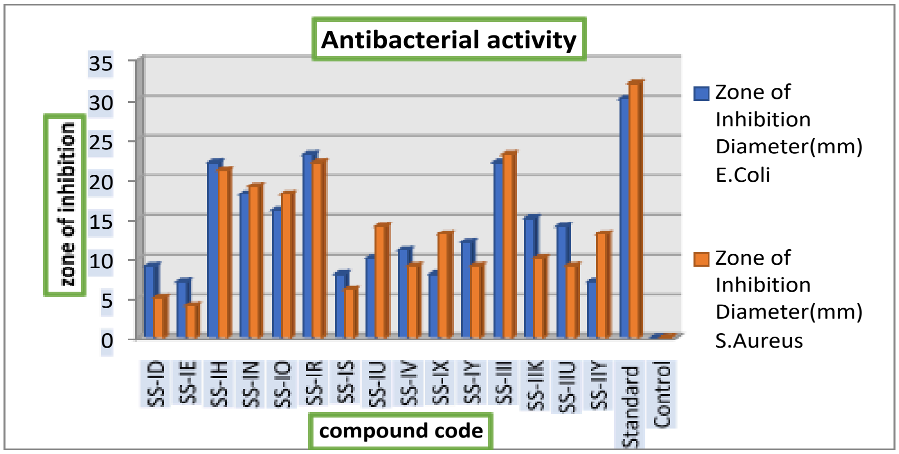
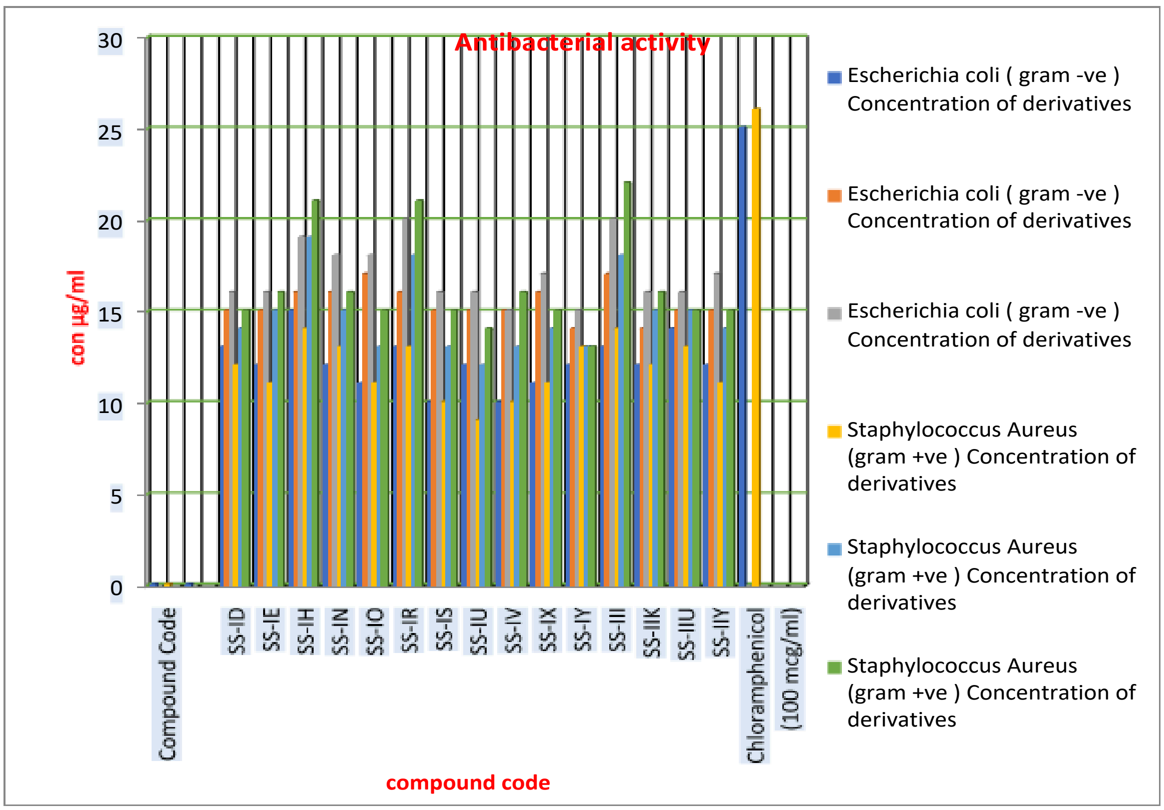


Figure No. 5.45: Zone of inhibition of antibacterial activity of Indole derivatives against *bacteria.*



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FigureNo.5.46:AntibacterialActivityofsynthesized Indole derivatives.

5.7.2 Anti-fungal activity

The zone of inhibition was determined by the cup plate method. Ketoconazole was employed during the test procedures as references. Zone of inhibition of the synthesized compounds ranges between 100µg/ml. SS-IH, SS-IR and SS-III was found moderately active, while SS-IN were found to have an average activity compared with standard. Test compounds were found to be more sensitive towards *Aspergillus niger and Candida albicans.*

Table No. 5.32: Zone of inhibition of antifungal activity of Indole derivatives (Against Fungi) Note: -Standard(S) = Ketoconazole Control (C) = DMF

Note: - 0-15 mm poor activity, 15-25 mm moderate activity, 25above good.

Sl. No.	**Product Code**	**Zone of Inhibition Diameter(mm)**	
		C. Albicans	***A. Niger***
1	**SS-ID**	13	11
2	**SS-IE**	11	10
3	**SS-IH**	20	22
4	**SS-IN**	18	19
5	**SS-IO**	23	20
6	**SS-IR**	22	21
7	**SS-IS**	07	09
8	**SS-IU**	08	12
9	**SS-IV**	10	09
10	**SS-IX**	14	13
11	**SS-IY**	13	12

12	**SS-III**	22	22
13	**SS-IIK**	18	19
14	**SS-IIU**	15	20
15	**SS-IIY**	14	17
16	Standard	35	33
17	Control	-----	-----

Fig No. 5.47: Zone of inhibition of antifungal activity of Indole derivatives against *fungus*.

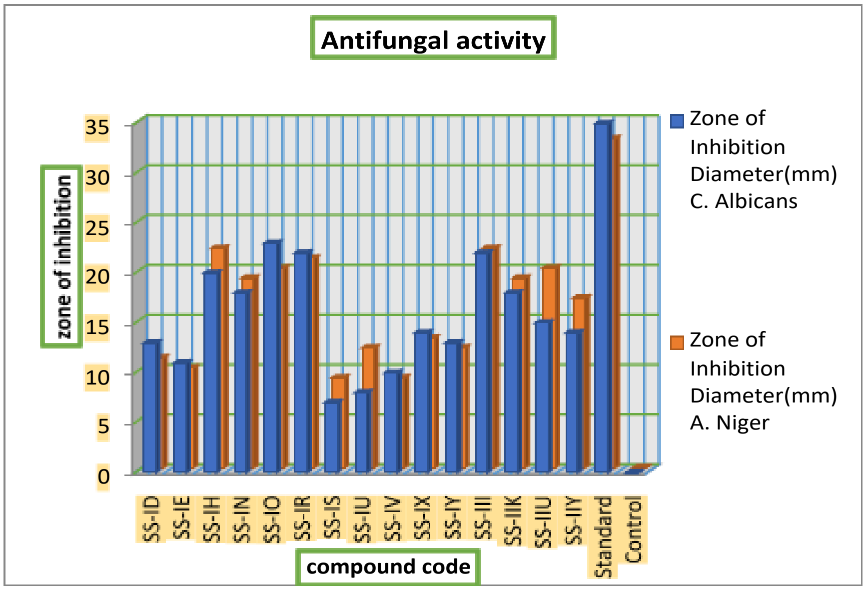

Figure No. 5.48: Zone of inhibition of antifungal activity of Indole derivatives against *Fungi*.

5.7.3 In-vitro cytotoxicity activity

The synthesized compounds were further screened for their in-vitro anticancer potential against various cell lines and the result of the same is given below:

Table 5.33: The anti-cancer activity of the synthesized compounds against various cell lines.

Indole Derivatives	**Cancer cell lines**							
	HeLa	**MDA-MB-231**	**MCF-7**	**A549**	**HEK-293**	**WEHI-164**	**L929**	**MCF-12A**
SS-ID	84.12	110.12	135.60	210.45	341.05	98.45	110.4	235.45
SS-IE	90.41	105.60	124.53	185.60	355.60	86.45	124.3	281.60
SS-IH	**78.45**	**83.45**	**68.45**	**120.61**	**220.45**	**55.43**	**79.62**	**140.56**
SS-IN	95.41	108.57	124.30	167.85	325.67	79.45	142.8	287.95

SS-IO	86.43	112.50	118.90	184.93	374.80	90.23	128.3	310.45
SS-IR	79.85	120.46	123.75	178.65	330.55	110.31	134.6	300.18
SS-IS	83.60	98.45	114.80	180.50	338.75	108.45	139.5	312.64
SS-IU	91.55	135.46	150.35	198.45	350.60	114.68	129.7	289.46
SS-IV	89.70	140.52	124.75	210.30	312.14	97.65	119.5	294.67
SS-IX	88.55	127.89	120.46	225.45	345.89	85.42	115.7	290.82
SS-IY	94.60	145.53	137.60	278.89	370.25	80.45	108.7	260.85
SS-III	84.23	115.60	122.45	190.52	289.65	90.65	114.6	284.65
SS-IIK	**70.45**	**84.75**	**88.65**	**126.40**	**190.75**	**70.86**	**80.65**	**140.55**
SS-IIU	**72.60**	**83.65**	**80.73**	**119.70**	**210.56**	**74.95**	**85.90**	**124.65**
SS-IIY	80.73	106.75	102.48	188.45	170.60	97.45	118.5	225.65
5-fluro uracil	18.60	19.45	40.75	64.32	98.35	40.45	23.45	60.75
Doxorubicin	19.45	20.06	55.67	59.76	65.84	35.60	30.95	84.20

The cytotoxic effect of indole derivatives were assessed based on the minimum concentration that giving at least 50% of the cancer cell survivability (IC50). The four categories of indole derivatives which are; very active (IC50 ≤ 20 μg/mL), moderately active (IC50 > 20–100 μg/mL), weakly active (IC50 > 100–1000 μg/mL) and inactive (IC50 > 1000 μg/mL) for pure compound or drug, IC50 value less than 4 μg/mL is considered potent.

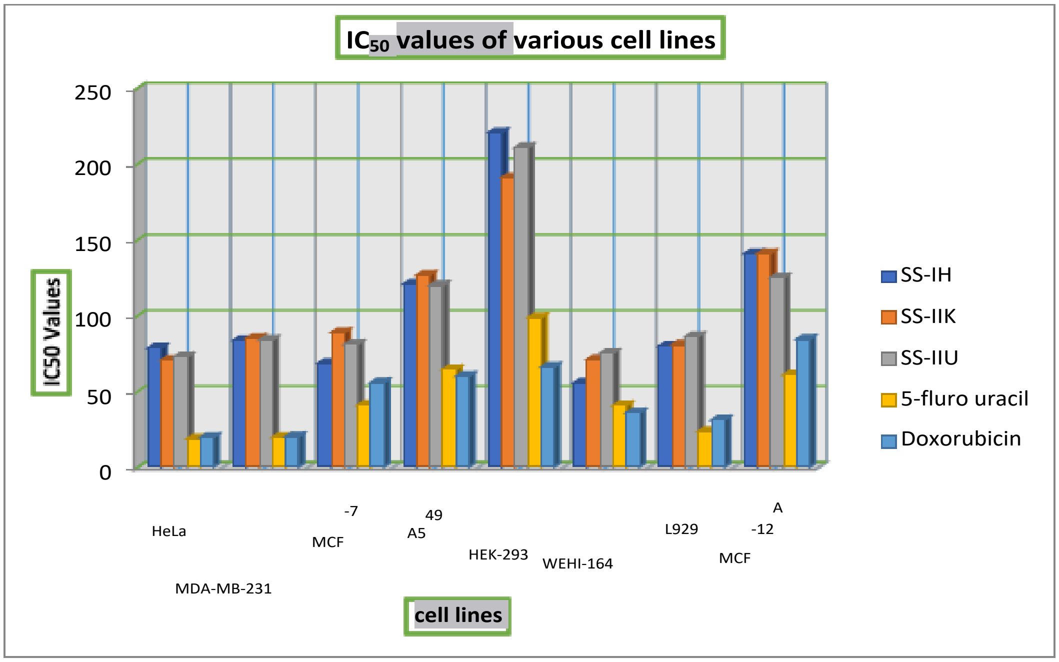

Figure No. 5.49: IC$_{50}$ values of various cell lines

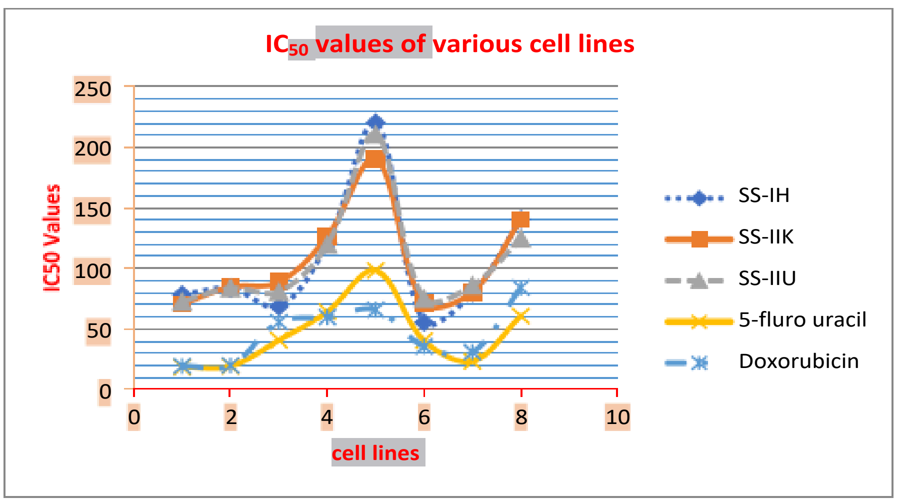

Figure No. 5.50: IC$_{50}$ values of various cell lines

Figure No 5.51: MDA-MB-231 cell line at 500µg/ml

Figure No 5.52: MCF-7 cell line at 500µg/ml

Cytotoxicity of the synthesized compounds was assessed on the basis of the measurement of the in vitro growth in the 96 well microtitre plates by cell-mediated reduction of tetrazolium salt to water insoluble formazan crystals by a previously described method. Cell lines for testing in vitro cytotoxicity included HeLa, MDA-MB-231, MCF-7, A549, HEK-293, WEHI-164, L929, and MCF-12A cell lines.

The Indole derivatives SS-IH has shown good cytotoxicity against MDA-MB-231 and MCF-7 (human breast adenocarcinoma cells), WEHI-164, L929, and MCF-12A cell lines The mouse fibrosarcoma cell line (WEHI-164), mouse nonmalignant cell line (L929), and MCF-12A cell lines (Michigan Cancer Foundation-12A, both estrogen receptor-positive and progesterone receptor-positive). SS-IIK has shown good cytotoxicity against HeLa (cervical cancer cells), HEK-293 (normal human embryonic kidney cells). SS-IIU has shown good cytotoxicity against A549 (human alveolar adenocarcinoma cells), MCF-12A cell lines (Michigan Cancer Foundation-12A, both estrogen receptor-positive and progesterone

receptor-positive). The synthesized derivatives revealed high safety level by exhibiting very low cytotoxicity against the normal cell line. The molecular docking studies validated the outcome results from the anticancer activity and signifies the potential of these derivatives as EGFR (Epidermal growth factor receptor) (pdbid: 6z4b) inhibitors. So, these compounds can be modified further for the development of new anticancer and antimicrobial agents.

CHAPTER -6

SUMMARY AND CONCLUSION

6.1. SUMMARY

The basic structure of many diverse compounds with important therapeutic characteristics is indole. Among all the heterocyclics, indole derivatives are a unique class that gave rise to several commercially successful medications, including NSAIDs like indomethacin, anti-psychotics like ergotamine, anti-asthmatics like zafirlukast, antihypertensive medications like resperpine, antiviral medications like Delavirdine, antipsychotic medications like oxypertine, and antibiotics like tulongicin, among others.
The introduction, literature research, computational analysis, synthesis, and antibacterial and anticancer assessment of several indole derivatives are all included in this thesis work. This thesis focusses on the biological significance of new derivatives of indole-2-carboxamide.

CHAPTER 1: INTRODUCTION

This chapter provides an overview of drug development techniques as well as the general chemistry of indole, with a particular emphasis on its physicochemical characteristics and commercial manufacture.

CHAPTER 2: AIM AND OBJECTIVES

This chapter includes the study's goals and work strategy.

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CHAPTER 3: REVIEW OF LITERATURE

According to reports in the literature, derivatives of indole-2-carboxamide have become quite important in medicine. This chapter also covered the various approaches for preparing indole derivatives. Furthermore, the structure-activity link was analysed in connection with pharmacological actions.Additionally, we spoke about the latest indole patents.

CHAPTER 4: METHODOLOGY

All the compounds were prepared by conventional method as outlined in the scheme.

CHAPTER 5: RESULT AND DISCUSSION

The current study aimed to discover biologically potent agents by creating two series of potent indole derivatives, taking into account the observations.

Utilising a variety of spectroscopic methods, the structure of these target derivatives was determined. Section 5.4 provided the results.

Each synthesised compound was evaluated for its antibacterial and cancer-prevention potential against a variety of breast cancer cell lines in vitro. In this section 4.8, the specific biological evaluation processes have been covered. In section 5.7 the biological screening results were given. The outcomes were noteworthy and incredibly promising.

6.2 CONCLUSION

In the current research work, by introducing new functionality on the nucleus achieving a better anti-microbial and anti-cancer profile.The design of different 2D-QSAR models against each scheme is the first step in the project. These models are then used to screen compounds by evaluating their anti-microbial and anti-cancer activity.

The 2D QSAR analysis, when compared to the predicted pIC50 value, demonstrates the design of more potent antibacterial and anticancer indole derivatives, which are SS-IH, SS-IU, and SS-IIK. Because these compounds include alternatives for amine, hydroxy, and nitro groups, the 2D QSAR model presented in this work may be helpful in designing the aforementioned indole derivatives with particular inhibitory activity.

According to the biological evaluation, the compound SS-1H exhibits the strongest antibacterial activity when compared to the other scheme analogues. The synthesized compounds did not exhibit as much promising activity in the anti-fungal activity, however the compound SS-1O did exhibit some moderate activity. After evaluating the synthesized compounds' anti-cancer activity against a range of cell lines, it was found that compounds SS-III, SS-IIK, and SS-IIU had the best activity against the greatest number of cell lines. Thus, molecular dynamic simulations were used to further assess the interaction and likely mechanism of action of these three molecules.The majority of the compounds that are synthesised, according to current research, appear to have interesting pharmacological profiles and may be fascinating therapeutic candidates. These derivatives may also be useful for developing more effective antibacterial, antifungal, and anticancer properties in the future.

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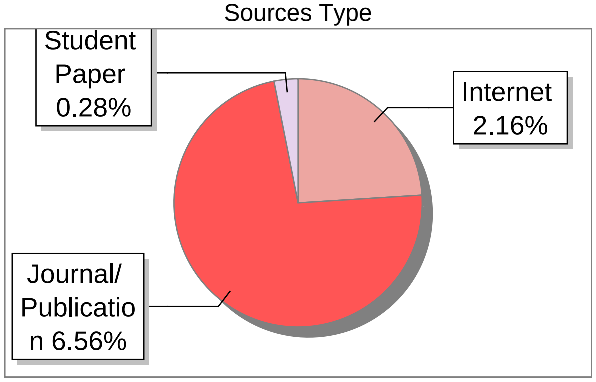

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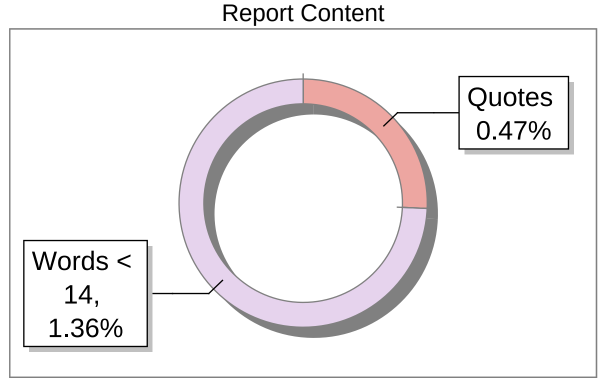

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58	scholarworks.umass.edu	<1	Publication
59	azooptics.com	<1	Internet Data
60	karnatakajudiciary.kar.nic.in	<1	Publication
61	qdoc.tips	<1	Internet Data
62	What Affects Use of Pretrip Public Transport Information Empirical Results of by Farag-2008	<1	Publication
63	www.teacheron.com	<1	Internet Data
64	acscollegesonai.edu.in	<1	Publication
65	blog.ipleaders.in	<1	Internet Data
66	dovepress.com	<1	Internet Data
67	REPOSITORY - Submitted to Kalinga University, Raipur on 2024-01-31 13-16	<1	Student Paper
68	towardsdatascience.com	<1	Internet Data

69	trace.tennessee.edu	<1	Publication
70	blog.linkedin.com	<1	Internet Data
71	e-apem.org	<1	Internet Data
72	ebmjournal.org	<1	Internet Data
73	Food, nutrition and health By E V McCollum, phd, scd and J Ernestine Bac by -1933	<1	Publication
74	repository.up.ac.za	<1	Publication
75	wikileaks.wikimee.org	<1	Internet Data
76	www.hindawi.com	<1	Internet Data
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A Study on Inter Relationship Between Academia And Industry: with Special Reference to National Capital Region, India

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CHAPTER 1

INTRODUCTION

1.1 CONCEPTUAL FRAMEWORK: AN OVERVIEW OF RELATED WORK

Industry and academia are like two sides of a coin and need to coexist for the growth and development of any nation. The education system is designed to prepare students for their future careers and also collaborate and closely associated with the industrial sector for developing an understanding with their present needs so that students can be prepared accordingly with a dynamic curriculum and pedagogy.

If there is no collaboration between industry and academia, then the students who graduate will be unemployable because they will lack the important skills that are required by industrialists and industry at the workplace. Employers think that more than 70% graduates from colleges cannot be employed because workforce are not adequately skilled or job-ready for jobs in the industry and workplace. In addition, the research and development that takes place when industry and academia come together can lead to the actualization of industry needs, which can be further fulfilled by academia.

At the Starting of the 21st century, we are witnessing the emergence of a new society that is driven by knowledge as well as the requirement for a quantum leap in the amount of students enrolled in higher engineering education. Higher education is a level of engineering education that is provided at academies, universities, colleges, seminaries, institutes of technology, and certain other institutions that confer academic degrees or professional certifications, such as vocational schools, many trade schools, and career colleges. Higher education is also referred to as engineering education at the collegiate level. In today's world, demand is rapidly growing growing demand for higher and professional education because it serves a range of essential functions in our society,

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Companies that build software or products and services that rely heavily on software are continuously working to improve their software engineering skills in order to maintain their competitive edge. For accomplishing this, everyone will need to cultivate the existing knowledge within the organization and gain access to individuals who possess the appropriate expertise. Universities strive to be a source for both aspects of competence by graduating software engineers who can find work in industry and by organizing pedagogy-oriented research that may contribute to the existing body and structure of the knowledge of the industrial sector. It will certainly help in the improvement of the industrial practices. This will allow universities to fulfil their mission of being a source for both aspects of competence. Although the relationship between academic research and industry has been acknowledged as a mechanism to share information and innovate, very little is known about how to manage the expectations and interactions of both parties.

Because the research cannot be carried out in complete seclusion in a university laboratory but must instead be carried out, at least in part, in real-world settings, there is an expectation that there will be a high degree of interaction with industry. This is particularly the case in applied research disciplines such as software engineering. Therefore, collaborative research projects have the potential to benefit both the private sector and the academic world (IA). Researchers receive access to real-world settings as well as insights into those settings. This allows researchers to better apply their findings to real-world problems.

Researchers have found a large number of barriers while integrating research and practice, despite the potential for both sides to profit. Both the areas and the topics of the proposed research and the tentative conclusions and results of the study need to be applicable to the corporate houses or the institutions. The findings of this research should provide software engineering professionals with actionable recommendations. There may be inconsistencies in the IA time views and incentive structures. IA must cultivate a mutually beneficial relationship in order to successfully bridge the gap between the two parties.

Within the framework of a collaborative project between IA, the primary objective of our research is to gain an understanding of (1) what elements can help enable communication between IA and (2) what results IA communication may contribute to. When we talk about communication, we are referring to the process of sharing information with one another, whether that information is vocal, written, or visual. We are also referring to the setting in which this communication occurs, such as meetings, reports, and e-mail. Communication is a means to promote outcomes of an IA research project; it is not a goal in itself, as could be the case for the exchange of knowledge. Further, we acknowledge that information is distinct from knowledge. This implies that communication is a means to promote outcomes of an IA research project. Nevertheless, we are operating under the assumption that communication is, in reality, a significant component of IA projects. In addition, as researchers in engineering, our main focus is on the organizational and practical features of communication within the perspective of an IA cooperation, rather than approaching the topic from pure communication science point of view.

During an era of an IA research project, researchers and nowadays the practitioners can effectively communicate with all the stakeholders for setting a variety of reasons. The choice of the research topic and the composition of the group or team are typically the primary focuses of conversation in the run-up to the official launch of a project. After commencing the project, the participants will come and work with holding hands. For defining the project plan, which may be more or less flexible depending on the participants' preferences. During the course of the project's execution, there are two distinct sorts of communication that take place. The first type of communication is related to the research work that is being done, such as when researchers collect empirical data and practitioners get part in the study process. The administration of the project and the reporting on its progress constitute yet another form of communication. In the end, the information is compiled into scientific articles and presented in the form of solutions, which are then shared with academics and practitioners.

A summary of the prior research that is relevant to our investigation is provided in this section. The first part of this article, we will discuss some viewpoints that should be taken into account by the researchers while analyzing IA research. First and foremost, everyone will be interested in the manner in which IA communication has been researched. In the second part of this paper, we discuss the findings of research in software engineering that pertain to collaborative IA work and the importance of communication. We came to the conclusion that our perspective on IA communication may be more all-encompassing than another scholars working in this area. On the basis of the result of this, it may be anticipated that the next part will contribute to the presentation of the IA communication perspective utilized in this research.

Interdisciplinary researchers from a wide variety of fields have approached IA research from a variety of angles. The authors of a review that was recently released by Salter and colleagues looked into the economic impact of research that was supported by the government, for instance. The authors identified six different types of contributions to economic growth. These contributions were related to the expansion of useful knowledge, the training of graduates, new scientific methods, networks and social interaction, increased scientific and technological problem solving, and the creation of new companies. An extensive literature review was studies by Good et al. from the standpoint of an organizational viewpoint of technology transfer ecosystems. These ecosystems are made up of university-affiliated organizations that participate in technology transfer operations. The authors focused their attention specifically on office of the technology transfer, the scientific parks, incubators, and university venue funds when conducting their research. The authors came to the conclusion that those structures had been investigated separately and brought attention to the fact that a holistic approach was required. The interaction pathways between IA and the contribution to open innovation are the topic of discussion in a different review that was published and written by Perkmann and Walsh. In this review, research collaborations are highlighted as one of the linkages between IA. One example of such a relationship is explored and found in the conclusion the research project that we conducted for our case study. Other links which have been established include the provision of research services, the commercialization of intellectual property rights, and the exchange of persons. Perkmann and Walsh discovered, in addition, that the primary focus of IA research has been on consequences rather than on how IA research is carried out. The latter is the question that our study addresses with regard to addressing the issue and challenges of the prevailing communication system.

The findings of the research that was done on how IA operate together, the most important factors is communication. Ankrah and Omar1 did a comprehensive assessment of 109 papers on the topic of IA collaboration across a variety of academic fields. They provide a model that may be used to depict IA initiatives. This model covers the motivations for collaborating, how the collaboration is formed and operated, the elements that improve and impede the joint work, as well as the consequences. In their paradigm, communication is brought up not once but twice: the first time, it is described as an activity that takes place all the way through the collaborative endeavor. Participants are able to connect with one another in a formal or informal setting using a variety of mediums including voice, email, video calls, etc., as well as through the publication of written content such reports, booklets, newsletters, bulletins, and research papers. The second way is as a factor that either helps or hinders the management of the organization and, as a result, the work that is done together. Our investigation covers both of these facets of communication as part of its scope.

In a similar vein, Rybnicek and Konigsgruber, the authors of a chapter about IA collaborations, acknowledge the significance of communication as a factor that plays a role in determining the nature of the relationship. They began their investigation based on the qualities that Ankrah and Omar1 had identified as being conducive to effective IA collaboration, and they discovered the factors listed below to be conducive to effective communication.

Frequent communication is vital to developing a common knowledge of how differences in cultural origins, hobbies, and interests can influence communication. It is impossible to build professional networks without first cultivating personal relationships and contacts. These connections are vital on both the managerial and the operational levels of the business. When choosing partners, companies frequently consider their level of knowledge as well as the reputation of the institution for its research. The quality of the relationship is improved when appropriate channels of communication and consistent in-person interaction are maintained. IA communication can also be affected by the usage of common languages and mutual understanding because researchers and practitioners may use distinct terminologies. Every partner needs to be familiar with the terminology used by the other partners. IA study could be hampered by cultural variations, such as differences in the way people work. As a consequence of this, the gaps that exist between the participants in the joint projects need to be determined and addressed at an early stage. In spite of the fact that our findings are consistent with a few of the factors that have been discussed thus far, we have discovered a few more factors that may promote IA communication.

A comprehensive literature assessment of IA partnerships was carried out by Garousi et al. in the field of software engineering, and the end result was a set of 33 primary research. The authors found both the difficulties and the most successful approaches to collaborating on IA projects. They decided to use the model that had been suggested by Ankrah and Omar to depict the process of putting together and running IA initiatives. Throughout the entirety of the project, difficulties with communication have been identified. There were gaps in the time horizon, areas of interest, and responsibilities; it was difficult to manage multiple collaborators; there was a massive lacking or insufficiency of standard terminologies; and there were few pre-existing networks before the projects. These are just some of the challenges that were associated with communication. In what follows, we will provide a quick overview of a very meagre or less examples of best practices that align with the results and findings of theresearch. One example of a best practice is to negotiate and elicit research subjects with practitioners before conducting industrial experiments. This may raise the level of trust that exists between the participants and contribute to the solution of specific industry-relevant problems. A second illustration of this would be to have a local advocate, also known as an engaged practitioner. The collaborative project will benefit from this in a number of ways, including a quicker start to the research, easier access to data, and more communication with business units and stakeholders. The ideal method of attracting the support of top management is one that strikes a balance between the research objectives of the collaborative project and delivers value to each member. Another recommended best practice is to hold weekly meetings, which may make it possible for practitioners to test and provide feedback on new ideas in a timelier manner. Establishing relationships for the long term is recommended as a best practice since both innovation and the impact it has on practice require time. Rather than being the outcome of a research effort that was only carried out for a brief period of time, high-quality and pertinent research findings are typically supported by long-term research. This research found that out of the 33 publications that were examined, 17 were written by writers from Scandinavia, which is an interesting finding (14 by Swedish researchers). This aspect may imply a willingness on the part of Scandinavian countries to create information architecture research and carry out study on this subject in order to further improve software engineering.

In a follow-up research of IA projects, Garousi et al. polled 64 respondents from around the world in order to determine which of the issues and patterns discovered in their earlier study largely impacted the ongoing research projects described by the respondents (101 projects). The authors discovered that issues linked to mismatches between IA, human and organizational challenges, and loss of interest or reduction in commitment had a greater impact than challenges connected to communication, which had a less significant influence. It is important to note that when the authors asked about difficulties with communication, they restricted their inquiry to communication channels that were used throughout the execution of the project. For instance, they asked about issues with Skype and working with several partners. Our understanding of communication in IA extends well beyond communication channels and communication that occurs solely throughout the course of the execution of certain projects. We consider every engagement that takes place between researchers and practitioners to be a form of communication. This is true regardless of whether the interaction takes place during the process of defining a research topic, conducting a research study, or disseminating research results.

In the era and the area of the software engineering, researchers have looked into and suggested a large number or variety of different models connected to IA research. A relational model that was presented by Sandberg and colleagues included ten guiding principles for the management of IA collaborations. Research on collaborative activities served as the foundation for the approach. Marijan and Gotlieb presented the Certus model as a reflection of the collaborative production of IA knowledge. The concept is predicated on the notion that in tune with research to be successful, it should carry out collaboratively by both academics and industry professionals, and this endeavor necessitates ongoing communication and coordination among all of the participants. In a similar vein, Mikkonen et al. created a model that describes the ongoing development of technology through collaborative efforts. Their model lends credence to the theory that innovation is not conceived in the research-oriented HEIs and then exported to the private sector. Instead, it is the collaborative effort of IA researchers that is responsible for innovation. The first two models were generated from research programmes in Sweden and Norway that were comparable to the one in our case study. The third model was derived from a national research programme in Finland. Both Sweden and Norway are located in Northern Europe. Although these models do not explicitly describe interaction analysis communication, they do model interaction analysis research, which, according to our beliefs, is dependent on and generates interaction analysis communication.

1.2 INDUSTRY AND ACADEMIA

The primary Obstacles to Interaction Between Industry and Academic Institutions Despite the fact that the primary principle of the interface between academia and industry has been adopted by the majority of private and only a very small number of public agencies in the past few years, its full potential has not yet been utilized and is still being nurtured for the benefit of both sectors.

1.2.1. **From Government**

When dealing with academia-industry collaboration, they are frequently too inert and generally very not flexible enough. This is because the collaboration itself is frequently not enterprising by nature and is plagued by bureaucrats. A common problem is that employees lack the compassion and quality that are desired. There has always been a significant amount of delay in funding to carry out or to conduct the research institutes, and delay in payments to some student sunder various central government research schemes. These issues are being experienced in the present.

day. There is a requirement for a very little quantity of ICT (information and communications technology) domain expertise in addition to a very large number of reporting. This will be financially beneficial for future planning to address the problem, as well as for furthering collaboration and achieving achievement.

1.2.2. From Academia

This may be a subject of significant debate, but it is unfortunately inescapable when academics (including professors, lecturers, and others of the same ilk) show a general lack of interest in continuing research and are unwilling to venture outside the safe confines of purely instructing classes. The academic world, as shown by universities, is notoriously rigid when it comes to the management of collaborative projects. Furthermore, academic institutions frequently present extra levels of internally restrictive policies and procedures, which stifle innovative thought. The academic community, for the most part, is unaware of the relevant industry criteria and is unable to adequately advertise its strong suit to the business world. The absence of sufficient motivation to professors and a specialized technical framework is another factor that contributes to the restricting effect (R & D Lab.),

1.2.3. From Industry

Any sector will inevitably be involved in some kind of business-related activity simply due to its very nature. Promptness in response time framework is maintained by the industry when interacting with particular academic institutions. The disinclination of the company to invest in its own internal R&D, which produces returns over the longer term, is often the driving force behind the investments. An unhealthy obsession with expensive, eminent professional consultants; an earlier unpleasant experience of exchanges with the academia; the oblige of on-going technical collaboration agreements; a concern to keep secret information of failure or success, confidential for fear of losing the competitive advantage are the other views which obstruct its interaction with a fresher's. The other view which obstructs its interaction with a fresher's is thoughtlessness to the tones of resource potential of the academia. More need on simply available foreign know-how.

1.2.4. Towards the mixing of Industry and Academia

The relationship between academia and industry is not like the one that exists between a technology producer and a technology receiver; rather, it is one that is interactive and collaborative, recognizing and ensuring joint respect for a mutual part, and contributing to the achievement of the correct purpose of such relationships, which is to bring about research-outcome synergy. Indeed, communications between universities and businesses are a system that call for the active and collaborative participation of all of the players. The fight that takes place at the interface between academia and industry in India today is restricted to a fine spectrum of actions. Therefore, in order to make this interface more robust, a variety of cooperation and engagement initiatives need to be put into place, observed on a level that is uniform across the board, and further developed. Identifying the scopes of expansions and incorporating them into the system are both tasks that need to be completed. The following are a few steps that have been discovered by employees and organizations working on the same issue of closing the industry-academia divide as that outlined in the previous sentence.

- The provision of academic and professional development opportunities and support.
- Participation of Former Students in playing the role of Counselor for Current Students
- The establishment of a Center of Excellence Foundation
- The Spreading of Information by Means of Collaboration Between Peers reviews
- Recruiting only the brightest minds to join the teaching staff.
- The establishment of an edge structures.
- A lab-based geared toward the industrial sector for students on research & development.

- Cell for the Nurturing of Technology
- Facilitating the transition of newly developed technologies from research laboratories to commercially available products.
- A Centralized Network for the Distribution of Knowledge to connect the many institutions.
- Improvements made to the ATKT session
- Research Park was established for encouraging the expansion of an existing enterprise organization.

Identifying and specifying that the partnership of academia and industry may lead to the tax inclusiveness and it may be spending research and development in they both will come forward and work together to achieve the goals. Additionally, the service tax in the form of any royalty by way of technology transfer from a research-oriented HEI. The beneficiaries (students) will be required to get experience in real-world workplace and in the industry through the completion of internships and other field and real projects. Additionally, the student practical training periods will be made longer and more presentable with the addition of feedback mechanisms, with the very aim of assisting the industry and the students. This would also be making it easier for businesses to design internship programmes that stay up with academic programmes, which would streamline the process. Introducing the ultimate beneficiaries (students) to the business world can play a very vital and important role in the learning process. Alumni who are currently working in a range of industries can serve as an ideal and role model for them mentor for Indian students to help them improve their employability skills and placements, as well as their having the understanding, knowledge and expertise of the international business nuances, global and overseas opportunities and the adequate and timely information on the expansion of technological advancements, among other things.

A tax exemption could be given for any expenditure that were incurred on the activities of research and development both in which the industry and academia can work together with holding hands. Additionally, a service tax exemption could be given for this as any royalty resulting from technology transferred from any research-oriented HEI to the industry an industry. Both of these measures will definitely be considered to encourage collaboration between academia and industry.

Students will be required to gain experience with real-world scenarios in the workplace through the completion of internships. Additionally, the student internships should be made more relevant by incorporating a feedback mechanism and by extending their duration to benefit both the students and the company. Hopefully, this would also be making it easier for businesses in the field to create and organize internship programmes that are in line with academic requirements. Teaching pupils about the working world serves two interconnected and equally important purposes.

Alumni who are currently working a large number of industries can play the role of mentors for Indian students by delivering lectures at their respective institutes to provide guidance to improve employability for their juniors', improving their skills, placements opportunities, knowledge of global and foreign business trends, overseas opportunities in business, and information of technological advancements, understanding and knowledge of the overseas business trends and opportunities etc. Alumni who are currently working in a variety of industries can also act as mentors for Indian students. Alumni can also generate money to assist in the growth and the development of entrepreneurial skills among the students who are interested in the programme by providing a feedback mechanism and operating under a set of specific terms and conditions.

Students should be informed about the requirements of society and industry, and the freedom, challenges, and sphere of entrepreneurship, therefore, they will be interested in becoming entrepreneurs rather than becoming entangled in conventional jobs. 43 The government may also think about the initiative to open various cells promoting to entrepreneurship in academic institutions, that is why it may be included in the curriculum. In the young minds of the pupils, this will instil a capacity for creative thought, a willingness to take risks, and a passion for resolving problems that are rooted in the real world.

During their brief stays within the physical premises and the arts of infrastructure of the institute, resourceful individuals from industry should be invited to give talks to students, academics, and scientific staff as well as participate in either teaching or research as part of intensive programmes developed under the Visiting Professorship scheme. These programmes should be designed to accommodate regular visits of these individuals. It is appropriate to confer the title of professor to an experienced professional who has worked in their field for a considerable amount of time. It is possible to refer to him as a Corporate Professor in order to help the individual receive the recognition they deserve from everyone involved.

Several appropriate programmes must be going to be or running to be adopted with the intention of focusing on critical and strategic areas of research and providing adequate financing assistance to the research that either maintains the pace with the market to step up with the market dynamics, needs or is market-driven. The ultimate goal of this endeavor is to improve R&D. During the process of evaluating the study, the commercial viability of the findings should be given the utmost priority for approval. This is in addition to the technical feasibility of the research. It may also be possible to orchestrate the reorganization of the many granted projects of research and development in the country; this would tend to streamline the goals and management of the existing grant projects under the oversight of a single management body.

1.3. **IMPORTANCE OF INDUSTRY-ACADEMIA COLLABORATION**

Industry and academic collaboration have become important because they support students' transition from educational institutions to the corporate world. It comes with many benefits and goes way beyond just placements. Let's look at the benefits of industry and academic collaboration:

Skill and Knowledge Development: When considering academics, industry, and academia, partnerships offer a platform for students to understand and develop capabilities to address challenges and issues with practical alternative solutions and options.

It helps the students be more aware of the practical aspects of research while developing new skills, data, and strategies. With industry and academia collaboration, most companies and organisations can improve their business performance by having access to many new ideas and thoughts from young minds while also extending their capabilities and expertise.

New Synergies: The industry-academia partnership also enhances the discovery of new synergies and models for companies. This is a collaboration that offers access to expertise and innovation, an extension of resources, and a sharpening of competitive benefits to companies. The academic faculty and students apply their brains to issues and challenges posed by the Industry and come up with a variety of solution options to try.

This partnership also leads the companies to hire students that match their requirements while making their businesses grow, which is beneficial both for the students and the companies because it short-circuits the selection and match-making cycle of recruitment.

Better Research: The industry-academia partnership also promotes advancing research and the formation of a skilled workforce. With this partnership, work-ready talent can gain specialist knowledge and practical training.

Moreover, universities also get the benefit of having opportunities to work on the latest technologies, challenges, and issues. This partnership helps reduce the cost of investment in research for any one partner. With joint efforts, [84] each partner brings its core expertise and resources already in place.

Better Access to Resources: The partnership with industries helps universities get more access to study resources for funding research and also diversifies into other research areas.

The universities can offer better education to MBA students when they get more opportunities to fund their research and innovation piloting from the industry. As a result, students can gain the best practical and theoretical knowledge.

Industry Jobs: The partnership between industry and academia also offers a much better platform for colleges to offer real-time jobs to students in the form of internships and on-the-job training programs.

The industry jobs and learning opportunities enable students to get involved in incubator projects and new initiatives of the company, making them learn intensely with length and breadth of exposure.

Full-time Employment: Students can get full-time employment as a long-term benefit of industry and academia partnerships. With partnership and collaboration between Industry and academia, trust and knowledge of each other are enhanced. This makes the partnership an effective tool for most colleges and universities.

When the university focuses on educating its students while keeping industry and academia's collaboration at the Centre, the result is high employability and job-ready students. This leads to less investment by the companies in fresher training to make them job-ready and better placement by academia for their students, which is a win-win model. This can be used to attract prospective students and corporate partners.

1.4. BRIDGING GAPS BETWEEN ACADEMIA AND INDUSTRY IN INDIA

1.4.1. Optimizing the Research focus: Because the goal of applied research should be to make it useful to society so that society can benefit from such research (as opposed to research that is oriented toward the development of a theory or concept through basic research), universities, particularly those offering courses in Master's and Doctorate programmes, should concentrate on the long-term objective of the research that is being conducted within a particular department or research group. The submission of a PhD thesis, the publication of a few papers, or the conferring of degrees and diplomas should not be the primary focus of the research. A strategy like this has the potential to be counterproductive due to the fact that potential researchers or academicians in the future may never become aware of fundamental industry requirements. One such requirement is the requirement for research and development of a product that is useful, along with a focus on timelines to deliver the product.

Therefore, it is necessary to have an optimized research focus in universities beginning at Master's degree courses themselves, or even better, at Bachelor's degree courses, in order to prepare a pool of candidates who are industry-ready in terms of their learning and thought-processes. This is because universities are the primary source of new knowledge. The research guide or Principal Investigator should have a more focused and long-term plan to bring the research project (once initiated) to a useful closure and at the same time ensure that his or her students pass the baton to their successors to reach to the long-term objectives of the research that was started under one group or Principal Investigator. This is necessary because students are a high-mobility population.

1.4.2. Increasing exposure to Industry: It is difficult to orient students toward research that is focused on industry unless there is adequate exposure of the entire academic team to the environment of the company. This exposure should include students, research guides, and administrative staff. This involves a continual conversation between academic research institutes and universities and the industry, as well as frequent visits to the industry, short-term training in the industry on specific activities, and frequent visits to the industry. An interaction of this kind might, in point of fact, become one of the primary duty areas for academic staff in a certain subject, as well as one of the required elements in the curriculum for students in that field. Regular meetings with the industry will provide an enhancement of the most recent ideas and major advancements in the sector, in addition to the construction of a mutual rapport between the organizations involved.

1.4.3. Academia-Industry Partnerships: Last but not least, the passion to have successful collaborations between academia and industry, such as public-private research partnerships, collaborative grant applications, and student trainings, is the most important component of bridging the gap. This is not to say that it is the only important component, however. According to my own personal experience, the most significant obstacle that stands in the way of successful partnerships between the academic world and the business world is the absence of a common understanding of the overarching objective, which is to develop a product that is beneficial to society as a result of the combined efforts of all parties involved in the research. When the business world finally wakes up to the fact that the majority of fundamental research is conducted in academic and university settings, this will finally become a reality. At the same time, it is essential that the academic community recognizes that turning proof-of-principle research into a product is not only a time-consuming process, but that it also requires industry to take on a significant amount of risk. For the partnership to be successful, both parties need to acknowledge and value the qualities that set the other apart from the pack, and then find ways to work together to capitalize on those qualities.

Training students in the business by providing them with hands-on experience through a research project is one example of a productive relationship between academia and industry. For optimal results, the company should support the students' research fellowships. Because of this process, a pool of skilled resources is created, which may then be utilized by the same industry or by other relevant industries. This presents a challenge in terms of maintaining difficult boundaries, such as the free pursuit of knowledge (which is important to academia) versus the strict confidentiality of information (which is important to industry). However, this challenge is one that could be successfully managed with appropriately planned projects and proper systems held in place within the organizations. Last but not least, the goal of any successful cooperation should be to put in place mechanisms that will enable the nation to keep its top workers by ensuring that there are sufficient employment possibilities.

a. **Product:** We can consider information or models a product delivered by the scholarly community. Thus, the first class identifies various features of the product (or in this case of the model) that either increase or decrease the hole among the scholarly community and practice.

b. **Relevance:** The first and foremost characteristic is relevance. At the point when intermediaries or practitioners come into contact with new research, the relevance to their business will be the essential determinant of whether they have any interest in really carrying out the research. Essentially, great models should clarify what users need to acquire from executing the model.

c. **Mindset:** Past the 'product' perspective - - pondering the features and characteristics of the decision support system or model, we also need to contemplate the setting of where and how the decision support system is being executed. The degree to which a model is viable may rely upon the decision climate. The second classification of 'mindset' attempts to catch association level attributes that would impact the successful execution of a decision support system.

d. **Analytical Maturity:** Analytical maturity reflects the skill level or capacity of practitioners to work with models and decision support systems. Past way of behaving and experience assume a significant part in this. Previous research has shown that earlier association with decision support systems was positively related with the use of a promoting the executives support system. The more encountered a supervisor or company is, the less distance that exists between that element and the scholarly community. However this may not be surprising, it's a significant component of understanding the 'distance' in model usage among the scholarly world and practice. Notwithstanding experience with previous models, analytical reasoning is a significant skill that contributes to the capacity of practitioners to work with models. Knowing this, it very well might be enticing to possibly target managers that are as of now high analytical thinkers while endeavoring model execution. Be that as it may, albeit insightful skills increase director's abilities to use new models, low-analytical decision makers have the most to acquire.

1.5. INDUSTRY-ACADEMIA INTERACTION-OBSTACLES OR IMPEDIMENTS

In his research, Fowler (1984) identified fifteen barriers or obstacles in university and industry collaborations or relationship. Some of them were related to the posing of problem while establishing a functional and practical relationship. All the universities or HEIs and academicians always have a reasonable desire to publish their research work like articles, research papers, patents etc. But at the same time industry do not protect their intellectual property right with enthusiasm and self-motivation. They have to protect them because of ethical compulsion or due to some legal or regulatory compliances. In addition to that academics focus on conducting some descriptive and fundamental research that generally leads to develop some new theories and hypothesis but industry needs to have some applied and problem solving research that can produce some instant solution of the persistent problem faced by the industry or industries.

Industries always tend to have the result in a time bound manner. They cannot allow a long span of time on research because they have to develop new products as per the needs and wants of the market scenario. This is the main obstacle in developing a healthy and sustainable relationship between industries and universities. There is a lack of strong linkage between industry and academia because of the following reasons:

- Generally, faculties do not possess any industry experience. They should earn some industry exposure before making their career in academics only then they can significantly contribute towards industry-academic linkage.
- There is also some issues in academic curriculum. There should be some provisions in their curriculum so that they can learn some practical skills and training during their program.
- State of art infrastructure and other physical facilities are also responsible in creating barriers because these thing prevent the free folw of information between industry and academia.
- Suitable and appropriate mechanism is also required for the collaboration between industry and academia. Presently, we are lacking of this.
- Some universities and HEIs are reluctant to produce outcomes and research in time bound manner.
- Because of above mentioned factors the dependence of our industry on foreign collaboration is chronic.

1.6. REMOVAL OF OBSTACLES OR IMPEDIMENTS IN INDUSTRY-ACADEMIA LINKAGE

This is the need of the hour that the universities and professional should come out from their offices and comfort zone. They should be keen to establish relationship with the rest of the world. They must understand that they are mutually associated and their requirement and existence is mutual.

Their benefits are not separated from each other but they are mutual and highly interdependent. It should also be noted and recognized that academics, industrial sector and Research & Development organizations are coming together with holding hands for the technological developments in many core areas and sectors of the country. The main aim of such collaborations and initiatives is provide bases for the further research and education. The survival of the industries will be entirely dependent on the innovations, creativity, continuous improvements in process that will support and motivate the academic sector to conduct further research. So far as in India, the industry-academia collaboration was kept away but now we are moving towards to develop such linkage between these two sectors for the furtherance of the both sectors.

1.7. RECENT INITIATIVES OF MINISTRY OF HUMAN RESOURCE AND DEVELOPMENT, GOVERNMENT OF INDIA

Today, we need (Pallam Raju, 2013a) a closer and sustained relationship and partnership between industry and academia. For conducting any kind of research the funding is the most crucial factor because without having adequate and timely funding, no research project can be undertaken. It is also noteworthy that most of the funding are coming from the Government bodies. Therefore, the active involvement and participation of the private sector has become very relevant and mandatory. Because without active and adequate participation of the private sector, not many research projects can be undertaken only with the help of government bodies. In today's scenario industries are not only expected for satisfying the funding requirements but also they are also required to actively engaged in the activities of skill development, innovation and develop entrepreneurial skills and to promote entrepreneurship through start up schemes and under the Make in India initiatives. This is the high time to bridge the gap between industry and academia in terms of the mutual interaction, mutual exchange of ideas and resource sharing and many more. In comparison to other countries, India is spending less on such initiatives. China is spending a large amount on this.

In continuation of promoting such initiatives, the Ministry of HRD, Government of India (MHRD), has compelled to set up three task forces. These task forces are as follows:

1. Research, innovation and entrepreneurship;
2. skill and employability; and
3. The ways to foster institutional mechanism, (Thakur 2013).

The main mandate of these task forces were to work on the status of the linkage between industry and academia, they recommended the recommendations in a broad spectrum and having a wider perspective. The Government is very motivated and eagerly keen to promote the research and skill development activities to foster the collaborative activities between the both of them (industry and academics).

It is necessary to have some knowledge hubs that can transform the institutions so that the dissemination of the information can take place uninterruptedly. This is an urgent need of the hour to work on some areas with the priorities like;

- improving learning outcomes at all levels;
- meeting the shortage of faculty/ teachers at all levels;
- Industry-academia linkages to ensure better employability of our graduates as also skilling of our youth.

Now the Gross Enrollment Ratio (GER) has substantially increased. Some initiatives from MHRD with regard to achieving the national mission on teachers and teaching that have been taken to address the current issues like lack of availability of adequate number of teachers so that teaching profession can be made more attractive. In this regard, the Ministry of HRD took some initiatives and notified the National Vocational Qualification Framework (NVEQF). This is the very unique platform where professional education as well as technical education is imparted by the technical institutions under the university system and polytechnics under the technical boards will provide basic skills required for transforming students as employable, (Pallam Raju, 2013b).

To bridge the gap between both stakeholders that is industry and academics, an 'Academia-Industry Interface Council' was set up by the Ministry of HRD, Government of India for serving the purpose of promoting the cutting-edge research, improving the quality of teaching and learning process. All these initiatives will improve and boost the employability of the graduates. The funding requirements can also be fulfilled by corporate sector by the way of collaborating with the academics. These funding can be allocated in different heads like undertaking the research projects, conducting faculty development program, creation of state of infrastructure facilities, student's scholarship and governance. The Narayan Murthy Committee recommended to set up the 'Council for Industry and Higher Education Collaboration' (CIHEC) to facilitate industry-institute collaborations is indeed the way forward, (Pallam Raju, 2013b). The main aim of establishing this council was to identify the students who are not ready for the job. Having identified such students, the HEIs and corporate sector will jointly work on it.

For strengthening the linkage between both stakeholders that is industry and academia, the concerned ministry has taken various steps with regard to setting up the unique fund called 'incubation fund'. This incubation fund can be utilized. The All India Council for Technical Education (AICTE) and University Grant Commission (UGC) also launched various funding schemes for the promotion and support of the research activities. The need of private sector involvement is very important and it is the need of the hour. Providing funds is not the end of the responsibility of the industry or corporate but also they have actively engage in skill development program, conducting faculty development programs and workshops.

The National Vocational Qualification Framework (NVEQF) is the unique platform which has been established to offers students an alternate career path that offers unique opportunity to acquire or earn a degree or diploma which will enhance the employability of the students and it will make the ready to industry needs. The same needs a greater involvement of the industry not only in providing skills, but also in promotion of innovation and encouragement of entrepreneurship among our youth, (Pallam Raju, 2013b).

The industries and corporate sectors must contribute more funds and other physical infrastructure to support and promote the research projects. It is also noteworthy that most of the funding are coming from the Government bodies. Therefore, the active involvement and participation of the private sector has become very relevant and mandatory. Because without active and adequate participation of the private sector, not many research projects can be undertaken only with the help of government bodies. In today's scenario industries are not only expected for satisfying the funding requirements but also they are also required to actively engaged in the activities of skill development, innovation and develop entrepreneurial skills and to promote entrepreneurship through start up schemes and under the Make in India initiatives. This is the high time to bridge the gap between industry and academia in terms of the mutual interaction, mutual exchange of ideas and resource sharing and many more. In comparison to other countries, India is spending less on such initiatives. China is spending a large amount on this.

Therefore, there are some key Initiatives to promote industries- academia collaborations in the country for greater national productivity are:-

- There is the need of an incubation funds for at least more than one hundred HEIs, which will provide and supply seed money for incubation the ideas and promoting the ideas of the scholars.
- The National Employability Enhancement Mission (NEEM) was launched through the All India Council of Technical Education (AICTE). This will provide a special purpose vehicle (SPV) for companies and entrepreneurs to provide employability, skills development and internship as value added proposition to student for all fields.
- An Academia- Industry Interface Council should have the representation from the industry, corporate and academia as well.

1.8. INDUSTRY-ACADEMIA LINKAGES- RECENT TRENDS IN INDIA

In early years, the cooperation between industries and academia were not up to the mark. They did not used to provide cooperation to each other because of many factors and reluctance also. But now, the scenario has quite change and the trend has shifted from no-cooperation to mutual cooperation between both of them. Now they are sharing their resources, exchanging their manpower and ideas to cooperate each other and produce some meaningful and sustainable output.

It has become desirable and necessary in one sense or in other after liberalization in government policies that academics in pure and in applied science must interact with industries to explore the new opportunities to get some funds and other resources to conduct research and other innovative measures and initiatives. Academics should focus on solving some real problems of the industries. There is a large scope to interact with small, medium, and large-scale industries in Private Sector including Multinationals, as well as in Public Sector, coupled with some appreciation of financial matters. The trends of the industry-academia linkage can be traced out as following:

- Earlier conventional methods were used but now state of arts in technology is being used.
- Earlier, the quality of manpower was not satisfactory but it is improved now.
- The involvement of faculty with industry was very less but now it has substantially increased.
- The exchange programs for staff were rarely conducted but nowadays it is frequently conducted.
- There was very less involvement of staff in research & Development and consultancy but now it has increased.
- There was no such compulsion for academia with industry but it has become compulsive for the faculties to collaborate with industries and also it is being incentivized.
- There was no such linkage with the performance appraisal of the faculty but now it has been linked with the faculty performance appraisal.
- There was no link with the assessment of HEIs performance bot now the scenario is reversed. The assessment is being done by NAC, UGC, AICTE, NBA and other accredited

agencies.

- Earlier, there was a need of providing training and retraining of the manpower and workforce but nowadays it has become a regular feature.

1.9. THE CONFEDERATION OF INDIAN INDUSTRY (CII)-RECENT INITIATIVES OF INDUSTRY-ACADEMIA LINKAGES

Nowadays, the scenario has quite changed and Indian industries are not exception and they are very keen to work with academia, (Forbes, 2013) not only for the benefit of the stakeholders but also because of their own profit also. For improving the quality of skilled manpower in the industry, it is necessary to improve the quality of the academic curriculum. That is why the Confederation of Indian Industries (CII) has been taking multiple steps for serving the same purpose.

1.10. INDUSTRY-ACADEMIA INTERACTION

There is more cutthroat competition is driving up the expectations of industrial recruiters in terms of a candidate applying for a job in terms of their ability to multitask, possess soft skills, and be self-motivated. Industries and management institutes should be aware of one another's expectations in order to achieve a better blend of interests and inclinations, which will ultimately lead to a commercial tie that is more meaningful and useful. However, it seems that there is a significant disconnect between the expectations of the corporate world and those of management institutes in terms of employability abilities. The ancient adage that water is a composite of hydrogen and oxygen, both of which are found in abundant supply in nature, is completely accurate with regard to the current scenario; yet, there is a severe shortage of water. A situation quite similar to this may be seen in employment exchanges, where there is an abundance of candidates despite the fact that business houses continue to complain about a lack of qualified applicants. In order to remedy the situation, there is a requirement for research to be conducted in order to understand the skill gaps, which will be followed by the suggestion of corrective activities that can be readily carried out.

Education in management should be structured to meet the objective of producing "marketable products" in the form of management students for the business sector. Therefore, it is up to management institutes to pro-actively prepare and supply the final products with all of the necessary skills for instant employment placement. This responsibility belongs with the management institutes.

We are living in a world of work that is frenetic, cutthroat, and international in scope. In today's knowledge-based economy, employers anticipate that educational institutions of management will equip their students with the employability skills necessary for a specific position (Bok, 2006). According to Cappelli (2008), the search for talent on the part of employers is intertwined with that of employees. Employers anticipate that a candidate will possess all of the necessary abilities while maintaining an affordable salary. Employees demand control over their careers as well as the opportunity for progress in their fields. To address the severe lack of available workers with relevant skills, educational institutions that focus on business and management should adopt a more strategic approach to the teaching of employability skills. Although businesses are making strategic shifts in their recruitment and training and development operations, the management education system still needs to make the transition to a more skill-based learning model in order to provide successful results. The business sector and academic institutions are aware of the importance of fostering employable skills through training and education in order to maintain India's competitiveness and growth in an international market that is extremely competitive. The vast majority of corporations have the expectation that newly hired personnel will grow along with the organization and are willing to contribute to the development of more value-added abilities. Students often view obtaining a higher education, and particularly a management education, as a necessary step toward landing a well-paying career. Students who take courses in management are better able to enhance their analytical, synoptic, and presentational skills, as well as their rationale for decision making, all of which are extremely important in today's economy. Some companies believe that more activities might be undertaken to help students acquire skills and traits like as working together as a team, communicating effectively, taking initiative, thinking critically, and solving problems. When it comes to increasing one's employability skills, everyone is in agreement that internships and work placements make a tremendous difference.

Due to globalization (Church, 2000; Friga, Bettis, and Sullivan, 2003; Weisman, 2000), changes in science, increasing competition, limited resources (Barret and Beesan, 2002), rapid technological changes, workforce diversity, and customer behaviour, Corporate is currently facing a number of challenges (Allen, Bordas, Hickman, Matusak, Sorenson and Whitemire, 1998; Weisman, 2000). For a corporation to be successful in overcoming the challenges listed above, its employees will need to possess a broad range of skills, knowledge, and traits (Weisman, 2000). In order for the students of management to be able to solve the issues that are currently being encountered by organizations, they need to have a blend of broad knowledge, qualities, and abilities. Reasoning, the capacity to influence and persuade various groups of people, and strategic thinking and planning in the context of application of technology (Allen et all, 1998; Weisman, 2000) are all important skills that the students should have (Friga et all, 2003). In order for them to be employable, they should also have strong communication and learning skills, adaptability skills, responsibility skills, interaction skills, proactive skills, appearance skills, operational skills, creativity and problem solving skills, technological savvy skills, team building skills, and task perseverance skills.

However, previous research has shown that management schools do not teach employability skills to their students in a manner that is consistent with the requirements of corporations (Fugate and Jefferson, 2001). The lack of skills necessary for employment among management students is a source of widespread frustration among business professionals. According to the literature review, businesses believe that management education is falling behind the growing demand for globally competitive employees. These days, academia and industry are working together to close the skills gap between what is anticipated by corporations and what management institutions teach their students in order to improve the employability of the graduates of these programmes. Different methods, including as actual on-the-job experience, internships, case studies, and simulations, are currently being assessed to determine the impact they have on the development of employability skills. With the help of this research, a feeble attempt has been made to present a comprehensive overview of the current situation.

1.10.1. Spectrum of Academia-Industry Interaction

In recent years, there has been an increasing awareness regarding the role and duty of education with regard to the context of the way in which education systems are organized and governed. The flow of knowledge, which ultimately leads to economic growth, is one aspect of the relationship between academia and industry that has a beneficial impact. Keeping up with the continually shifting expectations of industry is the most significant obstacle facing academia in the modern day. The modern economy is built on the accumulation of information, which calls for an increased level of collaboration between academia and industry that is mutually beneficial. The lack of qualified workers in India is having a negative impact on the bottom line of businesses around the world, which is shown in the attrition rate of trained manpower. This circumstance has worsened as a result of the increased demand for qualified professionals. In order to meet the ever-evolving requirements of corporations, it is essential to build various modes of collaboration, which requires an awareness of the sectored demands that exist. Management institutes in India were given a boost by a number of factors, including a substantial inflow of foreign direct investment (FDI), the proliferation of outsourcing businesses in the country, the country's cultural diversity, its pool of professionals fluent in English, and its expanding economy. It advocates for the transformation of curricula in order to make students more dynamic, to equip them with the most recent technologies.

and to make them capable of working with a diverse workforce through contact between academia and industry. The rapid expansion of management institutions was necessary to close the skill gap that had developed between academia and industry. Management institutions are able to train students to fulfil the needs of the market and transform them into global managers who are prepared to face the competition on a worldwide scale if they participate in new educational programmes. Management institutes have the potential to raise more people's knowledge as well as produce economic plans with a high economic growth rate as their primary goal. Interaction between academia and industry is essential for any management institute, as this is what determines the brand building of the institute.

Interaction between academia and industry is vital and helpful for both sectors; industry can profit from the knowledge base that is available with management institutes. On the other hand, management institutes can profit from field experience and internship programmes through their participation. The most crucial aspect of the connection between academia and industry is to have an accurate grasp of the expectations that corporations have of management institutions, so that academics can provide students with education that is relevant to their careers. The interaction between academia and industry can be improved through the implementation of a faculty exchange programme. Under this programme, industry professionals would travel to management institutes to talk about their real-world experiences and help bring the curriculum in line with current business requirements. The corporate five expresses the skill set mismatch that exists between their expectations from management candidates and the knowledge provided by management institutes. This mismatch can be seen as a gap between the two. In addition, there are numerous aspects of personality that are ignored by management colleges. These may include the non-focused and underestimated employability abilities that are required to break into the business world.

Because of their divergent points of view, academia and businesses in India have lost the sense that they are working together to achieve the common goal of increasing employability. Many experts in India have recommended that research-based education in management be provided in partnership with businesses. However, academia has not agreed with this recommendation and has thought that teaching can be done without research. They tried to promote skill-based learning in management education by following a western pattern, which involved dealing with research projects concerned by industries. However, Indian corporations did not provide meaningful assistance for research and case study writings. This prevented them from achieving their goal. Since the Indian economy has been growing at an unprecedented rate in recent years, many management schools in the country have begun to stress to their students the importance of being prepared for international competition.

1.11. THE CHANGING HIGHER EDUCATION SYSTEM IN INDIA

1.11.1. Massification of Higher Education

In more recent times, particularly during around last twenty or 25 years, an increasing trend on awareness has been seen about the role and responsibility of education, and along with it, there has been a growing concern in a number of countries about the manner in which educational systems were organized and administered. This has occurred in response to a growing awareness about the importance of education. Perhaps the beginnings of this issue can be traced back to when education went from being a pursuit of the elite to being something that was done by the masses. Higher education also evolved into a mass education endeavor as a result of the universalization of primary and secondary education in most developed countries.

The Robbins Committee, which was the Committee on University Education in the United Kingdom in 1963, stated that there is a social responsibility of the university being a part of the society and they should respond in that direction by fulfilling the social demand. They can fulfill this social demand by way of providing the quality education. This view states that the HEIs should provide the equality in the education of all. The domino effect of this event was a rapid expansion of higher education in the United Kingdom, including the establishment of a huge number of new universities and an increase in the percentage of high school graduates who went on to pursue higher education. The proportion of students in the age bracket of 18 to 20 years old or older who enrolled in universities had a precipitous rise, reaching 17 by the middle of the 1980s and 32 by 1995.

According to the World Development Indicators published by the World Bank in 2001, the percentage of people in the appropriate age range who were enrolled in tertiary education was 52 in the United Kingdom, but it was 88 in Canada, 81 in the United States, 80 in Australia, and 74 in Finland. According to this Report, in 1997, the High Income countries had a participation ratio in postsecondary education that was equivalent to 62% of the age group that was being considered. In comparison, the nations with a Middle Income only had a participation rate of 12 percent, even if the countries in the Upper Middle Income group had 22 percent of the relevant age group enrolled in tertiary education. The similar percentage for Low Income countries, which includes India (India's own contribution being 7 percent), was a measly 8 percent.

At the moment, there are over 15,000 colleges in India, which are attended by somewhat fewer than 10 million students. More than two-thirds of these institutions are categorized as "Arts, Science, Commerce, and Oriental Learning Colleges" by the University Grants Commission (UGC), which is the main government regulating authority for higher education. In recent years, enrollment has increased significantly at professional institutions (particularly those that focus on engineering, management, and medical), as well as at private vocational schools that offer instruction geared specifically toward the information technology industry. The fact that there are 1253 medical institutions in India but only two that focus on public health reveals the goals and interests that define higher education in India. In India, more people become lawyers than become medical physicians, and there are around 0.7 million students studying engineering and technology. Over the past two decades, there has been a significant increase in higher education, with student enrollment expanding at an average rate of roughly 5 percent per year. This growth has contributed to the rapid expansion of higher education. This expansion, which is approximately two and a half times the rate at which the population is growing, is the result of a population bulge in younger age cohorts as well as an increase in the demand for higher education.

Nearly two thirds of students are enrolled in subjects related to the arts and sciences, while another 18 percent are studying subjects related to business and management. This is of significant significance due to the fact that the majority of so-called "private investment" in higher education is focused on fields such as engineering, medicine, and management, and as a result, it does very little for the majority of students. Despite the fact that a slew of committee studies on alternate sources of finance for higher education have raised high hopes (World Bank, 2000), the state will have to continue to occupy the commanding heights of at least this sector of the economy.

The evolution of higher education into a system for educating large numbers of people ultimately resulted in questions being made about the ways in which it was organized and governed. To begin, the majority of nations' higher education systems are still reliant on funding from the public sector. As a result, it was only natural to question whether or not the money contributed by taxpayers was being spent wisely, whether or not the institution on which public money was spent was accountable to society and the government, and whether or not the resources that were allocated to these institutions were utilized efficiently. The search for answers to these concerns inevitably started using the established management methods, and the ideas of performance, productivity, accountability, and so on made their way into the field of educational administration gradually but surely through time.

1.11.2. Management of Education

Even at the turn of the millennium, India is unable to point to any noteworthy shifts in the way it approaches the administration of educational institutions as evidence of progress in this area. The outdated notions of how school administration should be conducted are still the norm here. The National Institute of Educational Planning and Administration is, as always, our most prestigious educational training establishment. It is not known whether any HEI or other universities in the country may offer such substantial programs in management discipline to prepare the management leaders who can lead the industry and world from the forefront. Earlier there were some IIMs who used to offer the management education but gradually other government institutes and private sector also began to start to establish the institutions. The main aim of the management education is to prepare the professionally trained graduates who can lead the corporate world effectively and efficiently. Today's need is too do the smart work. Nowadays, various degree and diploma programmes are being offered by the HEIs which are having a varying range of the programmes those have been customized as per the need of the industrial world.

In point of fact, we have not even been discussing about the structure and governance of the management of HEIs in India. The administration or governance of educational institutions did not become a focus of attention until 1986, when the United States first outlined its National Policy on Education. This issue was voiced by confirming that a revamp of the educational system. It leads to the major planning and management of education that will be given a high priority. In the following section of the policy, it was stated that the guiding principles for the process of remodeling the management of education would be decentralization, the creation of a spirit of autonomy for educational institutions, the evolution of long-term planning, and a management perspective that is integrated with the country's developmental and manpower needs. In addition, the policy stated that the principle of accountability would be established.

In the past, we had been happy to approach the problem of university management by framing it as an issue of governance. In point of fact, a high–powered committee that was constituted in 1969 to form a Group on Governance of Universities was requested to do so. This committee was chaired by Justice P.B. Gajendragadkar, who had previously served as Chief Justice of India. The maintenance of the university's capacity for self-governance and independence was the primary topic covered by this Committee in the report that it presented in 1971; the committee did not focus on issues related to the management of universities as organizations concerned with accountability, efficiency, productivity, and other such topics. Naturally, the Committee discussed in great depth topics such as who should sit on various university bodies, and in what combination between internal and external members, and how those individuals should be appointed to those bodies, and whether such appointments should be through elections or some other method, and how governments should keep a safe distance from the administration of universities.

Concerning the administration of higher education, it was proposed that the established patterns, which include the structure, roles, and responsibilities of various university bodies, should be reexamined in light of the new demands placed on the university system. This would be done with the intention of fostering the development of new management systems that are more productive, efficient, and user-friendly. The Committee that was constituted by the UGC in pursuit of these recommendations which were dealt in the National Policy and it dealt with a variety of topics involved in the structural modifications of the university management that was submitted in 1990. This report was submitted in response to the National Policy. In addition to this, it suggested other alternative organizational structures for universities, which varied according on the type of institution they were. Take, for example,

- The Executive Council and the Academic Council will make up the university's two-tiered organization in a unitary institution that does not have any colleges that are connected with it.

- Large universities that affiliate will have to affiliate the attached HEIs. It is in addition to the traditional bodies of Senate, Executive Council, and Academic Council, a Collegiate Council to decide academic matters relating to the colleges. This council will be responsible for accrediting and regulating the universities' affiliated colleges.

Regarding the more fundamental problem at hand, namely the structure under which universities are run, the Committee made the following observation that there is an urgent need of to be recognized that the academic administration is quite different and committed to provide the quality education. The administration should be cooperative to the government. It is safe to say that the Committee refrained from recommending any significant changes to the way universities are run; at the very most, the report proposed some minor tweaks to the various models of administrative structures already in place, along with slight or moderate alterations to the make-up and responsibilities of the various university bodies already in place.

1.11.3. Expanding Horizon of Higher Education

Developments have always some challenges and repercussions. Therefore, there are also two repercussions of these development.

1. First, it becomes very clear and imperative that a lot of work have to be done to bring about greater professionalism in the administration of education, and,

2. Second, this is a good thing that now education has started to look for good practices outside of its own confines in order to improve its image of efficiency. Both of these repercussions were brought about as a direct result of the developments described above. As a result, it should not come as a complete shock to learn that in the sphere of education, some characteristics of contemporary management methods are currently being adopted step by step. The tool kits of today's education managers must include, at a minimum, the following: planning, strategic development, performance measurement, quality improvement, professional development, institutional and cultural transformation, resource mobilization, marketing, and public relations.

3. On the eve of the new century, all of the parties involved, including industry, academia, and the government, are coming under great pressure to become more strategic, boost

employability, and reduce skill gaps. According to the findings of Rajshekaran and Rajasingh (2009), there is a significant perceptional gap between academia and industry about employability skills. This gap needs to be overcome in order to improve the employability of students. The business world has the impression that the percentage of graduates who are employable drops year after year; on the other hand, there is a significant need for skilled graduates in the labour market. According to Winbladh (2004), in order for students to improve their employability skills, they need to participate in collaborative learning activities. In addition, he came to the conclusion that recent college graduates lack the employability skills that are required by businesses. Hamatteh and Jufout (2003) proposed that there ought to be established at the national level a committee that is comprised of members drawn from both the business world and the academic world for the purpose of determining the requirements of one another and seeing to it that they are met. He also suggested that there should be regular assessments of the skills that are being taught to students, as well as regular revisions of the curriculum based on the needs of industry. If these things are done, it will be possible to cut down on the costs of pre-training for newly graduated workers in industry.

4. Employers, employees, educators, and students all understand now how important it is to build employable skills in order to maintain competitive growth in this highly competitive market. Those skills can be applied in a variety of settings. However, there are still a lot of obstacles to overcome in order to take effective action. This is due to the fact that all of the stakeholders are confused about employability skills, how they are related to jobs, and what strategy should be used to improve pupils. Employability skills, in addition to helping a person find work, can also lead to increased financial success for businesses and the nation as a whole, as well as greater personal satisfaction for the individual. People who possess the abilities necessary for employability are highly employable and in high demand. Those who do not have it are destined to suffer losses in the market. Anyone may

improve their employability skills and increase their chances of finding work. Ghosh et al. (2007) found that there are various models in operation in India that involve interaction between the academic community and industry. He placed a strong emphasis on the involvement of industry all the way from the creation of the curriculum to the absorption of students as trainees, arguing that this will reduce the amount of time and money that enterprises spend on the orientation of newly graduated workers. Zahid (2008) came to the conclusion that academic and industrial ties need to be maintained in order to keep up with the continuously shifting global market.

1.11.4. Indian Models of University – Industry Linkages

Research demonstrates the good influence that industry-academia ties have, as well as the positive spillover effects that these linkages have, through a significant flow of knowledge and information between the two sides. It is considered that this results in a significant dissemination of scientific and technical knowledge, which, in turn, has an effect on economic development. According to the findings of a study that was funded by the Alfred P. Sloan Foundation and the National Academy of Engineering, academic research in a single field can frequently contribute to more than one industry, and on the other hand, an innovation in a single industry is typically the result of complementary advances in many fields of research. Keeping up with the continually shifting demands placed on the industry in terms of research and human resources presents a significant obstacle for academic institutions.

The relevance of university–industry linkages, also known as UILs, in innovation and the knowledge–driven economy argues that universities and industries should form a stronger alliance. In India, there are now a few UILs in operation. The majority of UILs had, up until this time, been concentrated mostly in the pharmaceutical and chemical industries (see Mani, 2004). Since the year 2000, the Technology Business Incubator (TBI), which is the industry interface unit of the Indian Institute of Technology in New Delhi (IITD), has been in active operation within the

Institute. This incubator was programmed and implemented by the Foundation for Innovation and Technology Transfer (FITT), which is the institute's name for its technology transfer arm. Since that time, around 15 businesses have been started from scratch on the site. In November 2006, FITT and FICCI signed a Memorandum of Understanding (MOU) in order to allow a larger University–Industry Linkage. This was done in consideration of the fact that.

28 The Indian Institute of Science is now collaborating on 22 projects in the fields of aerospace, information technology, defense, and space research with a total of eight universities, seven colleges, and seven national research organizations (Vijayakumar 2005). In a similar vein, the Society for Innovation and Development, which can be found at the IISc, runs joint university-industry projects in a wide variety of R&D fields (www.sid.iisc.ernet.in 2005). BPL and Satyam Technology in Chennai successfully implemented UILs, with faculty members forming a new IC design company and teaming up with Analog Devices of the United States to manufacture chips. Other explicit UILs have been created between IISc and foreign and domestic companies such as Nortel, Motorola BPL and Satyam Technology in Chennai successfully implemented UILs (Basant 2003). Former members 35 of the faculty at the Illinois Institute of Technology and engineering doctoral students are also employed by a small number of companies, such as Sasken and Softjin that design intricate embedded systems for the Japanese telecom market (Field Research, Bangalore, and February 2005). However, the number of projects is modest, and they are frequently impromptu. They are also limited to a select group of research institutions and technical institutes, and the majority of their partnerships are with companies based in other countries (Anthony D' Costa, World Bank Report, 2006).

1.11.5. Focus Areas 94 for Higher Education Institutions

There is a detailed list of the challenges and issues issues about various studies, research, and talks between leading academic institutions and industry institutions have determined need to be the primary emphasis of the institutions:

- Make certain that the rate of curricular modification keeps up with the rate of change in the industry;
- There needs to be Collaborated on the development of "Learning Models";
- There must be some joint Academic – Industry Degree Models that can be offered to the students to enhance the employability. ;
- Faculty are expected and supposed to Develop research-based teaching material;
- The HEIs are needed to form some alumni association and alumni network so that the reach of the HEI can be spread at a larger scale.
- There should be a mutual building of relationship that will enable them to grow more.
- Investigate the possibility of establishing endowed chairs in various facets of management.

1.12. BENEFITS OF INDUSTRY-ACADEMIA PARTNERSHIP

The industry-academia collaborations have become the reason for the rise of blockbuster discoveries over the years, and supported a large number of students to go from educational institutions to the corporate world. It has a myriad of benefits for the participants. Here is how this partnership is beyond placements,

- **Develop skills and knowledge** – While considering academics, the industry-academia partnership provides a platform for the students to address challenging research questions with real-world applications and helps them to be aware of the tangible impacts of their research while developing new skills, data, or equipment. With industry-academia collaboration, companies improved their business performances by developing new technologies and techniques, while extending the capabilities and expertise available at the firm.

- **Discovery of new synergies –** The industry-academia partnership promote the discovery of new synergies and models for companies and this collaboration provides access to expertise and research that leads to innovation, extends the resources and sharpens the competitive advantage of the companies. It offers revenue streams to institutions and increased competitiveness in funding options.
- **Promote advanced research** – The industry-academia partnership promotes advancing research and creating a skilled workforce. This leads to the gaining of work-ready talent with specialist knowledge and practical training, while universities get the benefit of having opportunities to work on the latest technologies and challenging problems.
- **Access to more resources** – Partnership with industries can help universities to get access to more study resources for funding their research and diversifying research areas, and receive feedback and guidance from the industries, while helping them further.
- **Exposure to industry jobs** – The industry-academia partnership provides a platform for the colleges to offer real-time industry jobs to the students, along with encouraging them to involve in incubator projects that are offered within the firm post-graduation to the students.
- **Full-time employment to students –** The collaboration also helps the students to turn their internships into full-time employment, which makes it a powerful tool for colleges. This results in high placement numbers that can be used to entice prospective students and corporate partners.

1.13. OBJECTIVES OF THE STUDY

1. To study the nature and work of industry.

2. To study the nature and work of academia.

3. To analyze the interrelationship between industry and academia.

4. To find out the existing gaps between industry and academia.

5. To find out how full fill the gap between academia and industry.

1.14. FUTURE SCOPE

The industry and academic partnership do have the potential and possibility to assist any emerging nation in maturing into a mature nation. There are also possibility that the money can also be raised by the contribution made by some alumni who placed in better positions. It can be done in order to impact the entrepreneurial skill level among students who are interested in the programme by using a feedback mechanism, but this must be done in accordance with particular terms and restrictions. Students should be informed about the requirements for starting a business and the government should take the initiative to open diverse entrepreneurship cells in academic institutions. This should also be included in the curriculum to educate students about the requirements for starting a business. This will allow students to focus on becoming entrepreneurs rather than becoming entangled in routine employment. The students will emerge from this experience with innovative thought, the ability to take calculated risks, and a strong desire to tackle real-world challenges. In the context of the "Visiting Professorship" programme, stringent programmes should be shaped for the systematic visits of capable persons from industry to guide students, academic and scientific staff to comprise them in coaching or research during their brief stay in the premises of the institute. These visits should be organized in such a way that they take place on a regular basis. It is recommended that the position of professor be awarded to a seasoned professional who has been working in their field for a considerable amount of time. It is possible to refer to him as a Corporate Professor, which will allow the individual to gain the recognition they deserve from everyone concerned. Numerous suitable programmes need to be implemented in order to concentrate on important and strategic areas of research, as well as to offer sufficient money for research that is either market-driven or maintains pace with the needs of the market. In the course of the review process, the technical possibility of the research output ought to be given secondary weight to that of the commercial feasibility of the research output in terms of sanction.

It may also be possible to coordinate the reordering of various research and development grant initiatives in India, which would tend to streamline the goals of the existing grant projects and bring their management under the oversight of a single management organization.

CHAPTER 2

Reviews of Literature and Gap Analysis

The literature survey is the backbone of any study. It facilitates the deep understanding and develops a deep insights of the proposed problem to the investigator. It should always be an extensive and exhaustive study so that the various aspects of the problem can be assessed and evaluated and accordingly the plan of the study can be prepared. Before proceeding to conducting any research enquiry or investigation, it is necessary for the researcher to have an adequate knowledge and information about the problem so that study can be navigated in the right direction. The reviews of papers helped to list out various functional areas of academia industry interface. For the most recent year's communication between research Institutions, Universities, furthermore, firms have turned into a huge zone of approach, as governments are trying to develop economy. Approach producers, for example, national governments, progressively consider information to be the Centre asset of present day economies and fundamental for worldwide aggressiveness. The information economy postulation, focal in the present approaches, states that the primary wellspring of profitability and aggressiveness in current economies is learning, both as info, however progressively as creation itself (Cas.tells1996).

ACADEMIA-INDUSTRY INTERACTIONS (AII)

On the eve of the new century, all of the parties involved, including industry, academia, and the government, are coming under great pressure to become more strategic, boost employability, and reduce skill gaps. According to the findings of Rajshekaran and Rajasingh (2009), there is a significant perceptional gap between academia and industry about employability skills. This gap needs to be overcome in order to improve the employability of students. The business world has the impression that the percentage of graduates who are employable drops year after year; on the other hand, there is a significant need for skilled graduates in the labour market. According to Winbladh (2004), in order for students to improve their employability skills, they need to participate in collaborative learning activities. In addition, he came to the conclusion that recent college graduates lack the employability skills that are required by businesses. Hamatteh and Jufout (2003) proposed that there ought to be established at the national level a committee that is comprised of members drawn from both the business world and the academic world for the purpose of determining the requirements of one another and seeing to it that they are met. He also suggested that there should be regular assessments of the skills that are being taught to students, as well as regular revisions of the curriculum based on the needs of industry. If these things are done, it will be possible to cut down on the costs of pre-training for newly graduated workers in industry.

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SOME MAJOR LITERATURE SURVEY

Esangbedo Olufunke Caroline et al., (2024) concluded in their study that there is the huge role of the industry-academia collaboration in enhancing and refining more educational opportunities. The study also focused on the outcomes of the industry 4.0 using the advantages of the research, innovations, creativity, patenting, publications and research & development. Their study also focused on the use of the various tools and techniques of the statistical tools which could be very useful in analyzing the data and producing the more relevant outcomes. As we know that empirical studies produce more genuine, relevant, reliable and valid inferences and conclusions because nowadays the use of statistical tools and techniques has substantially increased and it leads to the generation of more sustainable and valid outcome and findings. The researchers in their study used purposive sampling as it was more convenient for them. They also used descriptive and inferential statistics in their study. They divided the whole respondents into different groups on the basis of some homogeneous attributes. Some structural educational models were used to estimate the specific objectives of their study. Their study also makes some significant contribution to the Triple Helix hypothesis by way of enquiring the pivotal role of collaboration of the industry and academia. It is also important that knowledge must be disseminated and innovative talents should be nurtured without making any discrimination.

Caviggioli, F. and Colombelli (2023) has examined novel evidence on co-evolution patterns of the technological specialization of innovation activities of firms and academic institutions located in the same European region during the years from 2003 to 2014. We exploit a novel and unique dataset merging data on EU-funded R&D projects, universities, patents, and economic region-level data for a large sample of universities and firms co-located in geographical areas at the third level of the Nomenclature of Territorial Units for Statistics (NUTS3), which correspond to a sub-regional scale of analysis. Our results indicate the presence of substantial heterogeneity across the analysed EU regions with respect to the co-evolution of industry and academia specializations. In particular, we find that the specialization into a new technological domain is led by the local academic research system only in a few cases. We also document that a number of factors, at both the university and region levels, are associated with convergent or divergent processes in the relative specialization of the innovation activities carried out by firms and universities co-located in the same region.

Sharma Pankaj (2023) concluded in his work that Education is one of the most powerful tools for transforming the whole nation into a digitally empowered society and an economy based on knowledge or knowledge economy. Today, education and technology cannot be separated from each other they are actually interconnected. Technology plays an important role in imparting the knowledge to the students without making any discrimination. We all are witness that how much and significant role was played by technology during covid-19 pandemic. It dealt with the various aspects of the life. There was the global crisis during covid-19 pandemic and government had to impose nationwide lockdown. In that difficult period technology played a very vital role. The global crisis of the COVID-19 virus and the subsequent lockdowns imposed by the government to control the situation has forced the people to stay indoors which has impacted the education sector tremendously. Without the aid of information and communication technology (ICT), it would have been impossible to continue the teaching-learning process during this unprecedented closure of educational institutions due to the pandemic. Information and communication technology (ICT) in learning institutions has enhanced learning by greater heights. Though students from different backgrounds especially those who are from the economically backward section of the society are facing considerable number of challenges to continue the learning process with the help of online education system still with the help of information and communication technology (ICT) educational institutions all over the world are trying their level best to address the situation. In order to keep pace with the current trend of globalization, there is a need of constantly improvising our skills. Proper implementation of the National Education Policy – 2020 in its true sense has the potential to bring remarkable changes by transforming the Indian education system. The main aim of National Education Policy – 2020 is to fill the gap of present education system which is totally mechanized which develops the cramming power of the students but curbs the individual thinking capability of the students. It also interrupts the free thinking of the students. Switching the method of education from rote learning to project/ activity based or experiential learning will enrich the learning experience of the learners through hands-on training experience. It will help to promote scientific temperament among the young learners.

Cui, Z. and Li, E. (2022) narrated in their study thatthe dislocation between regional innovation and economic development directly influences the economic effect of regional innovation. However, no in-depth researches have been made on how to solve this problem. Using data from Henan Province, China, employing geographical detector technology, this paper focuses on testing whether the industry-university-research cooperation can contribute to coordinating the relation between regional innovation and economic development. It is shown that: 1) the industry-university-research cooperation in Henan Province is increasing gradually, and the network presents a core-edge structure, and the coupling degree between regional innovation and economic development is spatially unbalanced, which is similar to the spatial distribution of the intensity of industry-university-research cooperation; 2) as an important approach to effectively connect scientific researches with market demands, the industry-university-research cooperation can help form an interactive, interconnected, coupled and coordinated virtuous relation between regional innovation and economic development. Compared with the cooperation between organizations of the same type and the separate innovation of organizations, the improvement of the industry-university-research cooperation level can better coordinate the relation between regional innovation and economic development; 3) the cooperative innovation model between enterprises and universities can better promote the coupling between regional innovation and economic development, compared with many industry-university-research cooperation models. For underdeveloped areas lacking local knowledge base, industry-university-research cooperation should be considered as a long-term development strategy, especially using the knowledge sources of external universities and scientific research institutions to enhance innovation capability and achieve economic growth.

Mukherji and Silberman (2021) posit that the phenomenon of industryacademic collaboration, commonly denoted as industry-academia collaboration (IAC) or university-industry collaboration (UIC), entails a mutually beneficial alliance between academic establishments (such as universities and research institutions) and industrial entities (including companies, businesses, and industries). The establishment of partnerships between universities and industries, frequently facilitated by government action, is widely recognized as a crucial factor in enhancing regional and national innovation systems (O’Dwyer et al., 2023). The purpose of this partnership is to leverage the respective experience, resources, and capacities of the involved parties in order to promote the advancement of research, innovation, and societal improvement in a mutually beneficial manner. Fischer et al. (2019) argue that the establishment of partnerships between industry and academics serves as a means to foster the flow of knowledge and expertise. Academic institutions play a vital role in generating theoretical knowledge and conducting research, whereas industry offer valuable practical insights and present real-world issues. Collaborative endeavors encompass cooperative research initiatives aimed at resolving industry-specific challenges, propelling technological advancements, and nurturing the cultivation of innovative ideas (Alexander et al., 2020). Academic research frequently generates novel technologies that are subsequently commercialized through collaborative efforts, effectively bridging the gap between academia and practical market applications. The partnership aims to synchronize educational curriculum with the requirements of the industry, so augmenting the competencies of graduates and facilitating their seamless integration into the labor market (O'Dwyer et al., 2023). Moreover, the institution provides opportunities for internships, training programs, and workshops, hereby facilitating the exposure of students and staff members to real-world industrial experiences.

S. Zeidan1 and M.M. Bishnoi (2020) focused on to investigate the gaps between academia and industry readiness and to identify skills and abilities organizations look for in terms of assessing Industry 4.0 readiness. The study investigates skills that are essential for 21st century workforce employability and takes into account the perspectives of alumni, university professors and employers. Data for this study was collected using surveys from undergraduate students, and focus groups comprising of Industry professionals, academics and alumni. Until today, there is a lack of consensus in the literature as to what the fundamental components for evaluating industry 4.0 readiness include. This study fills this gap by combining the perspectives of industry leaders/advisors, academic faculty, alumni and undergraduate students. Thus a triangular design approach is taken by considering the opinions of all parties involved to improve the validity of the results. It also provides a more holistic view of what can be improved on when it comes to the competences provided by universities. The results of the study showed that a gap exists between graduates' skills and competencies required by the industry. The results are significant as they have practical implications for both employers and academia in bridging the skills gap.

Mehmet Erdem(2019)offered a point by point description of the successful use of Experiential Learning Techniques in a hospitality classroom setting. The authors contended that the use of such instructional approaches will connect the existing hole between hospitality training and the competencies employers anticipate from graduates of hospitality programs.

Arturas, Kaklauskas et.al (2018) have drawn the results in their study and their study observed that there is an important linkage between university and industry partnership. They used a five-point Likert scale criteria in their study for concluding their results. They took the sample size 39 respondents for their study. This study drawn various aspects for the effective assessment of available alternative academic and industry partnership to evaluate and assess the market and try to find fair assessment in the most efficient and effective manner.

Hussain, Ashaq N. (2018) has examined and proved that industry has seen fast development in the last four decades still in the present serious work market hospitality graduates face uncertainties in terms of the needs and expectations of the hospitality industry. As a verifiable truth there is a considerable hole between what educators instruct in the classrooms and needs at the real work place. Thus the paper reasonably analyses the reasons behind the hole and the factors that will overcome any issues. The result indicates some of the normal drawbacks that are distinguished by the pass out hospitality graduates are as "lacking PC preparing, Multi-lingual obstruction, Short time of internship and so forth" while as hospitality practitioners have emphasized on some significant skills that should be infused in hospitality graduates which would assist them with being the piece of hospitality industry for example "functional skills, the board skills, human connection skills, and so on" Hospitality graduates need the previously mentioned skills that will empower them to work really in the hospitality sectors. These skills are intended to make them more useful to their employers and the customers they will serve.

Haspel, Patrick (2018) concluded in his study that Cadence Academic Network is to advance the multiplication of driving edge technologies and methodologies at universities prestigious for their designing and design greatness in the areas of check, design, and execution of microelectronic systems. Adopting a four-pronged strategy of enlisting, advancing the Cadence university software program, establishing scholastic partnerships, and advancing applicable events all over the planet, Cadence facilitates the sharing of innovation expertise with universities, research institutes, and industry advisors.

Sergio, Rico (2018) concluded in their study that despite the shared advantage of the industry-the scholarly community partnership, the degree of joint work is still low. Thus, the interest in interfacing research and practice has increased as of late in the scholarly local area. Objective: This research aims to design and apply approaches to further develop the information trade between scholastic researchers and software designing practitioners. Procedure: This work should be visible from a design science perspective. Following the design-science worldview, the information in regards to a peculiarity is acquired through the design and assessment of solutions that apply in a specific setting. Consequently, this research work proposes and evaluates approaches to connect the correspondence hole. Results: Two approaches have been investigated and to some degree assessed. The SERP-scientific classification design that can be used to describe and interface research results and industry challenges, and quick reviews to foster correspondence among industry and the scholarly world. Conclusion: This thesis will give exact proof of the utilization of cooperative approaches to further develop industry-the scholarly world correspondence and draw nearer research and practice.

Dr. Nimish Gupta (2018) carried out his study to highlight the importance of the academic and business empowerment. He concluded in his research that there is a vital role of the higher education in empowering business organizations. The main importance of his study was to point out the significance of the higher education, industry, business and their sustainability over each other. He emphasized that there are various strategic approaches and implementing practices on this subject and discipline suggested by many models and researchers to implement the strategies and policies in a manner that can effectively produce the output that can make some sense for the industry, academics and business. As we all know that higher education has become very important and necessary for the holistic and all round development of human kind. Earlier, these all were not in the reach or access of everybody. Nowadays, improvement in technology has brought so many changes in education system and it helped in education to make it more readily available to one and all. This has become in the reach of majority of the people. There is a set of economic, political and legal framework for operating and functioning the business. Every business always operates in an uncertain environment. Now the challenges faced by business are global and international because now the concept of liberalization, privatization and globalization was introduced in 1991. Since then the challenges are international. For the purpose of meeting these challenges effectively, all the business organizations need specific knowledge and expertise and also needed knowledgeable and qualified experts and workforce. Innovative and sustainable practices are also needed. In this regard the learning organizations may be very much effective for the sustainability. Education is the main motivational factor behind the sustainability of such practices. The main observations of his paper was to identify the challenges which are generally faced by the business houses and effectively these can be addressed by the existing solutions. Because the customer satisfaction is the ultimate goal of every business. There are many strategies which are based on educational set up and learning societies. Many stakeholders are around there and it is the responsibility of the business towards the society to satisfy all the stakeholders of the society. In conclusion, it can be said that efforts should be made towards the main challenges which are faced by the HEIs.

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Lorenz Lassnigg et.al (2017) in their study that there is a triangle among HEIS, knowledge and industries. This triangle gives a very logical and scientific structure in continuation with taking some two or three war connections included in the study. They used the interpolation and extrapolation techniques to draw their results. They used three-way relationship shown by knowledge triangle. There may be some knowledge triangle exercise which may foster the industrial growth through industry academia interaction. The main feature of their study is to develop the industry-academia interface and effectively implementing the knowledge triangle practices.

Chhikara, Manoj (2017) has provided the conclusions of his study that the constitutes the base for most of the industrial products used in our life. While the scholarly world contributes towards basic research; that research in itself does not translate into a product. This is the place where Industry plays a key job. Industry adapts the basic ideas and applied research to form, create and showcase a product for use in society. Consequently, the coordination between research performed at scholastic research institutions and its application in Industry becomes an essential necessity.

Kaur, JasbirSodi (2017), has given a reformation of the system and has conducted her study by preparing three Questionnaires which includes for Students, Universities and Corporates respectively. From his study the author has concluded that Guest Lecturers represented from Industry, Joint Seminars for faculty and students, Public private partnership, Research collaboration, Certification system are some of the ways to bridge the gap.

Prof. Lennart (2017) presented an approach to bridge the gap through Learning Factories, found that Technical and Social Competency match the requirements of the industry but there exists a gap regarding the methodological competency.

Saad Mohammad et al., (2017) emphasized in their study that there are various opportunities and possibilities and challenges also by National System of Higher Education with regard to align themselves in tune with the needs of the Regional and National Innovation System in developing countries and Least Developed Countries. It can be achieved by making comparison of various practices of industry-academia interface across all the selected countries for the study. The study made to develop the links between the academia and industries for motivating such practices and research habits. For this purpose, we have to develop a research-oriented mind set so that the research culture can be developed.

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Sushil Sharma, Ekta Sharma, Yatendra Sharma (2015) did their study on Academia-industry interaction: A win-win partnership. The outcome of their study was that there is a huge need of academia-industry partnership if we want to develop our society. Without their effective partnership, the development of the every stakeholders of the society is not possible. In this regard, businesses can play its role in improving the knowledge base of the academicians; provide them resources timely so that final cost of the innovation and research and development can be brought down. The faculty members need to update and refresh their knowledge time to time as we are living in a dynamic world. The role of the effective administration cannot also be ignored in this system. They have their own role. It should be noted that whether the expertise and mastery is being used in the favor of society or not. Its application must always be for the helpful and gainful purposes, broadening and extending the educational system and program.

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Kapil, Prachi (2014) did their study on identifying the skill gap of the students and how these skill gaps can be bridged with the help of the collaboration of industry and academia. The main motive of the study was to highlight the importance of the current and future initiatives those will be aiming onto providing a shape to the interdependence of both of them (industry and academia). In Indian context, the main focus needs to be on the development of research and development initiatives. There is n urgent need to bring the transparent governance system in management schools and institutions and attractive salary package to the faculty members. As the gap between academia and industry is increasing day by day that is why the industry and government must come together with folding hands. Higher learning must be in the focus of the HEIs.

Tiwari, Rajesh et al. (2014) did their study based on North Indian Universities. They took the sample from the North Indian Universities for drawing their conclusions with regard to highlight the importance of the industry- academia interface. The main objective of this study was to address the major issues related to the industry-academia interface. For their study they collected the information from the faculty members and teachers of the universities of North India. They tried to trace the exploratory factors which affect the industry-academia collaboration and interface at a larger extent. They considered various variables for the study and collected primary data for analyzing these variables. For collecting the primary data, random sampling method was used. Data was collected with the help of structured questionnaire. Final questionnaire was prepared having done the pilot study. The study revealed that collaboration for skill development is considered as the most important factor and it can enhance the employability as it directly related to the making the students fit for the industry needs.

Joseph, K. J. and Abraham, Vinoj (2014) conducted their study on a very relevant topic- university-industry interaction and Innovation in India. In their study the researchers focused on the modernization of the education, innovation and university-industry interaction. They realized in their study that innovation is very necessary for bringing the change in the state of mind of the stakeholders who are directly involve in the process of industry-academia interface and collaborating all those efforts which may be put forward in this regard. They took the example of developed states like Gujarat, Maharashtra, Tamil Nadu, Karnataka and Delhi as well. They found that only 14% of the organizations were not putting their resources into research & development projects. They also concluded that very few firms are actively involving in the process of collaborating themselves with the industry. The number of such firm was very low and their frequency was very low. They also gave the findings in their study that government approaches are very friendly now and the policies of the government are being formulated in such a manner that it will be helpful in this regard.

Tiwar R. et al., (2014) evaluates the impact of teaching and industry experience of university teachers with industry academia interactions. The industry academia interface is underdeveloped in India. Except few premier institutions, majority of the academia institutions work isolated with industry. Poor employability of graduates is a cause of concern. Effective industry academia interface provide opportunity to enhance the employability of graduates and improve research and academic outcomes. The survey method was used for collection of primary data. Faculties from private and public universities were respondents for the study. The data was analyzed by ANOVA. The results show that industry experience of faculties had no significant impact on industry academia interface. Senior faculties were more optimistic about willingness of industry and regulatory agencies for industry academia interface. Young faculties were willing to participate in industry academia interface. Majority of faculties were dissatisfied with involvement of student in industry projects. Industry academia interface may be made more effective by involvement of young faculties in execution and involvement of students for projects. Senior faculties should guide the young faculties for proper execution of projects and setting up of the collaborations.

Joshi, K.M. (2013) conducted his detailed study based on the investigation and enquiry of the Indian Advanced Education System and its challenges which have to be addressed. The main theme of his study was to target the administration of the advance education and how to comprehend the idea of privatization in advance education system in India. Study mainly based on secondary data and these secondary data was collected from the archives of Ministry of Human Resources and Development, UGC, AICTE and other bodies and associations. His investigation showed that the development is open for all but private sector is doing dominantly in education system. There are various complexities in Indian advance education system because India is diverse country having different religions, caste and creed. There are also many complications in terms of financing, value, effectiveness, quality, internationalization and many more.

Nangia, K. Vinay,and Pramanik, Cashmira (2011) did their study on the model of academia and industry interface and examined in their study that there are many issue and challenges before

Indian universities and academic world and colleges while collaborating with the industries and other corporate world. The stakeholders should focus onto the conducting research of high quality. Their research studies about various barriers and challenges which can adversely affect the industry and academia interaction and then developed a model that advocates various approaches of new collaborative opportunities which are possible between industry and academics. In today's scenario, there is an urgent need of developing trust among all the stakeholders of the academia and industry interface. There is a need of close tie ups between industry and academia for the holistic development of the students so that they can be placed in industries. Students should have adequate research facilities and infrastructure so that they can learn the skills and experimental learning can be enhanced.

Vinay K. Nangia, Cashmira Pramanik (2011) assesses their study the impact of teaching and industrial experience having industrial experience and exposures. As far as the industry and academia is concerned, it is still in underdeveloped stage, except some premier institutions. Actually the main problem is isolation that mean most of the institutions in India are working exclusively. They do not want to work with industry. There is some reluctance with go together with the industry. There is a main issue of poor employability because many graduates are not employed and it is a major concern for the graduates or post graduates. The whole study was based on primary data. Faculties from private institutions and universities were selected as the respondents. The survey method was used to collect the primary data. Various statistical tools and techniques were used to analyze the primary data like ANOVA and other techniques. The findings of the study indicate that it is not an issue to have an industry experience for the faculty members because it does not make an impact on the industry-academia interface. But now, young faculties are willing and very keen to participate in such initiatives.

Kurtulus Kaymaz Kadir Yasin Eryigit (2010) conducted their study on a very relevant topic-university-industry interaction and Innovation in India. In their study the researchers focused on the modernization of the education, innovation and university-industry interaction. They realized in their study that innovation is very necessary for bringing the change in the state of mind of the stakeholders who are directly involve in the process of industry-academia interface and collaborating all those efforts which may be put forward in this regard. They took the example of developed states like Gujarat, Maharashtra, Tamil Nadu, Karnataka and Delhi as well. They found that only 14% of the organizations were not putting their resources into research & development projects. They also concluded that very few firms are actively involving in the process of collaborating themselves with the industry. The number of such firm was very low and their frequency was very low. They also gave the findings in their study that government approaches are very friendly now and the policies of the government are being formulated in such a manner that it will be helpful in this regard.

Siegel et al. (2003) highlighted the issues in their empirical study related to University Industry Technology Transfer (UITT). For concluding the results of the study, five universities were selected for the study. The findings of the study were clearly imperative towards the comprehensions in relation to the colleges, universities and other HEIs. There should be comprehensiveness towards the logistics supports, research facilities, working conditions, administration and other amenities in any HEI. The rewards and honors can be introduced in the educational system to motivate the academician and scholars as well to do more and quality research. There are some significant barriers in developing the norms of the research. These need to eliminate to develop a smooth environment.

Vincent F. S. Wu (2000) conducted his study in Taiwan in relation to university-industry. The study was undertaken primarily for suggesting some directive guidelines to the government of Taiwan. Government of Taiwan needed to some assistance to help set 'middle people' for research centers. All these were needed for mechanical advancements, and other developments of the country for the societies. There were a strong feeling and realization among the people of that country that there must be sustainable developments that will sustain for a long time. It will assist and well spring of technologies to bring the resources together with the universities.

GAP ANALYSIS

Organizations need a trained staff and innovative sustainable practices to successfully address complex issues. Only learning organizations, of which education is a significant driver, can be successful for long-term sustainability. The capacity to endure with the possibility for long–term well–being maintenance is referred to as sustainability. Innovative sustainable practices are critical to building a long-term company that benefits consumers, stakeholders, and society. In order to tackle the problems of today's corporate environment, education and learning, as well as practices of pioneering sustainability solutions, are critical. The obstacles that Academia-Industry cooperation are now experiencing include concept awareness, identification, assessment, protection, and commercialization. Today's skill development requirements are diverse, and they depend heavily on cooperation between industry and academic institutions, knowledge creation, innovation, and technology transfer. As a result, it will aid in the promotion of new businesses and entrepreneurs. Collaboration between industry and academia generates new research and development agendas, as well as fresh investment in research fields, resulting in long-term competitive advantages. It establishes a form of synergy in the realm of technological capabilities and ensures the commercial application of the greatest ideas for the benefit of society. The partnership between industry and academics aids in the effective employment and use of human resources in both the public and commercial sectors. This partnership aids in the search for and development of new research and development areas.

NEED FOR THE PRESENT STUDY

Businesses may utilize the academic community's learning base to increase their cost, quality, and all-around focused metrics, reducing their dependency on distant talent and spending on internal R&D. Also benefits from the academia's administration improvement initiatives, which renew and update the learning base of business specialists. Institutions benefit from the satisfaction of seeing their learning and mastery put to use for socially beneficial and profitable purposes, the broadening and expanding of the educational programme and the viewpoints of educators and scientists, and thus improving their assurance as well as that of understudies, secure preparing and final situations all the more effectively for their understudies based on the respect earned from, and the relationship built with industry.

The educated community industry relationship idea recommends that this affiliation has to be:-

1. Most interactive and collaborative in character, according to the educated community industry connection concept.
2. It is the obligation of both business and educational institutions to foster mutual respect and recognize the critical role they play in meeting society's needs.
3. This entails creating a research and development synergy.
4. That it should be a network in which all stakeholders collaborate and participate in the most suitable way possible.

CHAPTER 3

RESEARCH METHODOLOGY OF THE STUDY

This chapter contains the objectives and description of the research method used in this research. First of all objectives of study are given as below:

OBJECTIVES OF THE STUDY

6. To study the nature and work of industry.
7. To study the nature and work of academia.
8. To analyze the interrelationship between industry and academia.
9. To find out the existing gaps between industry and academia.
10. To find out how full fill the gap between academia and industry.

FUTURE SCOPE

The industrial-academic partnership has the potential to assist any emerging nation in maturing into a mature nation. Some alumni can also raise money in order to impact the entrepreneurial skill level among students who are interested in the programme by using a feedback mechanism, but this must be done in accordance with particular terms and restrictions. Students should be informed about the requirements for starting a business and the government should take the initiative to open diverse entrepreneurship cells in academic institutions. This should also be included in the curriculum to educate students about the requirements for starting a business. This will allow students to focus on becoming entrepreneurs rather than becoming entangled in routine employment. The students will emerge from this experience with innovative thought, the ability to take calculated risks, and a strong desire to tackle real-world challenges. 17 In the context of the "Visiting Professorship" programme, stringent programmes should be shaped for the systematic visits of capable persons from industry to guide students, academic and scientific staff to comprise them in coaching or research during their brief stay in the premises of the institute. These visits should be organized 6 in such a way that they take place on a regular basis. It is recommended that the position of professor be awarded to a seasoned professional who has been working in their field for a considerable amount of time. It is possible to refer to him as a Corporate Professor, which will allow the individual to gain the recognition they deserve from everyone concerned. Numerous suitable programmes need to be implemented in order to concentrate on important and strategic areas of research, as well as to offer sufficient money for research that is either market-driven or maintains pace with the needs of the market. 4 In the course of the review process, the technical possibility of the research output ought to be given secondary weight to that of the commercial feasibility of the research output in terms of sanction.

It may also be possible to coordinate the reordering of various research and development grant initiatives in India, which would tend to streamline the goals of the existing grant projects and bring their management under the oversight of a single management organization.

The main purpose of any research is to discover some new facts and to add on some new knowledge. Every research is conducted in a set framework applying some specific knowledge and expertise that is called research methodology. It explains and describes a model and an approach that identifies any problem and decides that which research process will be applied to find out an optimum solution for the problem that can satisfy the objectives of the research study in the best way,(Bryman and Bell, 2077).

Generally research methodology provides some insights about to develop the better and deep understanding of the available previous studies those are related to the problem. It is used to plan out every detail regarding the proposed research study. It is used as an effective tool for conducting any research study as it combines various statistical tools and techniques which have to be employed for the study. This chapter in every research is the backbone of the study because it decides that what are the objectives of the study; what hypothesis have been formulated; which data collection method will be used; what statistical tools will be applied for drawing the conclusions?

The classification of research methods can be done on different basis. We need to understand the differences between qualitative and quantitative approaches. Although there are various research methods are available yet it is to be decided that which research method can be used for the proposed study as per the nature of the study. The nature of the proposed study always decides that what research methodology should be used to draw the appropriate conclusions. There msut be deeper understanding for the proposed study.

Qualitative approach in research is generally used in social science research for drawing the inferences. Social science research is conducted for now the social traits, social behavior, psychological studies and other that kind of studies. In such kind of researches, data can be collected with the help of interviews, questionnaires, observation, documents, mailed interviews, schedules and so on.

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Research Design:

When we do any study or task, we need to prepare an outline or blueprint of that activity before initiating that activity. This is an outline in which every steps needed for the study is considered. This is an exhaustive exercise because the success of such activity is largely depend upon that how efficiently you have prepared that blue print or outline. Actually, this blueprint or outline is known as research design in research methodology.

According to Kerlinger (2005) "Research design is the plan, structure and strategy of investigation conceived so as to obtain answer to research questions and control variances." In research design, all the requirements and resources required for the study are discussed that from where resource will be made available, from where data have to be collected, which method will be applied to collect the data, which statistical tools will used for classification of data, analysis of data, and what is the duration needed for the study. It is also decided in research design that what will be the financing resources? Some considerations are taken into account like what, where, when, how much and by what mean combines a plan of study or research design. As we know that conducting any research has become a scientific task that follows a systemic approach or process. There are certain components of a good research design. These components are as follows:

- Sources of information to be explored;
- Nature of the study or problem;
- Aim and objectives of the study;
- Socio-economic context of the proposed study;
- Scope and geographical area to be covered by the proposed study;
- Duration to be taken by the study;
- Dimensions and parameters of the study;

- Statistical tools and techniques to be used for the purpose of collecting and analyzing the data.

The proposed present study is empirical in nature based on mainly primary data that has been collected through the structured questionnaire circulated through mail and other sources. In addition to that, secondary data has also been used and collected for the purpose of extensive literature survey in order to develop the deep understanding of the proposed study.

Since every study or problems is always unique in itself and formulates some specific aim and objectives. The process of every research starts with the identification of the problem or determining the area of study which has to be conducted. Then after the objectives of the study or problem are decided that what exactly investigator want to conclude at the end of the study. This process is followed by extensive literature survey, data collection, classification of data, editing of data and analysis of data, interpreting the results and report writing of the study.

The component part as suggested by Young is relevant enough. For the purpose of the present study, all these components have been taken into consideration. It was a serious exercise and each and every component discussed seriously and included in the present study so that conclusions and findings can be rationally drawn. Keeping in mind the nature of the present problem, objectives of study, types of information needed, the geographical are to be covered, the time duration, tools and techniques of the data collection and the nature of the universe, the impact evaluation research design have been used in this study. While taking the decision for applying the research design some of the most needed and essential have been considered at the serious note. It was a tough task to review of the pertinent literature, experience survey and analysis of insight stimulating cases were the major essential which were consciously taken for granted for the planned scientific study of the problem in hand as it all was necessary for the study.

Research design

As far as the research design is concerned, it is a systematic methodology and preparation of an outline that indicates the subtle elements of the methods significant for getting the information expected to structure or deal with the assessment issue. It always gives the overall structure to be used as a helper to accumulate and investigate data. The plan of system used to accomplish set objectives of research. It will include hypotheses, information assortment methods, sample design, information analysis methods, and scope of study, among others.

This research is a descriptive, empirical and observational research, which tries to get the data from the respondents through the structured questionnaire made in the wake of considering the objectives and hypothesis of the study.

Sampling Technique

"Sampling techniques give a scope of methods that empower one to decrease how much information required for a study by considering just information from a sub-bunch instead of every possible component." (Saunders et al, 2009, p.210). There exist two types of sampling:

A. "Likelihood sampling, where the chances of each case being selected from the populace which is known and is usually equivalent for all cases.

B. Non-likelihood sampling, where the chances of each case selected from the all-out populace is not known, making it impossible to answer research questions" (Saunders et al., 2009, p. 213).

Data Collection

Once the research design and research plan or blueprint is decided

After deciding the research design and sampling frame, the data collection starts. On the basis of the nature of the identified problem or proposed study, the data collection (primary or secondary) is selected. The techniques for collecting the data is directly related to the tentative outcomes of the proposed investigation. Primary data are those which are assembled once more and suddenly and in this way end up being exceptional in character and discretionary data are those which have just been accumulated by someone else and which have just been gone through measurable strategy.

Primary Data

Primary data for this research has been collected through structured questionnaire. This questionnaire designed in the wake of considering the objectives and hypothesis. Two sets of questionnaires has been prepared. First set of questionnaire are related to students and faculty members of the universities and HEIS. Second set of questionnaire is related to factors motivating industry for academia collaboration and finding out potential areas where Industry's participation with Academia is more effective.

Secondary Data

Start of the research works started from the secondary data collection. The data collection will include Journal, Magazines and Internet. Top to bottom study of various research papers and thesis work on similar topics has been by the researcher. This will help the researcher with understanding the subject appropriately.

Scaling and Measurement

A structured questionnaire consisting of multi-thing scale and measures has been used with specific response options and alternatives. Measures are based on rigorous calculated improvement and hypothetical establishment all the constructs and variables are measured with the assistance of established scales from the writing.

Two types of questionnaires has been constructed. First set of questionnaire will contain the questions for student and employees connected with factors persuading the scholarly community for industry point of interaction and second piece of questionnaire consist of questions connected with barriers for the scholarly world industry interface.

Second part of the Questionnaire will deal the questions connected with Potentialities of Government and not for benefit bodies. These items were measured on a five-point Likert scale that went from "strongly agree" to "strongly disagree".

Sample size

S.No.	**Target Population**	**Sample size**
1	Students	200
2	HR Professionals & Recruiters	50
3	Faculty Members	50
4	Higher Educational Institutions (HEIs)	10
Total Sample Size		**300**

Data Analysis and Statistical Tools

The data has been regularly dispersed because of its diverse nature, that is why information have been gathered using an estimation scale, difference covariance networks within each phone of the outline has been examined from the same population fluctuation covariance network, and the specimen size has been fixed and set for acknowledging the parametric strategies, a researcher may use parametric procedures. SPSS Version 23.0 and AMOS Version 23.0 may or have been applied to analyze the data. Cronbach's Alpha may also be applied to determine the data's reliability.

a. Descriptive statistics

b. Factor analysis

c. Confirmatory factor analysis

d. Correlation and Regression analysis

CHAPTER 4

ANALYSIS AND INTERPRETATION OF THE DATA

This chapter has provided the detailed data analysis and interpretation. This chapter has given a deep insight on so as to how much these factors are important for the better relations between Industry and Academia.

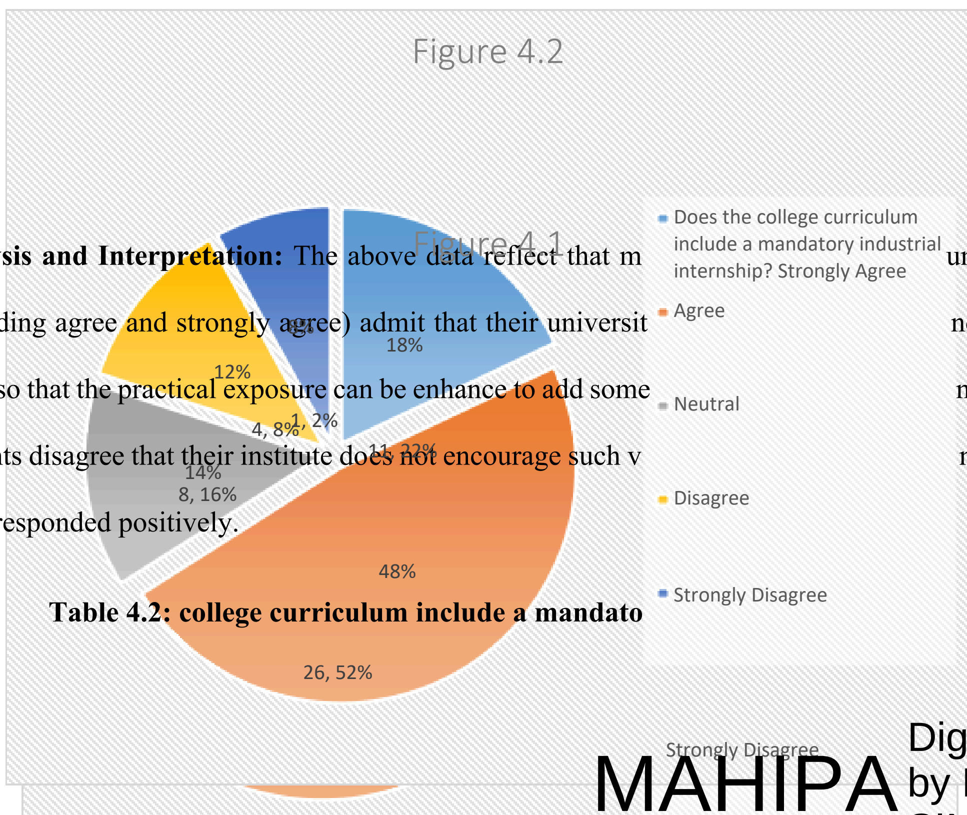
Analysis of Responses from the Students

Table 4.1: university encourage industrial visits for students

Question	**Options**	**Response**	**Percentage**
Does your university encourage industrial visits for students?	Strongly Agree	44	22
	Agree	104	52
	Neutral	32	16
	Disagree	16	8
	Strongly Disagree	4	2

Total		200	100

Question	Options	Response	Percentage
Does the college curriculum include a mandatory industrial internship?	Strongly Agree	36	18
	Agree	110	55
	Neutral	28	14
	Disagree	16	8
	Strongly Disagree	10	5
Total		**200**	**100**



Analysis and Interpretation: The above data reflect that m und 72% (including agree and strongly agree) admit that their universit ndustrial visits so that the practical exposure can be enhance to add some nly 10% students disagree that their institute does not encourage such v ntage of them responded positively.

Table 4.2: college curriculum include a mandato

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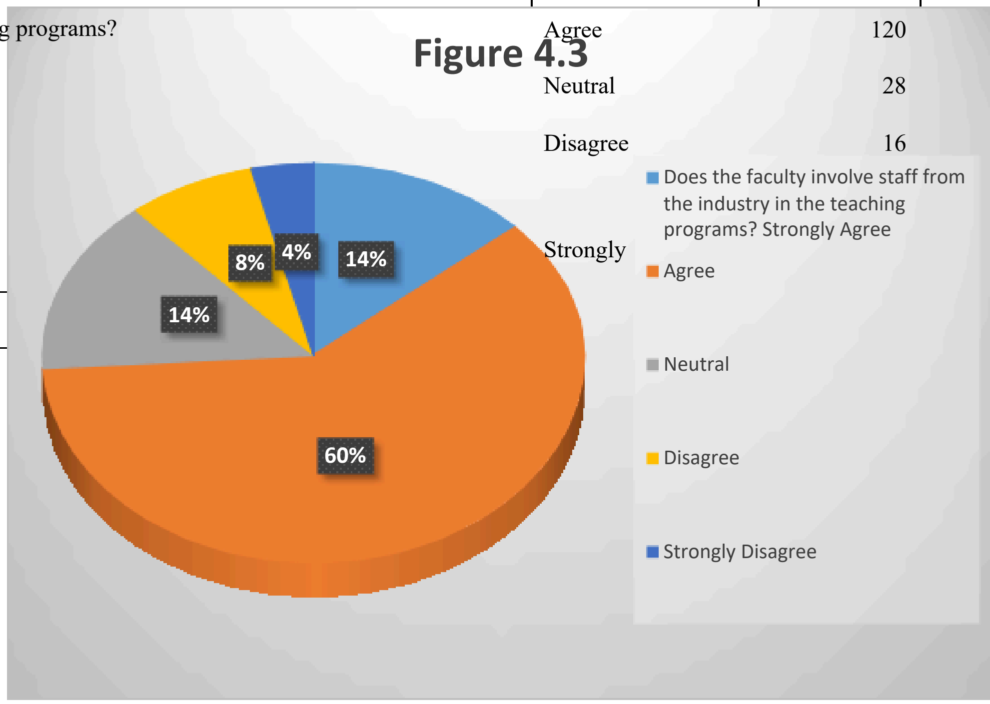
Analysis and Interpretation: Internships play a crucial role in building a successful career. They offer practical experience that complements theoretical knowledge gained through education. Internships provide opportunities to learn new skills, gain industry knowledge, and network with professionals in the field. Additionally, internships allow students to apply classroom knowledge to real-world situations, which enhances their employability. Internships don't always relate directly to your desired career field. Pursuing internships in adjacent fields may help you develop transferable skills, learn about new interests or reaffirm your preferred career path. For example, a public relations student may complete an operations internship with a local sports team to develop their event organization skills.

It was found that majority of the students admit that there is mandatory internship in their curriculum. 18% admits strongly, 55% agree and 14% were neutral. Only 13% responses were negative.

Table 4.3: Faculty involvement in Industry

Question	Options	Response	Percentage

Does the faculty involve staff from the industry in the teaching programs?	Strongly Agree	28	14
	Agree	120	60
	Neutral	28	14
	Disagree	16	8
	Strongly		4
			100

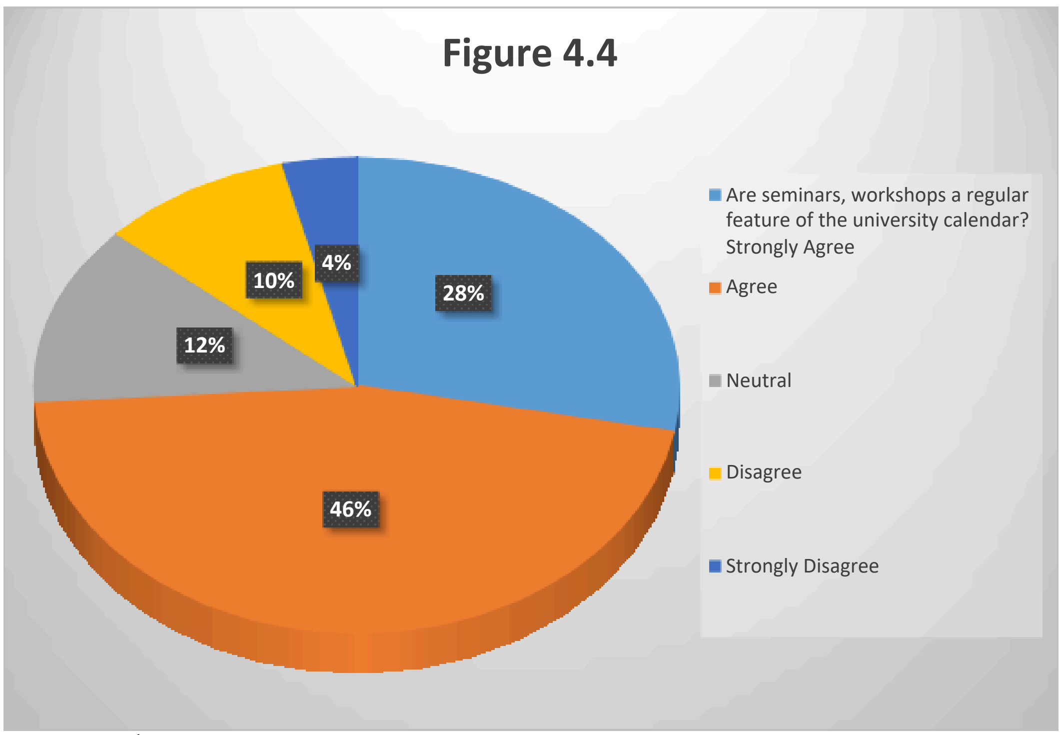


Analysis and Interpretation: Today we are talking about experiential learning, E-learning, flipped classrooms and what not. With all these innovations in the teaching methods do we still get the desired results? We still cope with issues like employers complaining about lack of skills in fresh students passing out of colleges, their lack of employability extra. Even the best students passing out of reputed management colleges and engineering colleges still have to cope with the issue of unemployment. It can be concluded with the help of above data that most of the students admit that most of the faculty members have some industry exposure in their teaching pedagogy. 148 students out of 200 students have agreed that the teachers are having the industry involvement while teaching.

Table 4.4: Workshops and Seminars are regular feature

Question	Options	Response	Percentage
Are seminars, workshops a regular feature of the university calendar?	Strongly Agree	56	28
	Agree	92	46
	Neutral	24	12
	Disagree	20	10
	Strongly Disagree	8	4
Total		**200**	**100**

Analysis and Interpretation*:* Nowadays, the market is very much demanding and we often come across the issue regarding the level of higher education not meeting the industry expectation. To bridge this gap and equip the students of current generation with new-age technologies, seminars and workshops play an imperative role. Ensuring a proper flow of knowledge Seminars and Workshops assist in passionate interaction and active participation boosting the skills and expertise of students. Importance of seminars and workshops for students is often acknowledged as a prime concern. Keeping in mind the importance of seminars for students and the benefits of workshops for students*,* seminars and workshops are an innovative and welcomed step towards modern education. Nowadays seminars in schools are encouraged recognizing the importance of seminars for

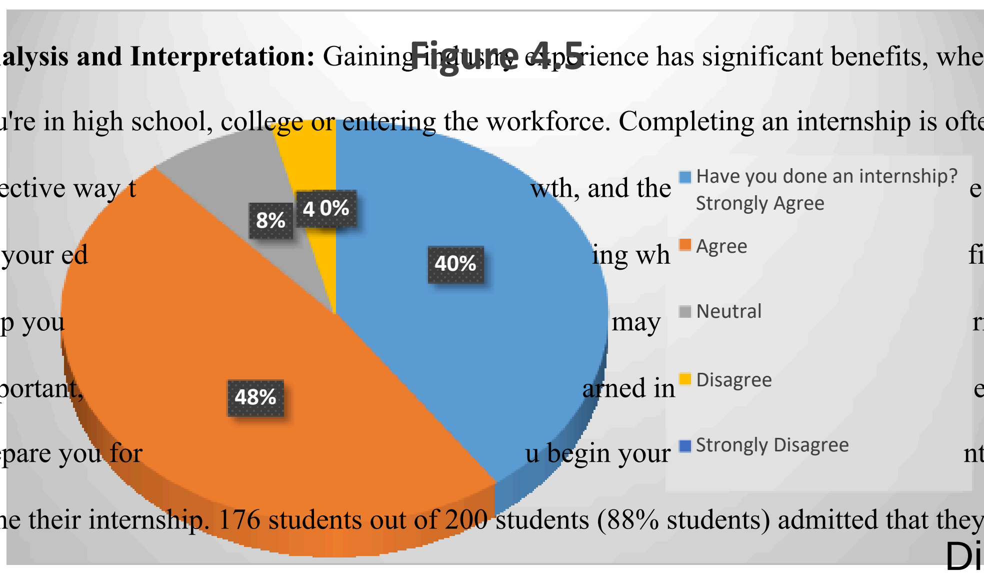


students at an early age.

Total 148 students out of 200 students (74% students) admitted during filling the questionnaire that their institute frequently and regularly organize seminars and workshops, guest lectures, invited talks. Maximum students responded positively that this is a regular feature of their institution.

Table 4.5: Status of Internship

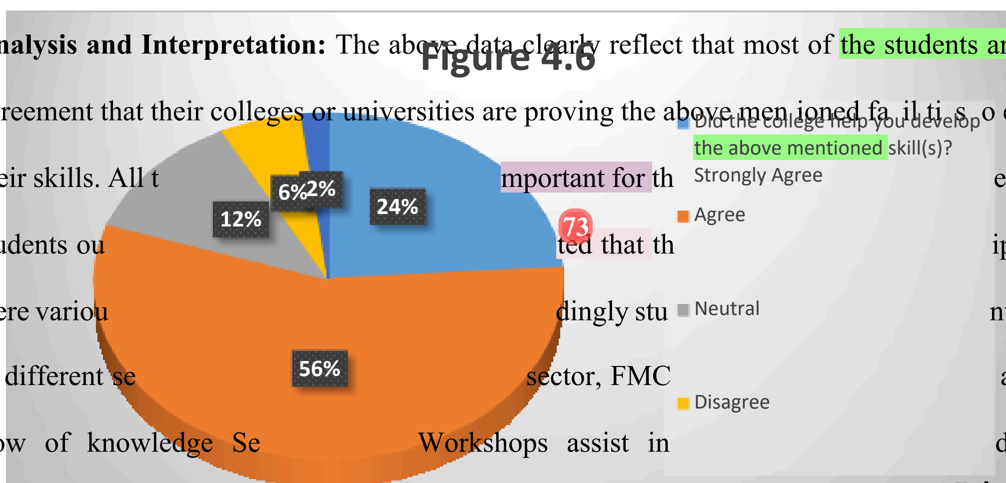
Question	Options	Response	Percentage
Have you done an internship?	Strongly Agree	80	40
	Agree	96	48
	Neutral	16	8
	Disagree	8	4
	Strongly Disagree	0	0
Total		**200**	**100**



Analysis and Interpretation: Gaining industry experience has significant benefits, whether you're in high school, college or entering the workforce. Completing an internship is often an effective way t wth, and the e based on your ed ing wh ficial may help you may rning is important, arned in elps prepare you for u begin your nts have done their internship. 176 students out of 200 students (88% students) admitted that they have done their internship. There were various internship options available and accordingly students were undergone their internship in different sectors like manufacturing, service sector, FMCG, IT, R & D etc.

Table 4.6: Development of Skills

Question	Options	Response	Percentage
Did the college help you develop the above mentioned skill(s)?	Strongly Agree	48	24
	Agree	112	56
	Neutral	24	12
	Disagree	12	6
	Strongly Disagree	4	2
Total		**200**	**100**

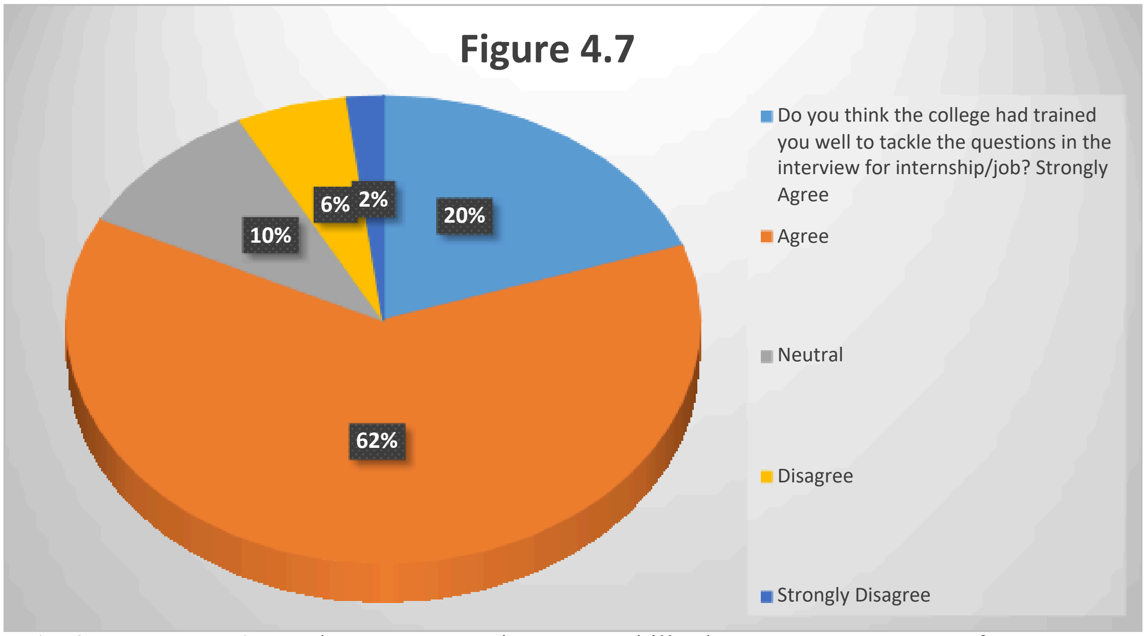


Analysis and Interpretation: The above data clearly reflect that most of the students are in the agreement that their colleges or universities are proving the above men ioned fa il ti s o enhance their skills. All t mportant for th ents. 176 students ou ted that th ip. There were variou dingly stu nternship in different se sector, FMC a proper flow of knowledge Se Workshops assist in d active participation boosting the skills and expertise of students. Importance of seminars and workshops for students is often acknowledged as a prime concern. Keeping in mind the importance of seminars for students and the benefits of workshops for students, seminars and workshops are an innovative and welcomed step towards modern education. Nowadays seminars in schools are encouraged recognizing the importance of seminars for students at an early age.

Total 148 students out of 200 students (74% students) admitted during filling the questionnaire that their institute frequently and regularly organize seminars and workshops, guest lectures, invited talks. Maximum students responded positively that this is a regular feature of their institution.

Table 4.7: Regarding the Training to the students

Question	Options	Response	Percentage
Do you think the college had trained you well to tackle the questions in the interview for internship/job?	Strongly Agree	40	20
	Agree	124	62
	Neutral	20	10
	Disagree	12	6
	Strongly Disagree	4	2
Total		**200**	**100**



Analysis & Interpretation: There are some important skills those are necessary to face any interview to get selected. Effective communication, active listening for deeper connection, unleashing problem solving and critical thinking, embracing adaptability and flexibility, and leadership and teamwork are the skills those are crucial for the students. Effective communication skills are crucial in every aspect of our lives, and they play a significant role in the interview process. Being able to articulate your thoughts clearly and concisely, actively listen to the interviewer, and ask insightful questions demonstrates your ability to communicate effectively.

Practice speaking confidently and maintaining good eye contact. Pay attention to your body language, as it can convey confidence and engagement. Active listening is an often underrated skill, yet it plays a pivotal role in establishing rapport and understanding during interviews. By attentively listening to the interviewer's questions and comments, you demonstrate genuine interest and thoughtfulness in your responses.

Avoid interrupting and take a moment to comprehend the question or statement before offering your answer. Develop active listening skills by engaging in conversations with friends, colleagues, or mentors, actively seeking to comprehend their perspectives and practicing reflective listening.

Employers highly value candidates who possess strong problem-solving and critical thinking abilities. Interviews often include scenarios that require quick thinking and efficient problem-solving. Prepare by reflecting on past challenges you've faced and the strategies you employed to overcome them. Emphasize your analytical skills, creativity, and decision-making prowess.

Hone your critical thinking by engaging in puzzles, riddles, or hypothetical scenarios. Such exercises will sharpen your problem-solving acumen and enable you to navigate challenges with ease, leaving a lasting impression on interviewers.

Highlight your adaptability by showcasing instances where you adjusted your approach or thrived in diverse settings. Practice flexibility by actively seeking new experiences, volunteering for varied projects, or taking on different roles. Such endeavors will not only broaden your skill set but also demonstrate your capacity to embrace change and excel in any work environment.

Employers value candidates who can lead teams, inspire others, and collaborate effectively. Highlight your leadership experiences, such as leading projects or mentoring others. Discuss how you've motivated and influenced team members to achieve collective goals.

Demonstrate your ability to work well in teams by providing examples of successful collaborations and effective communication within a group setting. Leadership and teamwork skills show that you can contribute to the organization’s success and work harmoniously with others.

Mastering these key skills is essential for excelling in your job interviews. By developing effective communication and active listening abilities, honing critical thinking and problem-solving skills, showcasing adaptability and flexibility, demonstrating emotional intelligence, and investing time in thorough preparation and research. The majority of the students that 82% students are in the agreement that their institutes are offering all such facilities which have been mentioned above.

Response from the Faculties

As chief architects of curriculum, faculty are largely responsible for student learning outcomes. Given the cost of higher education and the amount of debt students incur, higher education stakeholders want to know if higher education is worth the investment. Student career preparedness is an important goal of higher education. While research has been dedicated to college student development, career decision-making, and student-faculty interaction from a student perspective, little is known about the faculty perspective and their role in student career preparedness in a specific articulated way. This study recognizes that students can acquire career preparedness through background contextual affordances, such as exposure to social and learning opportunities, and directly through learning experiences. Faculty can influence these through their interactions with students. This study identified environmental conditions, environmental response, social knowledge, self-knowledge, socio demographic characteristics, and career influences on faculty behavior related to student career preparedness. Faculty believe that students need support and guidance in determining their career direction, especially first-generation students; faculty feel the goal of preparing students for employment after college is an essential or very important priority; faculty feel confident in their ability and willingness to support students' career preparedness in varying degrees and in multiple ways; responsibility for student career preparedness is shared among the institution, students, and least of all faculty, but ultimately, students' career preparedness is dependent on students' willingness to accept responsibility for it and seek help when needed. A sample of fifty faculties were taken for this study.

Table 4.8: Status of faculties regarding working with industry

Question	Options	Response	Percentage
Have you ever worked in the corporate field?	Yes	38	76
	No	12	24
Total		**50**	**100**

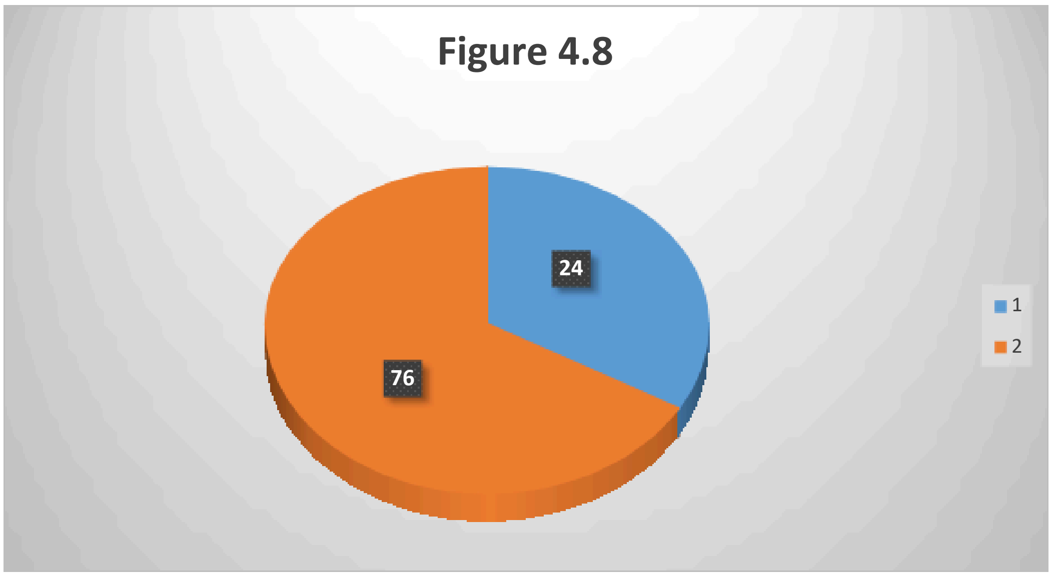


Figure 4.8

Analysis & Interpretation: 76 percent faculty members said that they had worked with industry for any point of time in their career. Working with industry develops a different kind of exposure of the faculty and it also enable them to impart the practical knowledge of the corporate sector. The faculty members are very crucial to develop and providing a shape to the career of the students and they will be able to develop them only when they will possess that kind of knowledge and exposure. Nowadays the competition has become very tough and in order to sustain in the market it is very necessary to have some unique skills to compete with the rivals. Core competencies are very much important and faculty must focus to inculcate these core competencies in the students.

Table 4.9: Academic Research is at par with industry requirements

Question	Options	Response	Percentage
Do you think the academic research is at par with the industrial requirements?	Yes	44	88
	No	6	12
Total		**50**	**100**

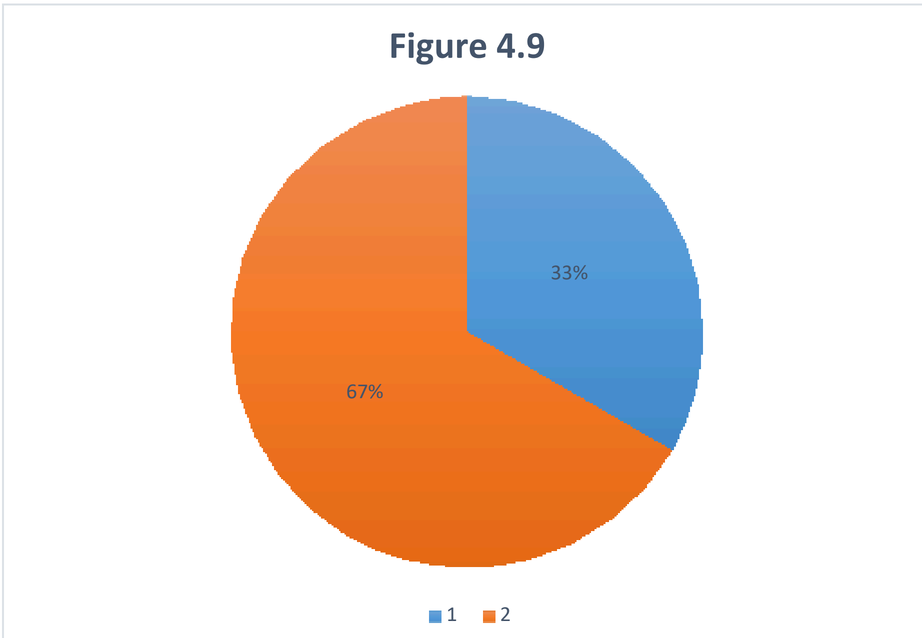


Figure 4.9

Analysis & Interpretation: The universities and other HEIs can serve the industries in many ways. But here, we will discuss only two areas where universities can offer their services to the industries. One, it provides the plenty of skilled manpower the industries so that industries can navigate and run their business smoothly. Second, they can incubate new and innovative ideas to come up with some start-ups and entrepreneurial undertakings that can make them job provider rather than job seeker. This relations is very apparent between both of them but it not that simple. It is complex in many ways. There are inherent differences between both of them. They can be seen together but still they will be far from each other like the two sides of the river. For getting into any collaboration between academia and industry there are many formalities and procedural works have to be done. And not only to be collaborated is enough but also their collaboration must be functional only then it will benefit to the stakeholders. Engineering and science discipline are very much need to have the collaboration and tie-ups with the industries and research and development organizations.

The above data reflect that 70% faculties are think in a manner that there must be clear procedure and process to support and facilitate industry-academia collaboration.

The above response received from the academicians shows that 88% faculty members admit the fact that academic research is playing an important role for the growth of the industry. The quality of academic research is at par for fulfilling the requirements of the industries. Many of the universities and HEIs are establishing Research and Development Cell to promote and encourage to undertake research projects and other academics research to solve the persistent problems and challenges of the industries.

Table 4.10: Contribution of Academic Curriculum

Question	**Options**	**Response**	**Percentage**
"How did the academic curriculum of your field of study contribute to developing the skills and competencies that align with the industry requirements?"	Strongly Agree	8	16
	Agree	27	54
	Neutral	8	16
	Disagree	4	8
	Strongly Disagree	3	6
Total		**50**	**100**

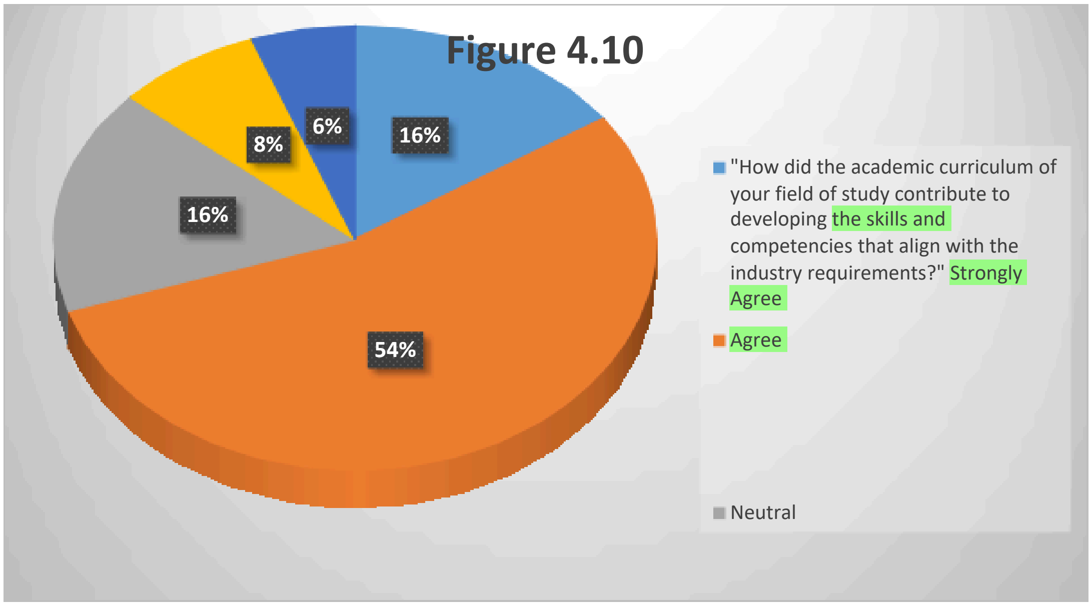


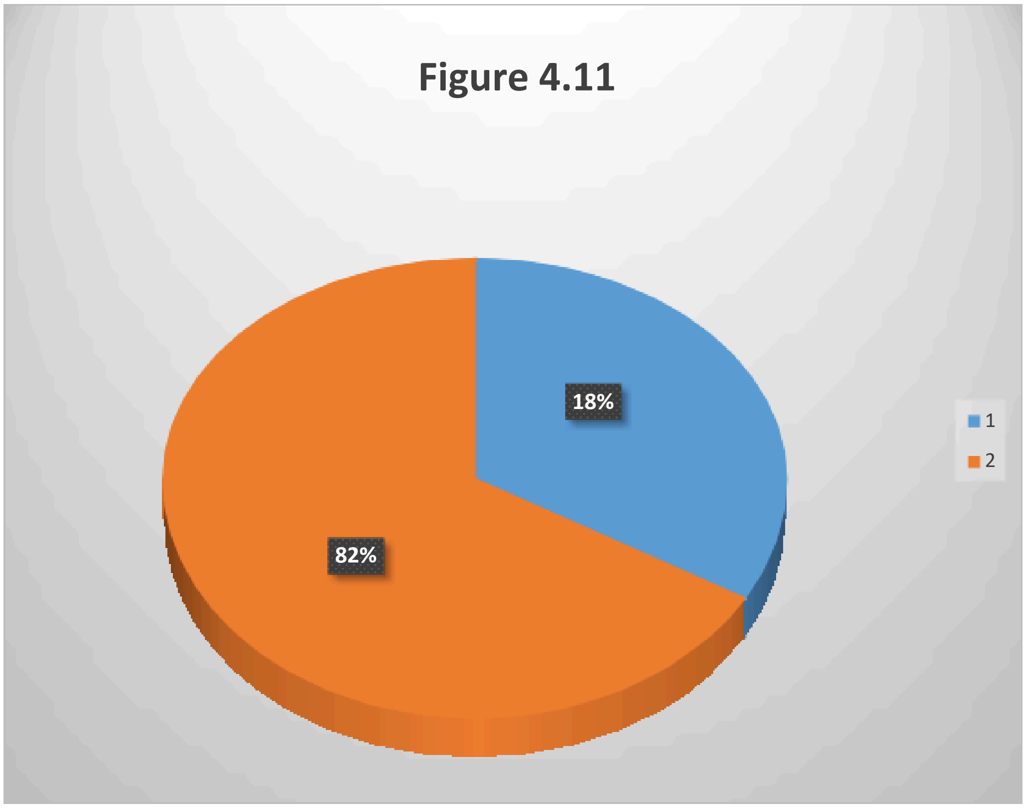
Figure 4.10

Analysis & Interpretation: As a higher education professional, you know how important it is to keep your curriculum relevant and up-to-date with the changing needs and expectations of the industry. But how do you achieve this alignment without compromising your academic standards and learning outcomes? In this article, we will share some of the most effective ways to align your curriculum with current industry trends and ensure that your students are prepared for the future. The first step to align your curriculum with current industry trends is to identify the skills and competencies that are in demand in your field of study. You can do this by conducting a market analysis, reviewing job postings and descriptions, consulting with employers and industry experts, and surveying your alumni and current students. This will help you to understand what employers are looking for, what challenges they are facing, and what gaps they are trying to fill. The next step is to update your learning objectives and outcomes based on the skills and competencies that you have identified. You should ensure that you're learning objectives and outcomes are clear, measurable, and aligned with the industry standards and expectations. You should also review your assessment methods and criteria to make sure that they reflect the level of mastery and performance that you want your students to achieve. The third step is to incorporate relevant and authentic learning activities and resources into your curriculum. You should design your learning activities and resources to simulate real-world scenarios, problems, and tasks that your students will encounter in the industry. You should also use a variety of formats and modalities, such as case studies, simulations, projects, portfolios, podcasts, videos, and online platforms, to engage your students and cater to their diverse learning styles and preferences. The fourth step is to engage with industry partners and stakeholders to enhance your curriculum alignment and relevance. You should seek feedback and input from industry partners and stakeholders on your curriculum design, content, delivery, and evaluation. You should also collaborate with them to provide opportunities for your students to interact with industry professionals, such as guest lectures, mentorships, internships, placements, and capstone projects. This will help your students to gain exposure, experience, and network in the industry. The final step is to monitor and evaluate your curriculum alignment and impact on a regular basis. You should collect and analyze data and evidence from various sources, such as student performance, feedback, and satisfaction, employer feedback and satisfaction, graduate outcomes and employability, and industry trends and developments. You should also use this data and evidence to identify the strengths and weaknesses of your curriculum alignment and make adjustments and improvements as needed.

The majority of the faculty members responded that their academic curriculum significantly contributes to develop the core competencies skills in students. 70% academicians from various HEIs were in the agreement with the fact that academic curriculum plays an important role in inculcating the spirit of developing the core competencies for taking the strategic advantages. Only 30% faculties were either in the denial mode or not able to comment anything on the topic that was put before them to comment.

Table 4.11: Academicians' confidence to undertake Industrial Projects

Question	Options	Response	Percentage
Do academicians feel confident to undertake industrial projects?	Yes	41	82
	No	9	18
Total		**50**	**100**



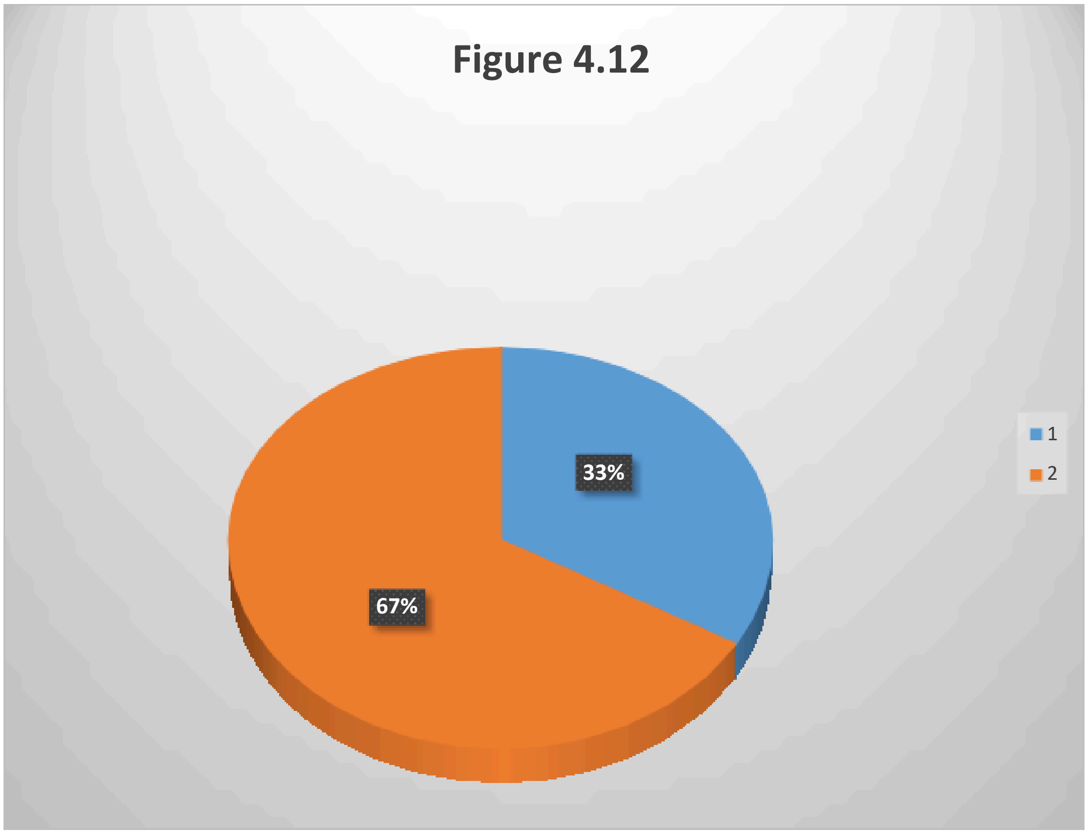
Analysis & Interpretation: Nowadays, the industrial scenario has completely changed and all the industries are undergoing a structural transformation. Therefore, the well-equipped and well qualified with expertise and core professionalism professionals are required to navigate the industries in such a challenging environment so that industries and corporate houses can sustain in long run. Academia and industries are two sides of the same coin as they cannot be separated from each other. They have to play a complementary role for each other. They have to realize that they are exclusive but mutual. On the one hand academia imparts the knowledge and skills to the students and prepares a foundation of knowledge to compete the rivals in the market. On the other hand, industries apply their theoretical knowledge and skills in the business and to solve the real life problems. Academicians should focus on the industry-oriented or job-oriented curriculum so that it can play a very crucial and vital role in getting the jobs in the market after completing their course. The project-based learning imparted by the academicians may play an important role in bridging the gap between industry and academia. This need has to be realized by the academicians as well only then the scenario will take a paradigm shift because the academicians are in the core of this entire process of bridging the gap between industry and academia.

Now the faculty members and academicians are taking interest in undertaking the industry projects. As the above analysis also reflects that the confidence of the academicians have substantially increased during few years. This is an indication that witnesses that the academia world are shifting towards imparting more skill based knowledge to the students that could be more relevant with regard to the job providing and it will enhance the employability. During their internship and apprenticeship of the students they should engaged in real life projects which are facing some technical or profession gulch so that their practical leaning can start at the very beginning of their career.

The above data shows that the majority of the academicians consider themselves as the most confident for undertaking the industry-oriented projects in align with the industry requirements. 82% faculty members from various universities or HEIs are ready to undertake such endeavors. Only 18% faculty members of the selected sample were in denial mode or reluctant to take such projects due to some reasons or others.

Table 4.12: Motivation of Faculties

Question	Options	Response	Percentage
In your opinion, is the faculty motivated for industry oriented research?	Yes	37	74
	No	13	26
Total		**50**	**100**

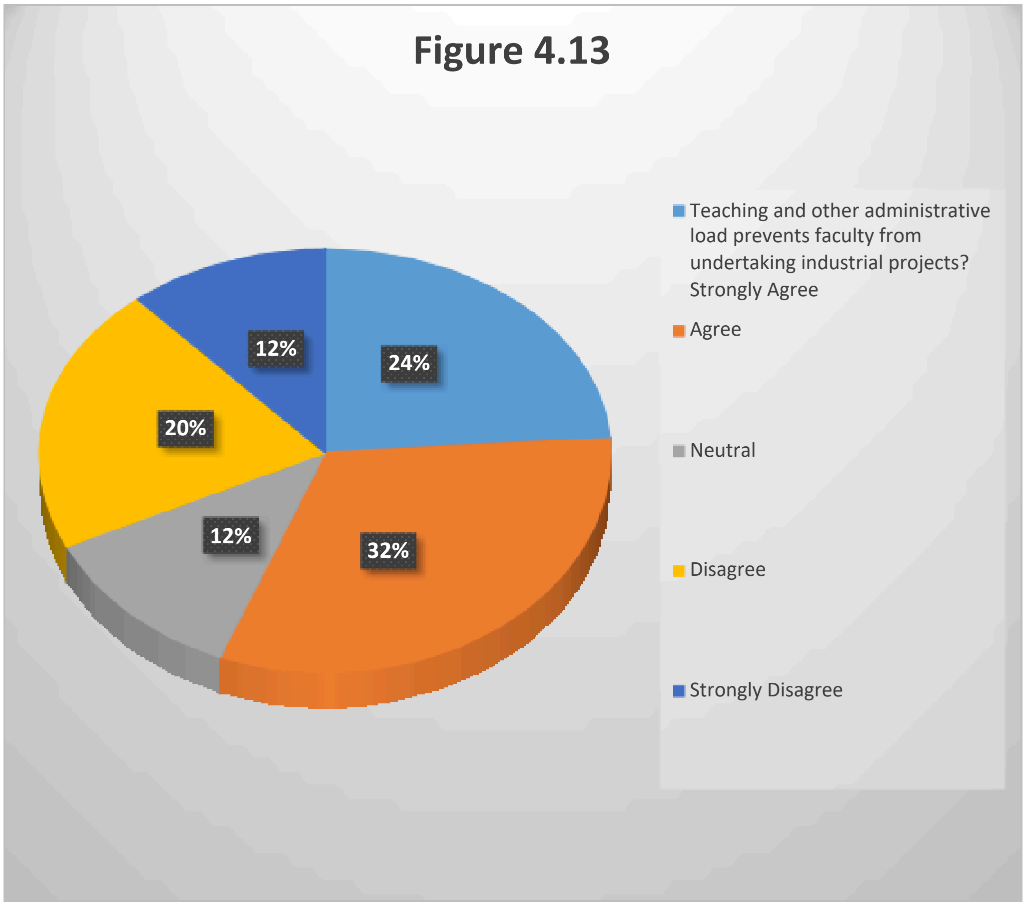


Analysis & Interpretation: The basic aim of the students to go to college or university is to gain some knowledge and skills so that they can be eligible for getting jobs and conduct some research and developmental projects in the betterment of themselves as well as in the betterment of the society and nation as a whole. The students expect from the universities and institutions in which they are pursuing their degree or diploma courses that they will be imparted job-oriented education that will help them to get a job when they complete their course. Today's world has changed and having only conventional knowledge to the students is not enough because today's time demands to be multi-dimensional and versatile only then you can survive in the market. Therefore, the HEIs must offer a complete package of skills, knowledge, expertise and training to them. There is cut-throat completion in the market among all the stakeholders. Students are coming from various parts of the country and they are diverse in knowledge and skills. There are many cultures and traits so you must be experts in two or more languages also. The universities and HEIs are expected to motivate their faculty members to undertake the industry projects and involve students too in such projects. It will work from many points of view. First, students can assist faculty members in the functioning of the projects and second, students will learn something new and innovative and practical that may lead to the overall growth of them. The training programs should be organized for them to learn the skills like communication skills, personality development programs, mock interviews, and other job-oriented training. There is an urgent need of such faculty members who have some industry experience so that they can provide the practical knowledge and skills to the students. The academia must have the collaborations and tie-ups with the industry and corporate. Such tie-ups can contribute in the holistic development of the students.

The analysis of the above data of the current study justifies that the majority of the faculty members are motivated and encouraged to undertake the industrial projects. 74% academicians of the selected sample from the various institutions responded that they are motivated to undertake such projects and some of them are already engaged in some industry projects.

Table 4.13: Impact of Teaching and other Administrative Load

Question	**Options**	**Response**	**Percentage**
Teaching and other administrative load prevents faculty from undertaking industrial projects?	Strongly Agree	12	24
	Agree	16	32
	Neutral	6	12
	Disagree	10	20
	Strongly Disagree	6	12
Total		50	100



Analysis & Interpretation: Teaching is a profession that holds the key to shaping the future, but the responsibilities and administrative burdens placed on educators can sometimes overshadow their primary focus on student learning. As schools and educational institutions evolve in the digital age, it becomes imperative to explore innovative strategies to alleviate the administrative challenges faced by teaching staff. In this comprehensive exploration, we will delve into a range of strategies aimed at reducing administrative burdens, fostering an environment where educators can dedicate their time and energy to what matters most – the education and well-being of their students. Teachers, often referred to as the backbone of the education system, face a multitude of administrative tasks that extend beyond lesson planning and classroom instruction. Grading assignments, tracking student progress, managing communication with parents, and navigating complex reporting systems are just a few examples of the administrative burdens that educators encounter daily. These tasks, while essential, can divert their attention and energy away from the core of their profession – teaching.

The increasing demands of paperwork and administrative responsibilities can contribute to stress, burnout, and a potential decline in job satisfaction among teachers. Recognizing and addressing these challenges is crucial not only for the well-being of educators but also for the overall quality of education provided to students.

56% respondents agreed that teaching and other administrative load hamper their productivity or efficient to undertake industrial projects. Excessive teaching workload and administrative responsibilities provide opportunities to learn many new things but it consumes a handsome amount of time. Having performed all these duties, very little time left to take up such industry oriented projects. But 32% respondents do not think that teaching workload and other administrative duties create any barrier to undertake industrial project. They believe that it is all about our time management that how effectively we manage our time. So, some balanced opinions were there regarding the question.

Table 4.14: Academician's Role for Industrial Collaboration

Question	Options	Response	Percentage
Academicians do not consider industrial collaboration as part of their job	Strongly Agree	10	20
	Agree	13	26
	Neutral	5	10
	Disagree	16	32
	Strongly Disagree	6	12
Total		**50**	**100**

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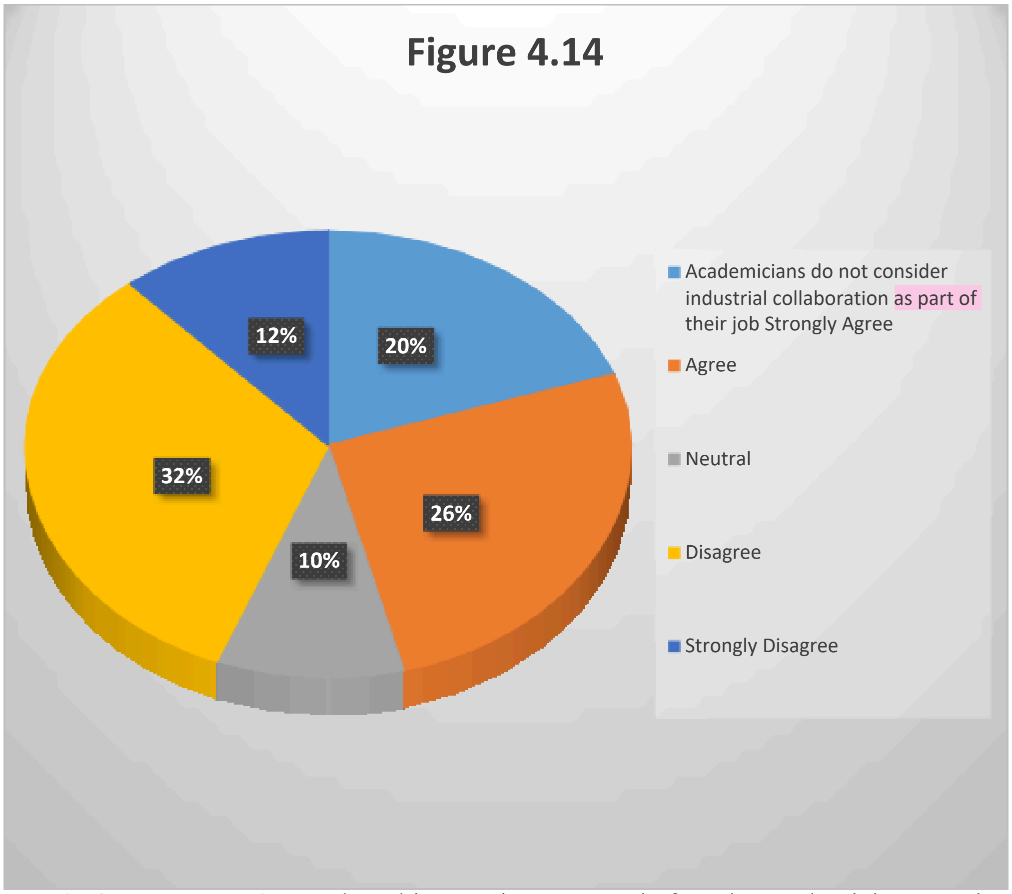
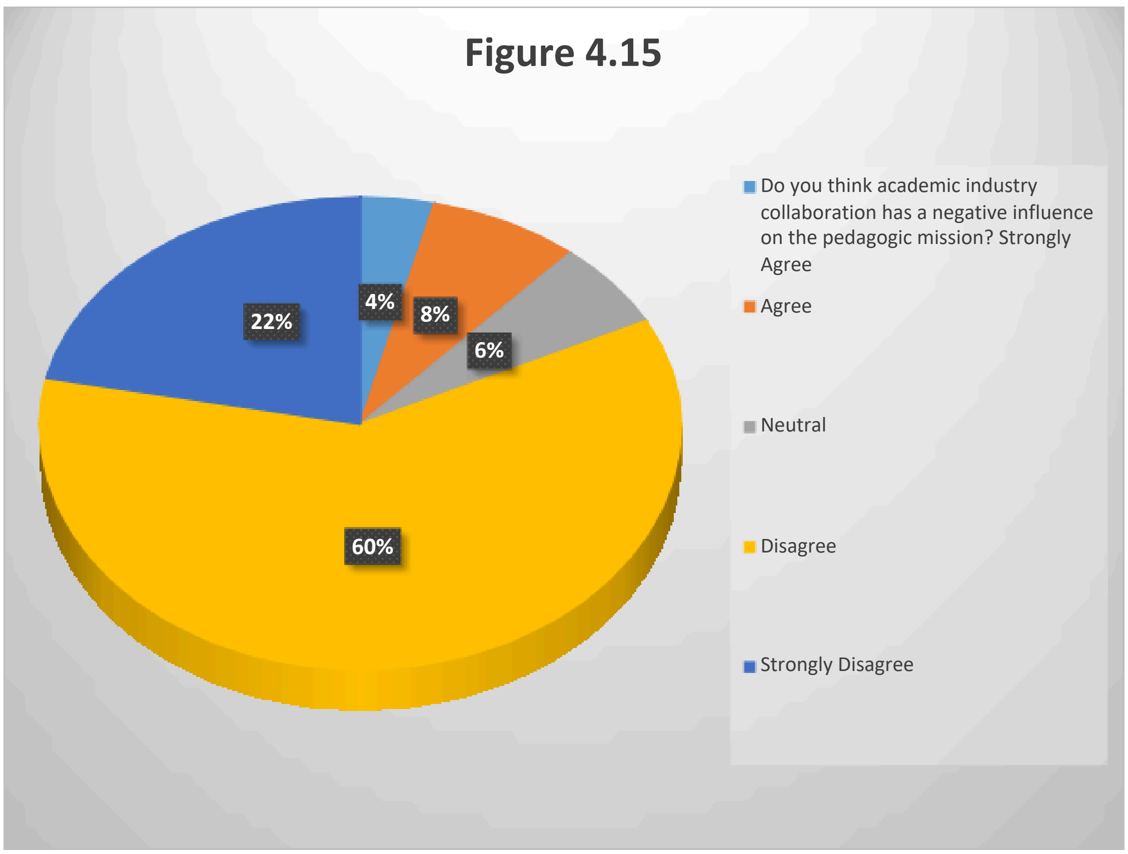


Analysis & Interpretation: When this question was put before the academicians, a mixed reaction and responses were received from them. 46% respondents said that this is true that it is not a part of our job to take up industrial projects. There must be some experts of that kind who can be involved exclusively in such tasks. On the other hand, 42% respondents were disagree and they believed that keep involving and engaging in undertaking industrial projects is an essential part of their job.

Table 4.15: Impact of Academic-Industry Collaboration on Pedagogic Mission

Question	Options	Response	Percentage
Do you think academic industry collaboration has a negative influence on the pedagogic mission?	Strongly Agree	2	4
	Agree	4	8
	Neutral	3	6
	Disagree	30	60
	Strongly Disagree	11	22
Total		**50**	**100**



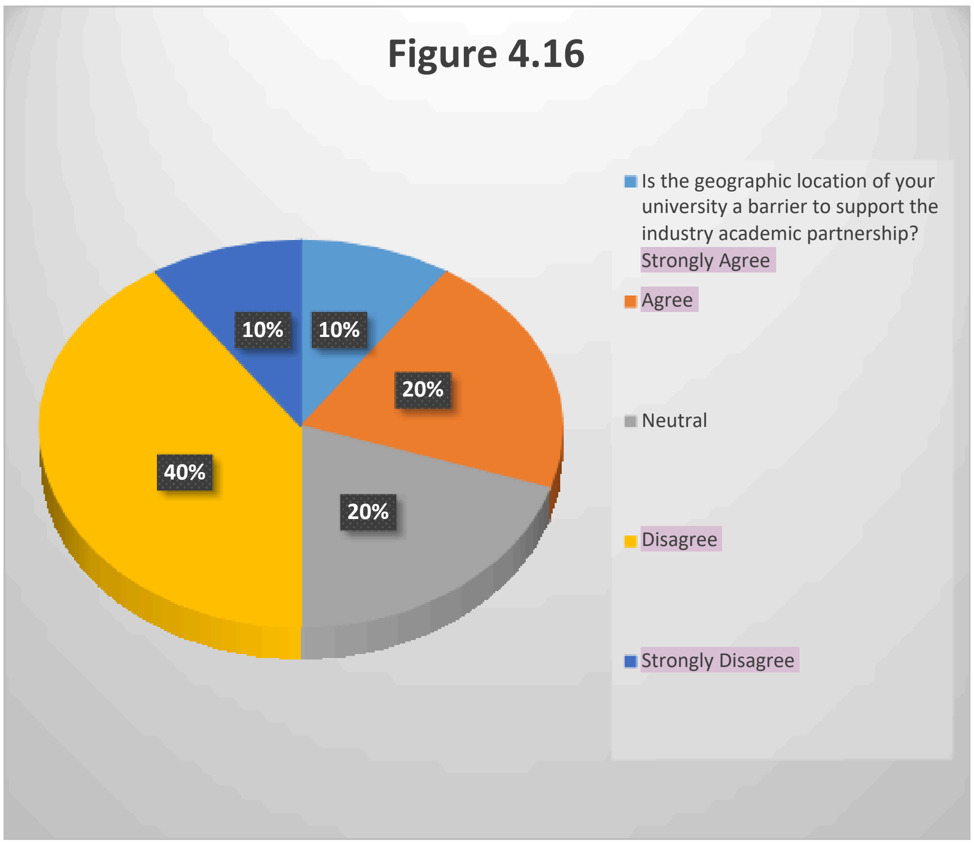
Analysis & Interpretation: Collaboration between universities and industries has become increasingly important in recent years. The traditional classroom model of education is no longer enough to prepare students for the workforce. By working with companies, students can gain real-world experience and develop job-ready skills. A report by the National Association of Colleges and Employers showed that students who had completed internships or cooperative education assignments were more likely to receive job offers and have higher starting salaries than those who did not. Furthermore, according to a study by Harvard Business Review, companies with higher levels of collaboration with universities had higher innovation output, higher quality patents, and more successful new ventures. This highlights the importance of industry-academia collaboration in driving innovation and growth.

Effective collaboration requires active participation and engagement from both sides. Universities must identify the needs of the industry and align their curriculums accordingly. This could involve incorporating industry projects into coursework, offering practical training sessions, or providing access to the latest industry equipment and technology. Similarly, industries should provide internships, mentorship programs, and other opportunities for students to gain practical experience. However, some may argue that industry-academia collaboration can lead to the commercialization of research and a potential conflict of interest. To avoid this, universities should maintain academic independence and transparency in research partnerships with industries.

The analysis of above data strongly believes that majority of the respondents consider that collaboration between industry and academia does not carry any negative impact on the pedagogic mission of the HEIs. 82% respondents disagree or strongly disagree with question put before them.

Table 4.16: Impact of Geographic Location of the Universities

Question	Options	Response	Percentage
Is the geographic location of your university a barrier to support the industry academic partnership?	Strongly Agree	5	10
	Agree	10	20
	Neutral	10	20
	Disagree	20	40
	Strongly Disagree	5	10
Total		**50**	**100**



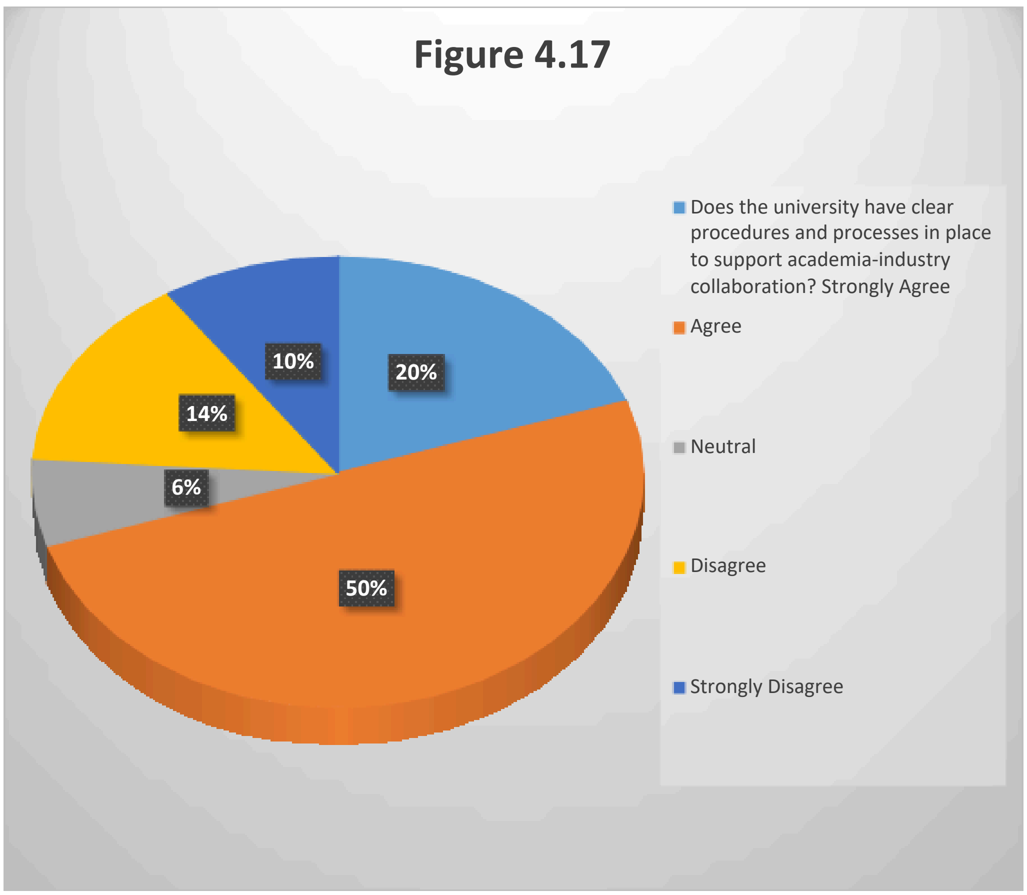
Analysis & Interpretation: The geographic location of a university can influence the strategy of leadership. Different universities operate in complex international environments and need to balance global relevance with local identity. Changes in governance structures of European universities have been proposed to enhance their democratic nature and degree of centralization.

The leadership exercised during the formation of University had a significant impact on the challenges experienced by the institution. Additionally, regional characteristics can shape university performance and their ability to contribute to their regions. Therefore, the geographic location of a university can affect the leadership strategy employed, considering factors such as international dynamics, governance structures, and regional engagement. The fundamental purpose of university geographic clustering is to gather resources through "agglomeration" to improve the performance of higher education and scientific research. The empirical challenges prevalent in the aforementioned studies are related to issues of sample representativeness and endogeneity. First, existing empirical studies are often based on case studies or a small number of research institutions and lack representativeness. This weakens external validity and prevents reliable conclusions from being drawn. Second, university or research institution cluster projects conducted at the national level suffer from serious endogeneity problems in sample selection, making it difficult to effectively identify the net effect of clustering. Indeed, examining the impact of geographic clustering on university scientific research performance should be of interest not only to scientific scholars but also to policy makers. Therefore, the effects of geographic clustering of universities need to be further explored.

The analysis of the above data reflects that the responses are mixed regarding the geographic location of the universities or Higher Educational Institutions. Only 30% respondents consider that the geographic location may be a barrier to establish a partnership between industry and academia. 50% respondents believe that geographic location does not create any barrier between the industry and academia. 20% respondents were not able to respond anything. Their responses were neutral.

Table 4.17: Procedure and Process

Question	Options	Response	Percentage
Does the university have clear procedures and processes in place to support academia-industry collaboration?	Strongly Agree	10	20
	Agree	25	50
	Neutral	3	6
	Disagree	7	14
	Strongly Disagree	5	10
Total		**50**	**100**

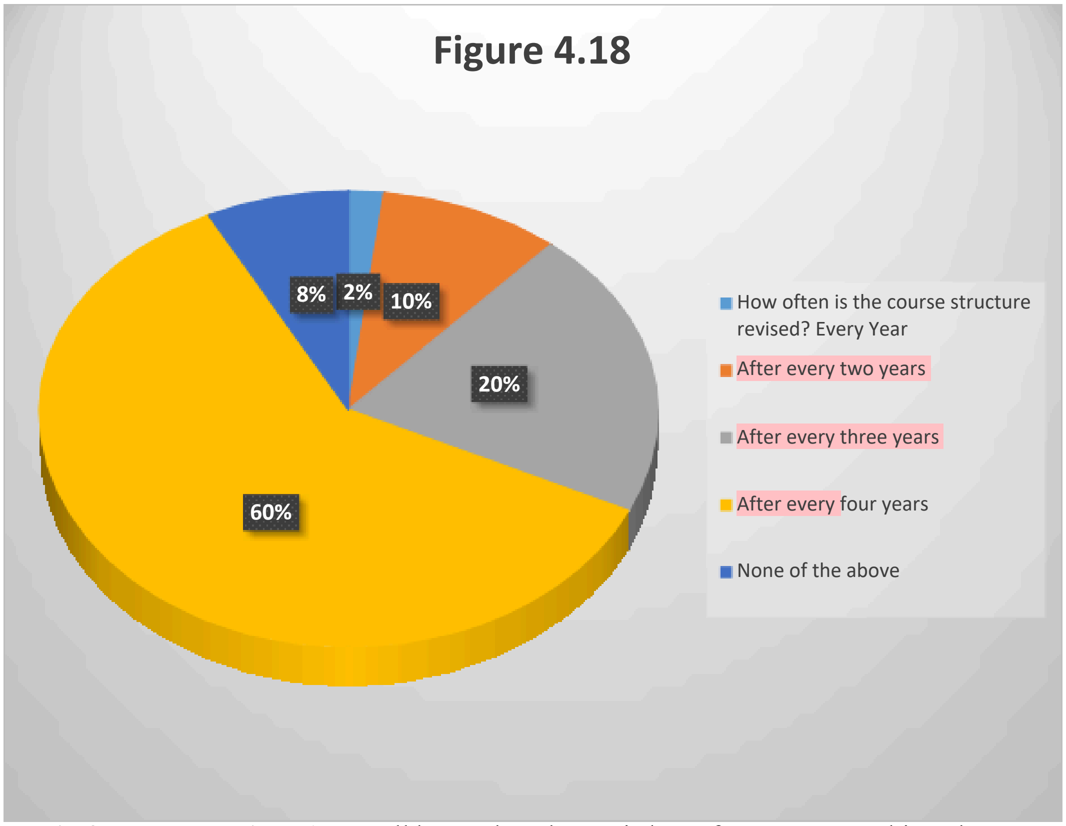


Analysis & Interpretation: The universities and other HEIs can serve the industries in many ways. But here, we will discuss only two areas where universities can offer their services to the industries. One, it provides the plenty of skilled manpower the industries so that industries can navigate and run their business smoothly. Second, they can incubate new and innovative ideas to come up with some start-ups and entrepreneurial undertakings that can make them job provider rather than job seeker. This relations is very apparent between both of them but it not that simple. It is complex in many ways. There are inherent differences between both of them. They can be seen together but still they will be far from each other like the two sides of the river. For getting into any collaboration between academia and industry there are many formalities and procedural works have to be done. And not only to be collaborated is enough but also their collaboration must be functional only then it will benefit to the stakeholders. Engineering and science discipline are very much need to have the collaboration and tie-ups with the industries and research and development organizations.

The above data reflect that 70% faculties are think in a manner that there must be clear procedure and process to support and facilitate industry-academia collaboration.

Table 4.18: Frequency of Curriculum Revision

Question	Options	Response	Percentage
How often is the course structure revised?	Every Year	1	2
	After every two years	5	10
	After every three years	10	20
	After every four years	30	60
	None of the above	4	8
Total		**50**	**100**



Analysis & Interpretation: As we all know that change is law of nature. Everything changes over the period of time. And it also true with the academic curriculum. The academic curriculum must be revised time to time according to the changing needs of the industry and society. As per the need of the market and industry, course curriculum and pedagogy should be revised aligning with the dynamic needs of the industry. The industrial sector has become global and economy is integrated economy. That is why, there must be some innovative teaching pedagogy which may provide more skills. Outcome-based education system can be introduced. Along with this Teaching-Learning & Assessment system should also be introduced. The main focus of the curriculum and pedagogy should be on the enhancement of the employability of the program only then it will have some value for the students and they can contribute in the growth of the society and the nation as a whole. Such academic curriculum and pedagogy focus more on practical training rather than the theoretical knowledge. Theoretical knowledge is necessary but knowing the application of that knowledge to solve the problem is the main theme of the today's scenario. The course curriculum and pedagogy should be so structured and sequential that will lead to the students towards becoming an expert of the area. New models, approaches, theories, practical and experiments, case studies etc. should be included in the curriculum.

The above analysis shows that 60% respondents said that they revise their academic curriculum after every four years. HEIs are not stuck with the old and traditional curriculum rather they are keen to revise and update their curriculum as per need of the hour.

Table 4.19: Two-way Communication between Industry & Academia

Question	Options	Response	Percentage
Is two-way communication between the university and the industry is a regular activity of the university calendar?	Yes	31	62
	No	14	28
	Can't say	5	10
Total		**50**	**100**

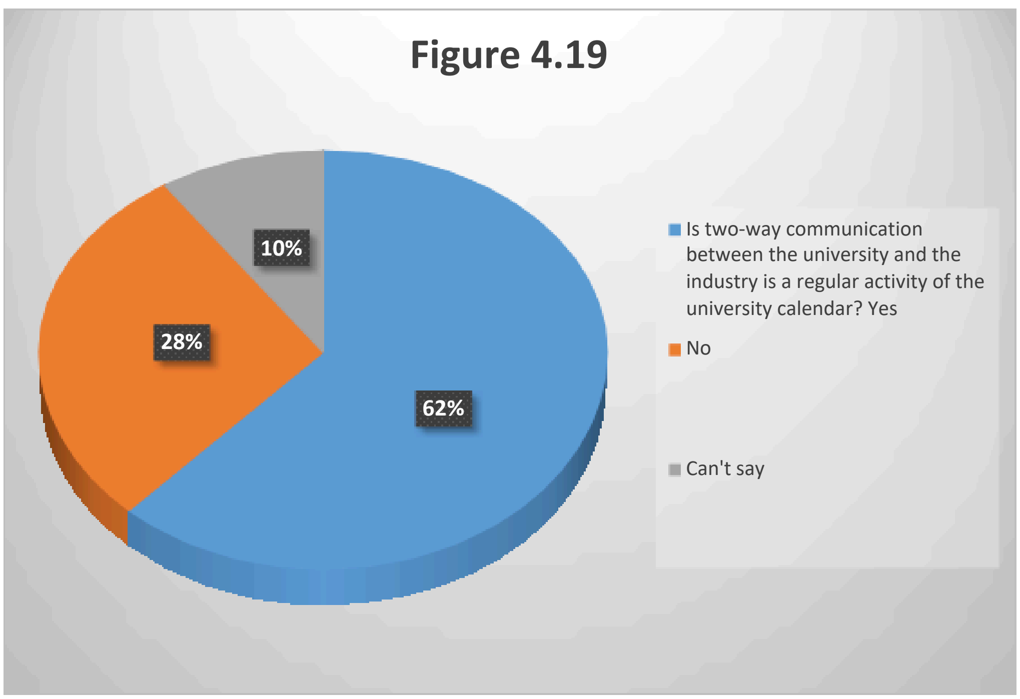


Figure 4.19

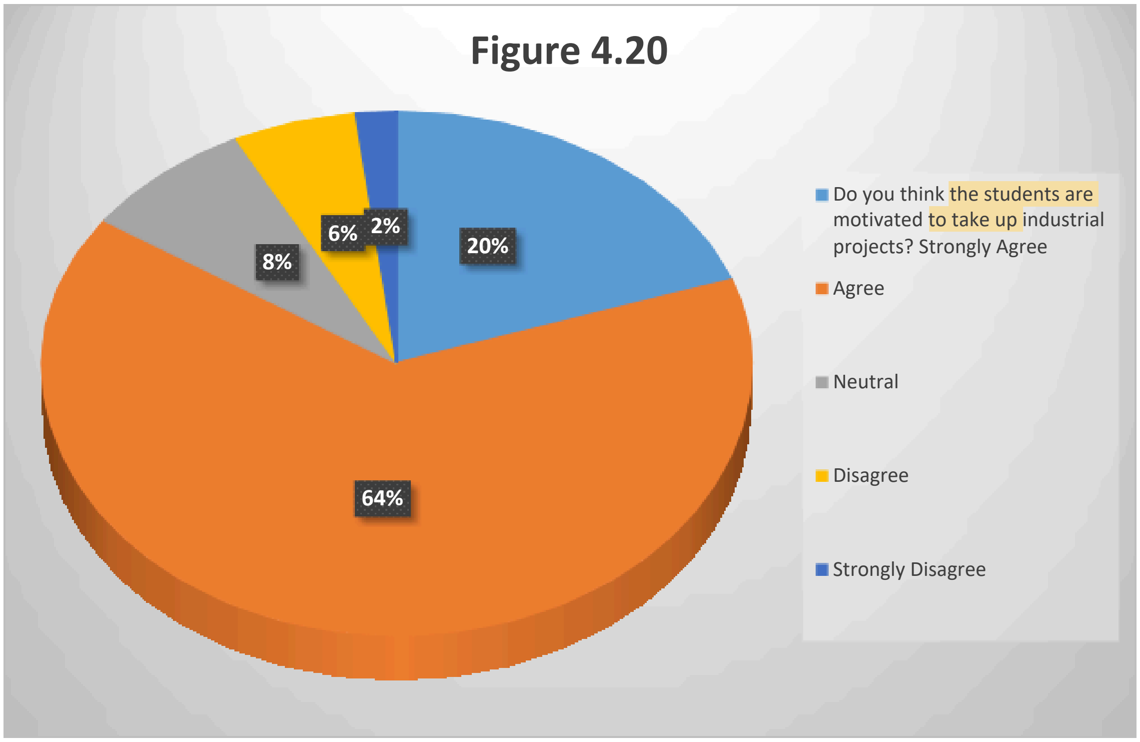
Analysis & Interpretation: Two-way communication in an organization is important because it allows for effective interaction, understanding, and collaboration among team members and departments. It enables the sharing of knowledge, ideas, and feedback, leading to improved problem-solving and decision-making processes. Effective communication also helps in building and maintaining relationships, both within the organization and with external stakeholders. It plays a crucial role in achieving organizational goals, motivating employees, and creating a trustful environment. Additionally, two-way communication helps in overcoming language barriers, especially in multinational organizations, by facilitating smooth communication between different departments and locations. Cultural differences also need to be considered to improve communication between parties. Overall, effective two-way communication is essential for organizational success and productivity. Two-way communication is the process of sharing information back and forth between two parties. In other words, it's a conversation where both the sender and receiver invite and offer feedback. And most importantly, two-way communication is never a monologue.

To maximize the benefits of two-way communication in the workplace, dialogue should be continuous. In other words, the flow of information between the sender and the receiver should be consistent. Effective internal communications tools, methods, and channels are vital in facilitating this process. 62% responses received in positive mode that two-way communication between the universities and industry is the regular activity. 28% respondents said no that it is not a regular activity but it is done as and when it requires.

Question	Options	Response	Percentage
Has the college made it obligatory for faculty to undertake a certain amount of work with industry?	Yes	10	20
	No	34	68

	Can't say	6	12
Total		**50**	**100**

Table 4.20: Regarding certain amount of work with industry



Analysis & Interpretation: As we all know that undertaking industrial projects is very much important for the faculty members but still most of the institute did not make it obligatory or compulsory for the faculty members. They motivate them, support them and also provide the adequate facilities and other resources to undertake and accomplish such projects but they do not impose such willingness of the institute on them. Only 20% faculties said in yes that their institute has made it obligatory and compulsory to undertake such industrial project and 68% faculties said no. 12% didn't said anything.

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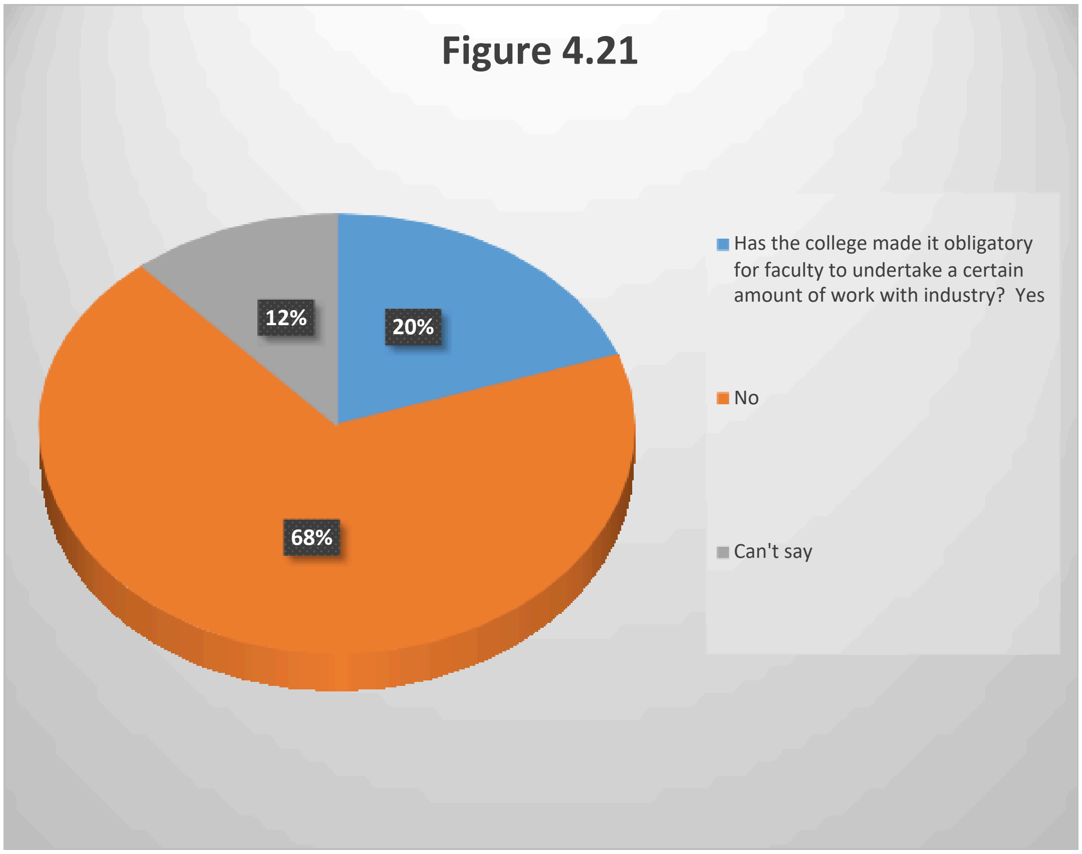
Table 4.21: Students' Motivation regarding Industrial Projects

Question	Options	Response	Percentage
Do you think the students are motivated to take up industrial projects?	Strongly Agree	10	20
	Agree	32	64
	Neutral	4	8
	Disagree	3	6
	Strongly Disagree	1	2
Total		**50**	**100**



Analysis & Interpretation: Industrial visits and industrial projects often referred to as industry visits for students, has become an important and vital part of the academic curriculum in almost all the programs whether it is under graduate or post graduate. Such industrial visits provide very unique and practical exposure to the students. It teaches and provides them an environment in which they can learn the nuances of the industry and corporate culture. Students can learn and

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apply their theoretical knowledge for solving the real problems. Actually, the main motive of such industrial is to bridge the gap between industry and academia.

The main intention and very objective of conducting industrial visits is to develop and inculcate the thought process of thinking out of the box. It is not about the classroom teaching but it focuses on the holistic development of the students and make them ready for the industry need. The current scenario is very dynamic and technological developments and advancements are changing rapidly so students must develop an adaptability in their nature.

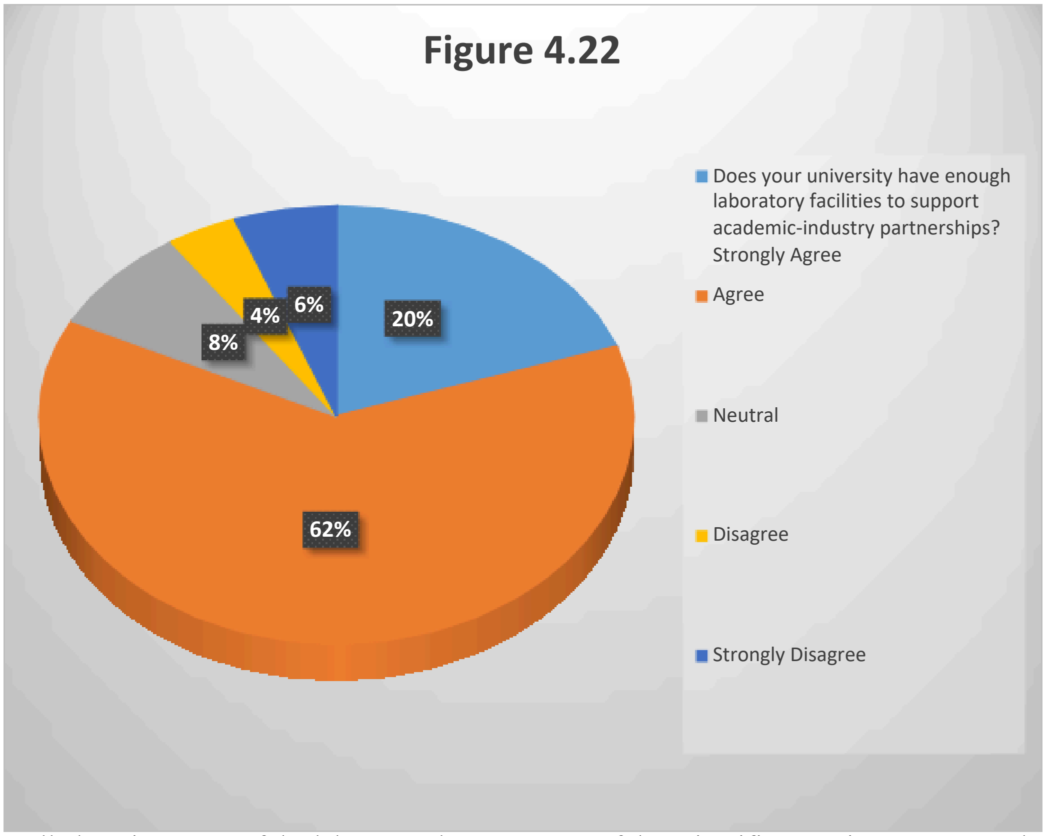
With the help of industrial visits they can take many live inputs to develop their own knowledge and understanding. Before seeking any job in industry, they will be able to know about the industrial growth, and actually, it provides them first point of getting interacted with the corporate and industrial personnel. They can also improve and enhance their skills with the help of the industrial visits. The students can also undertake some industry projects

The above data of the current study clearly explains that 84% responses are positive that affirms that majority of the students are motivated and willingly ready to undertake such industrial projects. Maximum students of all the selected HEIs said that their faculties and institute support and motivate them to undertake such projects.

Table 4.22: Status of Adequate Lab Facilities at Universities

Question	Options	Response	Percentage
Does your university have enough laboratory facilities to support academic-industry partnerships?	Strongly Agree	10	20
	Agree	31	62
	Neutral	4	8
	Disagree	2	4
	Strongly Disagree	3	6
Total		**50**	**100**

Analysis & Interpretation: Laboratory personnel must be much trained. They should have possess specific knowledge of the chemicals and how other experimental equipment's are operated. They should ensure that the existing infrastructure of the laboratory and the available resources are adequate and sufficient to meet the needs of experimentation. There must be very



controlled environment of the laboratory because most of the scientific experiments are conducted in a controlled environment. Ventilation must be adequate, cleanliness is very important, sanitation is very much crucial. Whether safety and efficiency measures are being effectively followed or not. Trained laboratory personnel must understand how chemical laboratory facilities operate. Every laboratory should adopt the standard operating procedures (SOPs) so that the standardization can be effectively implemented. All the functional and operational requirements must be easily available and insufficiency should avoided. Space of the laboratory must be sufficient and should be as per the regulatory requirements and also according to the intake of the students. Given the chance, they should provide input to the laboratory designers to ensure that the facilities meet the needs of the functions of the laboratory. Laboratory personnel need to understand the capabilities and limitations of the ventilation systems, environmental controls, laboratory chemical hoods, and other exhaust devices associated with such equipment and how to use them properly. To ensure safety and efficiency, the experimental work should be viewed in the context of the entire laboratory and its facilities.

82% respondents believe that there universities or institutions have adequate and sufficient lab facilities. There are only 18% responses were negative or they believed that there are insufficient facilities available in their institutions.

Chapter-5

Conclusions and Findings of the Study

Findings

On the basis of data analysis of responses collected from industry representatives and student representatives, the following conclusions were drawn:

The above data reflect that majority of the students around 72% (including agree and strongly agree) admit that their university or institute encourages industrial visits so that the practical exposure can be enhance to add some value in the curriculum. Only 10% students disagree that their institute does not encourage such visits otherwise a large percentage of them responded positively.

It was found that majority of the students admit that there is mandatory internship in their curriculum. 18% admits strongly, 55% agree and 14% were neutral. Only 13% responses were negative.

Today we are talking about experiential learning, E-learning, flipped classrooms and what not. With all these innovations in the teaching methods do we still get the desired results? We still cope with issues like employers complaining about lack of skills in fresh students passing out of colleges, their lack of employability extra. Even the best students passing out of reputed management colleges and engineering colleges still have to cope with the issue of unemployment. It can be concluded with the help of above data that almost all the students admit that most of the faculty members have some industry exposure in their teaching pedagogy. 148 students out of 200 students have agreed that the teachers are having the industry involvement while teaching.

Nowadays, the market is very much demanding and we often come across the issue regarding the level of higher education not meeting the industry expectation. To bridge this gap and equip the students of current generation with new-age technologies, seminars and workshops play an imperative role. Ensuring a proper flow of knowledge Seminars and Workshops assist in passionate interaction and active participation boosting the skills and expertise of students. Importance of seminars and workshops for students is often acknowledged as a prime concern. Keeping in mind the importance of seminars for students and the benefits of workshops for students, seminars and workshops are an innovative and welcomed step towards modern education. Nowadays seminars in schools are encouraged recognizing the importance of seminars for students at an early age.

Total 148 students out of 200 students (74% students) admitted during filling the questionnaire that their institute frequently and regularly organize seminars and workshops, guest lectures, invited talks. Maximum students responded positively that this is a regular feature of their institution.

Gaining industry experience has significant benefits, whether you're in high school, college or entering the workforce. Completing an internship is often an effective way to encourage your professional growth, and there are often some available based on your education level and desired career path. Learning what makes internships beneficial may help you better understand the professional impact they may have. While classroom learning is important, internships 18 allow you to apply what you learned in a practical setting. This helps prepare you for tasks you may complete once you begin your career. Most of the students 37 have done their internship. 176 students out of 200 students (88% students) admitted that they have done their internship. There were various internship options available and accordingly students were undergone their internship in different sectors like manufacturing, service sector, FMCG, IT, R & D etc.

The above data clearly reflect that most of the students 20 are in the agreement that their colleges or universities are proving the above mentioned facilities to enhance their skills. All these facilities are very much important for the holistic growth of the students. 176 students out of 200 students (88% students) 37 admitted that they have done their internship. There were various internship options available and accordingly students were undergone their internship in different sectors like manufacturing, service sector, FMCG, IT, R & D etc. Ensuring a proper flow of knowledge Seminars and Workshops assist in passionate interaction and active participation boosting the skills and expertise of students. Importance of seminars and workshops for students is often acknowledged as a prime concern. Keeping in mind the importance of seminars for students and the benefits of workshops for students, seminars and workshops are an innovative and welcomed step towards modern education. Nowadays seminars in schools are encouraged recognizing the importance of seminars for students at an early age.

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There are some important skills those are necessary to face any interview to get selected. Effective communication, active listening for deeper connection, unleashing problem solving and critical thinking, embracing adaptability and flexibility, and leadership and teamwork are the skills those are crucial for the students. Effective communication skills are crucial in every aspect of our lives, and they play a significant role in the interview process. Being able to articulate your thoughts clearly and concisely, actively listen to the interviewer, and ask insightful questions demonstrates your ability to communicate effectively.

Practice speaking confidently and maintaining good eye contact. Pay attention to your body language, as it can convey confidence and engagement. Active listening is an often underrated skill, yet it plays a pivotal role in establishing rapport and understanding during interviews. By attentively listening to the interviewer's questions and comments, you demonstrate genuine interest and thoughtfulness in your responses.

Avoid interrupting and take a moment to comprehend the question or statement before offering your answer. Develop active listening skills by engaging in conversations with friends, colleagues, or mentors, actively seeking to comprehend their perspectives and practicing reflective listening.

Employers highly value candidates who possess strong problem-solving and critical thinking abilities. Interviews often include scenarios that require quick thinking and efficient problem-solving. Prepare by reflecting on past challenges you've faced and the strategies you employed to overcome them. Emphasize your analytical skills, creativity, and decision-making prowess.

Hone your critical thinking by engaging in puzzles, riddles, or hypothetical scenarios. Such exercises will sharpen your problem-solving acumen and enable you to navigate challenges with ease, leaving a lasting impression on interviewers.

Highlight your adaptability by showcasing instances where you adjusted your approach or thrived in diverse settings. Practice flexibility by actively seeking new experiences, volunteering for varied projects, or taking on different roles. Such endeavors will not only broaden your skill set but also demonstrate your capacity to embrace change and excel in any work environment.

Employers value candidates who can lead teams, inspire others, and collaborate effectively. Highlight your leadership experiences, such as leading projects or mentoring others. Discuss how you've motivated and influenced team members to achieve collective goals.

Demonstrate your ability to work well in teams by providing examples of successful collaborations and effective communication within a group setting. Leadership and teamwork skills show that you can contribute to the organization's success and work harmoniously with others.

Mastering these key skills is essential for excelling in your job interviews. By developing effective communication and active listening abilities, honing critical thinking and problem-solving skills, showcasing adaptability and flexibility, demonstrating emotional intelligence, and investing time in thorough preparation and research. The majority of the students that 82% students are in the agreement that their institutes are offering all such facilities which have been mentioned above.

Response from the Faculties

As chief architects of curriculum, faculty are largely responsible for student learning outcomes. Given the cost of higher education and the amount of debt students incur, higher education stakeholders want to know if higher education is worth the investment. Student career preparedness is an important goal of higher education. While research has been dedicated to college student development, career decision-making, and student-faculty interaction from a student perspective, little is known about the faculty perspective and their role in student career preparedness in a specific articulated way. This study recognizes that students can acquire career preparedness through background contextual affordances, such as exposure to social and learning opportunities, and directly through learning experiences. Faculty can influence these through their interactions with students. This study identified environmental conditions, environmental response, social knowledge, self-knowledge, socio demographic characteristics, and career influences on faculty behavior related to student career preparedness. Faculty believe that students need support and guidance in determining their career direction, especially first-generation students; faculty feel the goal of preparing students for employment after college is an essential or very important priority; faculty feel confident in their ability and willingness to support students' career preparedness in varying degrees and in multiple ways; responsibility for student career preparedness is shared among the institution, students, and least of all faculty, but ultimately, students' career preparedness is dependent on students' willingness to accept responsibility for it and seek help when needed. A sample of fifty faculties were taken for this study.

76 percent faculty members said that they had worked with industry for any point of time in their career. Working with industry develops a different kind of exposure of the faculty and it also enable them to impart the practical knowledge of the corporate sector. The faculty members are

very crucial to develop and providing a shape to the career of the students and they will be able to develop them only when they will possess that kind of knowledge and exposure. Nowadays the competition has become very tough and in order to sustain in the market it is very necessary to have some unique skills to compete with the rivals. Core competencies are very much important and faculty must focus to inculcate these core competencies in the students.

There are many ways for universities to serve the industries. First, it supplies the all kind of workforce whether skilled, semi-skilled and unskilled. Manpower is the most important factor for the industry to function it. Without manpower, the existence of any industry cannot be imagined. Universities are the place where the idea generation of many innovations takes place and is translated into realty with logistic support of the industries. The main function of the university is to evolve or develop an idea and transforms that idea into the realty with the help of industries. Such linkage and collaborations are much required in case of science and engineering institutions as to place the students for technical internship and apprenticeship. It will be the betterment for both-industry and academia.

It is the best tool to develop or enhance knowledge and to facilitate learning. Academic research conducted by students is important not just for students only, also for the entire scholastic world. Knowledge is associated with research objectives and findings. Arguments framed by the researcher in the academic paper provide a pathway to the mind of the scholar. Research allows comprehension of specific issues through varied angles that were never identified or talked much about. While conducting the research, a scholar goes beyond personal experience and collects the evidence based on facts and rationality. That is how academic research papers open the gates for further discourse and discussions.

Indian universities help in producing and delivering knowledge by conducting research work. The output of Ph.D. theses also forms an important source of information for the research community. High-caliber research programs should be sponsored by the universities to produce quality research and development of various disciplines, leading to growth and economic gains for our country.

The above response received from the academicians shows that 88% faculty members admit the fact that academic research is playing an important role for the growth of the industry. The quality of academic research is at par for fulfilling the requirements of the industries. Many of the universities and HEIs are establishing Research and Development Cell to promote and encourage to undertake research projects and other academics research to solve the persistent problems and challenges of the industries.

As a higher education professional, you know how important it is to keep your curriculum relevant and up-to-date with the changing needs and expectations of the industry. But how do you achieve this alignment without compromising your academic standards and learning outcomes? In this article, we will share some of the most effective ways to align your curriculum with current industry trends and ensure that your students are prepared for the future. The first step to align your curriculum with current industry trends is to identify the skills and competencies that are in demand in your field of study. You can do this by conducting a market analysis, reviewing job postings and descriptions, consulting with employers and industry experts, and surveying your alumni and current students. This will help you to understand what employers are looking for, what challenges they are facing, and what gaps they are trying to fill. The next step is to update your learning objectives and outcomes based on the skills and competencies that you have identified. You should ensure that you’re learning objectives and outcomes are clear, measurable, and aligned with the industry standards and expectations. You should also review your assessment methods and criteria to make sure that they reflect the level of mastery and performance that you want your students to achieve. The third step is to incorporate relevant and authentic learning activities and resources into your curriculum. You should design your learning activities and resources to simulate real-world scenarios, problems, and tasks that your students will encounter in the industry. You should also use a variety of formats and modalities, such as case studies, simulations, projects, portfolios, podcasts, videos, and online platforms, to engage your students and cater to their diverse learning styles and preferences. The fourth step is to engage with industry partners and stakeholders to enhance your curriculum alignment and relevance. You should seek feedback and input from industry partners and stakeholders on your curriculum design, content, delivery, and evaluation. You should also collaborate with them to provide opportunities for your students to interact with industry professionals, such as guest lectures, mentorships, internships, placements, and capstone projects. This will help your students to gain exposure, experience, and network in the industry. The final step is to monitor and evaluate your curriculum alignment and impact on a regular basis. You should collect and analyze data and evidence from various sources, such as student performance, feedback, and satisfaction, employer feedback and satisfaction, graduate outcomes and employability, and industry trends and developments. You should also use this data and evidence to identify the strengths and weaknesses of your curriculum alignment and make adjustments and improvements as needed.

The majority of the faculty members responded that their academic curriculum significantly contributes to develop the core competencies skills in students. 70% academicians from various HEIs were in the agreement with the fact that academic curriculum plays an important role in inculcating the spirit of developing the core competencies for taking the strategic advantages. Only 30% faculties were either in the denial mode or not able to comment anything on the topic that was put before them to comment.

Nowadays, the industrial scenario has completely changed and all the industries are undergoing a structural transformation. Therefore, the well-equipped and well qualified with expertise and core professionalism professionals are required to navigate the industries in such a challenging environment so that industries and corporate houses can sustain in long run. Academia and industries are two sides of the same coin as they cannot be separated from each other. They have to play a complementary role for each other. They have to realize that they are exclusive but mutual. On the one hand academia imparts the knowledge and skills to the students and prepares a foundation of knowledge to compete the rivals in the market. On the other hand, industries apply their theoretical knowledge and skills in the business and to solve the real life problems. Academicians should focus on the industry-oriented or job-oriented curriculum so that it can play a very crucial and vital role in getting the jobs in the market after completing their course. The project-based learning imparted by the academicians may play an important role in bridging the gap between industry and academia. This need has to be realized by the academicians as well only then the scenario will take a paradigm shift because the academicians are in the core of this entire process of bridging the gap between industry and academia.

Now the faculty members and academicians are taking interest in undertaking the industry projects. As the above analysis also reflects that the confidence of the academicians have substantially increased during few years. This is an indication that witnesses that the academia world are shifting towards imparting more skill based knowledge to the students that could be more relevant with regard to the job providing and it will enhance the employability. During their internship and apprenticeship of the students they should engaged in real life projects which are facing some technical or profession gulch so that their practical leaning can start at the very beginning of their career.

The analysis of the data shows that the majority of the academicians consider themselves as the most confident for undertaking the industry-oriented projects in align with the industry requirements. 82% faculty members from various universities or HEIs are ready to undertake such endeavors. Only 18% faculty members of the selected sample were in denial mode or reluctant to take such projects due to some reasons or others.

The basic aim of the students to go to college or university is to gain some knowledge and skills so that they can be eligible for getting jobs and conduct some research and developmental projects in the betterment of themselves as well as in the betterment of the society and nation as a whole. The students expect from the universities and institutions in which they are pursuing their degree or diploma courses that they will be imparted job-oriented education that will help them to get a job when they complete their course. Today’s world has changed and having only conventional knowledge to the students is not enough because today’s time demands to be multi-dimensional and versatile only then you can survive in the market. Therefore, the HEIs must offer a complete package of skills, knowledge, expertise and training to them. There is cut-throat completion in the market among all the stakeholders. Students are coming from various parts of the country and they are diverse in knowledge and skills. There are many cultures and traits so you must be experts in two or more languages also. The universities and HEIs are expected to motivate their faculty members to undertake the industry projects and involve students too in such projects. It will work from many points of view. First, students can assist faculty members in the functioning of the projects and second, students will learn something new and innovative and practical that may lead to the overall growth of them. The training programs should be organized for them to learn the skills like communication skills, personality development programs, mock interviews, and other job-oriented training. There is an urgent need of such faculty members who have some industry experience so that they can provide the practical knowledge and skills to the students. The academia must have the collaborations and tie-ups with the industry and corporate. Such tie-ups can contribute in the holistic development of the students.

The analysis of the data of the current study justifies that the majority of the faculty members are motivated and encouraged to undertake the industrial projects. 74% academicians of the selected sample from the various institutions responded that they are motivated to undertake such projects and some of them are already engaged in some industry projects.

The universities and other HEIs can serve the industries in many ways. But here, we will discuss only two areas where universities can offer their services to the industries. One, it provides the plenty of skilled manpower the industries so that industries can navigate and run their business smoothly. Second, they can incubate new and innovative ideas to come up with some start-ups and entrepreneurial undertakings that can make them job provider rather than job seeker. This relations is very apparent between both of them but it not that simple. It is complex in many ways. There are inherent differences between both of them. They can be seen together but still they will be far from each other like the two sides of the river. For getting into any collaboration between academia and industry there are many formalities and procedural works have to be done. And not only to be collaborated is enough but also their collaboration must be functional only then it will benefit to the stakeholders. Engineering and science discipline are very much need to have the collaboration and tie-ups with the industries and research and development organizations.

The analysis and interpretation of the data reflect that 70% faculties are think in a manner that there must be clear procedure and process to support and facilitate industry-academia collaboration.

As we all know that change is law of nature. Everything changes over the period of time. And it also true with the academic curriculum. The academic curriculum must be revised time to time according to the changing needs of the industry and society. As per the need of the market and industry, course curriculum and pedagogy should be revised aligning with the dynamic needs of the industry. The industrial sector has become global and economy is integrated economy. That is why, there must be some innovative teaching pedagogy which may provide more skills. Outcome-based education system can be introduced. Along with this Teaching-Learning & Assessment system should also be introduced. The main focus of the curriculum and pedagogy should be on the enhancement of the employability of the program only then it will have some value for the students and they can contribute in the growth of the society and the nation as a whole. Such academic curriculum and pedagogy focus more on practical training rather than the theoretical knowledge. Theoretical knowledge is necessary but knowing the application of that knowledge to solve the problem is the main theme of the today's scenario. The course curriculum and pedagogy should be so structured and sequential that will lead to the students towards becoming an expert of the area. New models, approaches, theories, practical and experiments, case studies etc. should be included in the curriculum.

The analysis in the fourth chapter shows that 60% respondents said that they revise their academic curriculum after every four years. HEIs are not stuck with the old and traditional curriculum rather they are keen to revise and update their curriculum as per need of the hour.

Two-way communication in an organization is important because it allows for effective interaction, understanding, and collaboration among team members and departments. It enables the sharing of knowledge, ideas, and feedback, leading to improved problem-solving and decision-making processes. Effective communication also helps in building and maintaining relationships, both within the organization and with external stakeholders. It plays a crucial role in achieving organizational goals, motivating employees, and creating a trustful environment. Additionally, two-way communication helps in overcoming language barriers, especially in multinational organizations, by facilitating smooth communication between different departments and locations. Cultural differences also need to be considered to improve communication between parties. Overall, effective two-way communication is essential for organizational success and productivity. Two-way communication is the process of sharing information back and forth between two parties. In other words, it's a conversation where both the sender and receiver invite and offer feedback. And most importantly, two-way communication is never a monologue.

To maximize the benefits of two-way communication in the workplace, dialogue should be continuous. In other words, the flow of information between the sender and the receiver should be consistent. Effective internal communications tools, methods, and channels are vital in facilitating this process.

62% responses received in positive mode that two-way communication between the universities and industry is the regular activity. 28% respondents said no that it is not a regular activity but it is done as and when it requires.

As we all know that undertaking industrial projects is very much important for the faculty members but still most of the institute did not make it obligatory or compulsory for the faculty members. They motivate them, support them and also provide the adequate facilities and other resources to undertake and accomplish such projects but they do not impose such willingness of the institute on them. Only 20% faculties said in yes that their institute has made it obligatory and compulsory to undertake such industrial project and 68% faculties said no. 12% didn't said anything.

Industrial visits and industrial projects often referred to as industry visits for students, has become an important and vital part of the academic curriculum in almost all the programs whether it is under graduate or post graduate. Such industrial visits provide very unique and practical exposure to the students. It teaches and provides them an environment in which they can learn the nuances of the industry and corporate culture. Students can learn and apply their theoretical knowledge for solving the real problems. Actually, the main motive of such industrial is to bridge the gap between industry and academia.

The main intention and very objective of conducting industrial visits is to develop and inculcate the thought process of thinking out of the box. It is not about the classroom teaching but it focuses on the holistic development of the students and make them ready for the industry need. The current scenario is very dynamic and technological developments and advancements are changing rapidly so students must develop an adaptability in their nature.

With the help of industrial visits they can take many live inputs to develop their own knowledge and understanding. Before seeking any job in industry, they will be able to know about the industrial growth, and actually, it provides them first point of getting interacted with the corporate and industrial personnel. They can also improve and enhance their skills with the help of the industrial visits. The students can also undertake some industry projects

The above data of the current study clearly explains that 84% responses are positive that affirms that majority of the students are motivated and willingly ready to undertake such industrial projects. Maximum students of all the selected HEIs said that their faculties and institute support and motivate them to undertake such projects.

When this research study was being undertaken, during that period it was found that there is a lacking of a strong partnership between industry and academia or in other sense between the knowledge providers and the users of the knowledge. It is necessary because to sustain and remain in this global society. The relationship of academicians and industrialists are not exclusive rather it is mutual. Industrialists tell them to prepare the graduates as per their needs and academician perform that.

Industry-academia relationship serve the society in many ways. It may develop in conducting quality research and their collaboration and association may also develop such products and innovative technologies which can be beneficial for the every stakeholder of the society. Generally. The research of the academia is developed and evolved in light of the practical application by the industry. Such collaborations may lead to the coming up of the new start-ups, undertakings of entrepreneurial activities. Eventually, it will produce some opportunities of employment for the society.

The final result and outcome of this research study can conclude that university and industry collaboration and interface always assist in developing the new and innovative technologies and upgraded processes equipped with the advanced technical know-how. And it will not be a realty until faculty members will take an active role and interest in industry academia interaction and association. They may play a key role or play the role as a link between HEIs and industry. They should also motivate and encourage the students to take part in the process of such collaboration, associations, and interface so that their visibility in terms of gaining knowledge can be practically enhanced. The study clearly reveals that industrial exposure imparted to the students enhances their employability and skills.

The research also reveals that recruitment of the qualified employee is important but more important is to retain that employee. It is to be further added that the research concludes that academia-industry association can help in the process of recruiting the best employee but also it may also assist in retain such employees. If the employee retains in an industry for a long time, its cost to company and industry remain less. On the other hand, if there is high ratio of incoming and outgoing employee, the cost of employee will be higher to company. And it will also affect adversely the productivity because industry have to provide orientation training to employee and it will happen again and again. The result of the study also indicates that in the government set up, the bureaucracy also sabotages the effective implementation of the policies.

It was also found in the research that there are many factors which promote the academia-industry collaboration. These factors may play an important role to promote such initiatives. These factors are employability, entrepreneurial development, collaboration for skill enhancement, advancement in research, teaching enhancement, financial support and assistance, recruitment and selection of the staff, retention of the staff, innovations and advertisement or publicity. These are factors which can promote the academia and industry interface.

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The main intention and very objective of conducting industrial visits is to develop and inculcate the thought process of thinking out of the box. It is not about the classroom teaching but it focuses on the holistic development of the students and make them ready for the industry need. The current scenario is very dynamic and technological developments and advancements are changing rapidly so students must develop an adaptability in their nature.

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There is a paradigm shift in universities from traditional teaching towards providing the job-oriented and industry-ready education. Academic curriculum are being revised in line with the industry needs. The academic curriculum and pedagogy should cater the needs of the industries and the corporate world. For imparting such sort of knowledge, universities can invite guest faculties and also adjunct faculties. Knowledge is diverse. Therefore, diverse faculty members should be take an active role in interacting with students so that they can gain more and diverse knowledge. Such practice will boost the growth of the students. Because in today's scenario, universities are focusing onto prepare industry ready graduates so that they can take the challenges as the opportunities. They are providing them industry related training and workshops to train them as per the need of the industry.

The major finding of the present study is that there is a positive and significant impact of the academia and industry collaboration and association in terms of improving the employability, enhancement of skills of the students. In addition to that it also enhances the scientific approach of the academicians. It compels them to change themselves and also change their pedagogy to deliver and impart the knowledge to the students in such a manner that can improve the personality of the students. Such collaboration can improve the Indian higher education system towards fostering the growth.

The manpower and personnel who works in laboratory need to be highly trained about the functioning of the laboratory equipment and they must know the use of chemicals and its ratio of mixture. They also ensure that the available facilities of the library must meet their needs. They should know their strength and limitations of the laboratory that can be able to cater the needs of the research and other experiments. They must be so capable to operate and navigate the machines and equipment properly. There must be very controlled environment of the laboratory because most of the scientific experiments are conducted in a controlled environment. Ventilation must be adequate, cleanliness is very important, sanitation is very much crucial. Whether safety and efficiency measures are being effectively followed or not. Trained laboratory personnel must understand how chemical laboratory facilities operate. Every laboratory should adopt the standard operating procedures (SOPs) so that the standardization can be effectively implemented. All the functional and operational requirements must be easily available and insufficiency should avoided. Space of the laboratory must be sufficient and should be as per the regulatory requirements and also according to the intake of the students. Given the chance, they should provide input to the laboratory designers to ensure that the facilities meet the needs of the functions of the laboratory. The ventilation system of the laboratory is very important and they (laboratory personnel) should know the challenges and limitations of the laboratory ventilation system. If there is any challenge in laboratory premises, that must be addressed without any compromise. Any leniency in that can be a cause of major tragedy. Safety is also another important aspect, and it should be ensured that safety measures are not compromised. Ventilation system, environmental control, laboratory chemicals, and other storage logistics system must be safe and efficient.

82% respondents said that there are adequate lab facilities available at their campus to support any kind of academia-industry partnership.

The geographic location of a university can influence the strategy of leadership. Different universities operate in complex international environments and need to balance global relevance with local identity. Changes in governance structures of European universities have been proposed to enhance their democratic nature and degree of centralization. The leadership exercised during the formation of University had a significant impact on the challenges experienced by the institution. Additionally, regional characteristics can shape university performance and their ability to contribute to their regions. Therefore, the geographic location of a university can affect the leadership strategy employed, considering factors such as international dynamics, governance structures, and regional engagement. The fundamental purpose of university geographic clustering is to gather resources through "agglomeration" to improve the performance of higher education and scientific research. The empirical challenges prevalent in the aforementioned studies are related to issues of sample representativeness and endogeneity. First, existing empirical studies are often based on case studies or a small number of research institutions and lack representativeness. This weakens external validity and prevents reliable conclusions from being drawn. Second, university or research institution cluster projects conducted at the national level suffer from serious endogeneity problems in sample selection, making it difficult to effectively identify the net effect of clustering. Indeed, examining the impact of geographic clustering on university scientific research performance should be of interest not only to scientific scholars but also to policy makers. Therefore, the effects of geographic clustering of universities need to be further explored.

The analysis of the above data reflects that the responses are mixed regarding the geographic location of the universities or Higher Educational Institutions. Only 30% respondents consider that the geographic location may be a barrier to establish a partnership between industry and academia. 50% respondents believe that geographic location does not create any barrier between the industry and academia. 20% respondents were not able to respond anything. Their responses were neutral.

Collaboration between universities and industries has become increasingly important in recent years. The traditional classroom model of education is no longer enough to prepare students for the workforce. By working with companies, students can gain real-world experience and develop job-ready skills. A report by the National Association of Colleges and Employers showed that students who had completed internships or cooperative education assignments were more likely to receive job offers and have higher starting salaries than those who did not. Furthermore, according to a study by Harvard Business Review, companies with higher levels of collaboration with universities had higher innovation output, higher quality patents, and more successful new ventures. This highlights the importance of industry-academia collaboration in driving innovation and growth.

Effective collaboration requires active participation and engagement from both sides. Universities must identify the needs of the industry and align their curriculums accordingly. This could involve incorporating industry projects into coursework, offering practical training sessions, or providing access to the latest industry equipment and technology. Similarly, industries should provide internships, mentorship programs, and other opportunities for students to gain practical experience. However, some may argue that industry-academia collaboration can lead to the commercialization of research and a potential conflict of interest. To avoid this, universities should maintain academic independence and transparency in research partnerships with industries.

The analysis of above data strongly believes that majority of the respondents consider that collaboration between industry and academia does not carry any negative impact on the pedagogic mission of the HEIs. 82% respondents disagree or strongly disagree with question put before them.

When this question was put before the academicians, a mixed reaction and responses were received from them. 46% respondents said that this is true that it is not a part of our job to take up industrial projects. There must be some experts of that kind who can be involved exclusively in such tasks. On the other hand, 42% respondents were disagree and they believed that keep involving and engaging in undertaking industrial projects is an essential part of their job.

Teaching is a profession that holds the key to shaping the future, but the responsibilities and administrative burdens placed on educators can sometimes overshadow their primary focus on student learning. As schools and educational institutions evolve in the digital age, it becomes imperative to explore innovative strategies to alleviate the administrative challenges faced by teaching staff. In this comprehensive exploration, we will delve into a range of strategies aimed at reducing administrative burdens, fostering an environment where educators can dedicate their time and energy to what matters most – the education and well-being of their students. Teachers, often referred to as the backbone of the education system, face a multitude of administrative tasks that extend beyond lesson planning and classroom instruction. Grading assignments, tracking student progress, managing communication with parents, and navigating complex reporting systems are just a few examples of the administrative burdens that educators encounter daily. These tasks, while essential, can divert their attention and energy away from the core of their profession – teaching.

The increasing demands of paperwork and administrative responsibilities can contribute to stress, burnout, and a potential decline in job satisfaction among teachers. Recognizing and addressing these challenges is crucial not only for the well-being of educators but also for the overall quality of education provided to students.

56% respondents agreed that teaching and other administrative load hamper their productivity or efficient to undertake industrial projects. Excessive teaching workload and administrative responsibilities provide opportunities to learn many new things but it consumes a handsome amount of time. Having performed all these duties, very little time left to take up such industry oriented projects. But 32% respondents do not think that teaching workload and other administrative duties create any barrier to undertake industrial project. They believe that it is all about our time management that how effectively we manage our time. So, some balanced opinions were there regarding the question.

Conclusions

On the basis of data analysis of responses collected from industry representatives and student representatives, the following conclusions were drawn:

- When this research study was being undertaken, during that period it was found that there is a lacking of a strong partnership between industry and academia or in other sense between the knowledge providers and the users of the knowledge. It is necessary because to sustain and remain in this global society. The relationship of academicians and industrialists are not exclusive rather it is mutual. Industrialists tell them to prepare the graduates as per their needs and academician perform that.

- Industry-academia relationship serve the society in many ways. It may develop in conducting quality research and their collaboration and association may also develop such products and innovative technologies which can be beneficial for the every stakeholder of the society. Generally. The research of the academia is developed and evolved in light of the practical application by the industry. Such collaborations may lead to the coming up of the new start-ups, undertakings of entrepreneurial activities. Eventually, it will produce some opportunities of employment for the society.

- The final result and outcome of this research study can conclude that university and industry collaboration and interface always assist in developing the new and innovative technologies and upgraded processes equipped with the advanced technical know-how. And it will not be a realty until faculty members will take an active role and interest in industry academia interaction and association. They may play a key role or play the role as a link between HEIs and industry. They should also motivate and encourage the students to take part in the process of such collaboration, associations, and interface so that their visibility in terms of gaining knowledge can be practically enhanced. The study clearly reveals that industrial exposure imparted to the students enhances their employability and skills.

- The research also reveals that recruitment of the qualified employee is important but more important is to retain that employee. It is to be further added that the research concludes that academia-industry association can help in the process of recruiting the best employee but also it may also assist in retain such employees. If the employee retains in an industry for a long time, its cost to company and industry remain less. On the other hand, if there is high ratio of incoming and outgoing employee, the cost of employee will be higher to company. And it will also affect adversely the productivity because industry have to provide orientation training to employee and it will happen again and again. The result of the study also indicates that in the government set up, the bureaucracy also sabotages the effective implementation of the policies.

- It was also found in 76 the research that there are many factors which promote the academia-industry collaboration. These factors 56 may play an important role to promote such initiatives. These factors are employability, entrepreneurial development, collaboration for skill enhancement, advancement in research, teaching enhancement, financial support and assistance, recruitment and selection of the staff, retention of the staff, innovations and advertisement or publicity. These are factors which can promote the academia and industry interface.

- Industrial visits and industrial projects often referred to as industry visits for students, has become an important and vital part of the academic curriculum in almost all the programs whether it is under graduate or post graduate. Such industrial visits provide very unique and practical exposure to the students. It teaches and provides them an environment in which they can learn the nuances of the industry and corporate culture. Students can learn and apply their theoretical knowledge for solving the real problems. Actually, the main motive of such industrial is to bridge the gap between industry and academia.

- The main intention and very objective of conducting industrial visits is to develop and inculcate the thought process of thinking out of the box. It is not about the classroom teaching but it focuses on the holistic development of the students and make them ready for the industry need. The current scenario is very dynamic and technological developments and advancements are changing rapidly so students must develop an adaptability in their nature.

- With the help of industrial visits they can take many live inputs to develop their own knowledge and understanding. Before seeking any job in industry, they will be able to know about the industrial growth, and actually, it provides them first point of getting interacted with the corporate and industrial personnel. They can also improve and enhance their skills with the help of the industrial visits. The students can also undertake some industry projects. The above data of the current study clearly explains that 84% responses are positive that affirms that majority of the students are motivated and willingly ready to undertake such industrial projects. Maximum students of all the selected HEIs said that their faculties and institute support and motivate them to undertake such projects.

- There is a massive setback in India for the fresher's students that they do not have any experience and they are asked to earn some experience then come again. It is a massive problem at the entry level that should be addressed as early as possible. This problem can be overcome by way of providing the long internship so that they can dedicate more time to the industry during pursuing their degree or diploma course. Internship in industry provides an opportunity to learn the basics of the industrial sector and also learn the functioning of the industry.

- There is a paradigm shift in universities from traditional teaching towards providing the job-oriented and industry-ready education. Academic curriculum are being revised in line with the industry needs. The academic curriculum and pedagogy should cater the needs of the industries and the corporate world. For imparting such sort of knowledge, universities can invite guest faculties and also adjunct faculties. Knowledge is diverse. Therefore, diverse faculty members should be take an active role in interacting with students so that they can gain more and diverse knowledge. Such practice will boost the growth of the students. Because in today's scenario, universities are focusing onto prepare industry ready graduates so that they can take the challenges as the opportunities. They are providing them industry related training and workshops to train them as per the need of the industry.

- The major finding of the present study is that there is a positive and significant impact of the academia and industry collaboration and association in terms of improving the employability, enhancement of skills of the students. In addition to that it also enhances the scientific approach of the academicians. It compels them to change themselves and also change their pedagogy to deliver and impart the knowledge to the students in such a manner that can improve the personality of the students. Such collaboration can improve the Indian higher education system towards fostering the growth.

Chapter-6

Limitations and Suggestions

Suggestions

Findings and conclusions of the present study clearly reveal that there are some of the recommendations for the stakeholders of Industries and educational institutions to bring some of the improvements and also it is the need of the hour to introduce some innovative initiatives to fasten and enhance the skills and employability of the students. These suggestions are as follows:

- The trends of the global economy is economy is changing rapidly and the needs and requirements of the industry from the Higher Education Institutions have also changed. Therefore the role of Indian universities and HEIs have changed and they should modify their role as per the changing requirements of the industry. They cannot go alone. They must try to understand that they are the important stakeholders of the society. Therefore, they are complimentary to each other. Universities and HEIs try to explore the opportunities in their local areas where some industries are located. Indian universities and HEIS need to collaborate with industries and R & D so that ample opportunities can be available for the students not only for their placement or jobs but also for their internship, summer training and other industrial projects.

- It is always taught and known that resources are scarce not unlimited and it is true with the organizations also. Therefore, every organization needs to utilize their resources optimally and efficiently. The allocation of their resources must be very rational, efficient and cost effective as well. In this regard, the academic institutions can play a vital and crucial role to develop and to train the industry personnel to rationally use the limited resources of the organization so that the profitability can be maximized on the cost of the resources consumed. There must be a free and uninterrupted flow of skills, idea and techniques between both the stakeholders

- There are always some unsolved and complex problems and situations before the management of the industry and other businesses to be resolved effectively and timely. For this purpose, researchers and academicians can be invited for conduction gang research or investigation to find out an optimal solution of the persistent problem. There are some brainstorming sessions can be conducted to solve the cases of the industry. Industries may offer some remuneration or incentives to the researchers, academicians and research scholars also.

- It is the need of the hour that academic curriculum must be designed as per the industry needs and expectations. Academic curriculum should be strongly industry oriented which can solve the industry issues and technological challenges. It is also important that universities and HEIS Institute/University should design their curriculum, which is strongly oriented towards solving industry issues as well technological challenges of the industries. It is also important that while recruitment such candidate must be given preference who have some industry experience in their profile.

- Innovations are very important across all the sectors whether it is industries, academics, technology, research and development etc. There should be an interdependence between industries and HEIs. The synchronization is very much needed between the industry and academics for bridging the gap. They should adopt multidisciplinary approach.

- It can be concluded and suggested in general that the faculties should be encouraged and promoted to gain some industry experience or exposure by attending workshops, conferences, seminars, and also they can pursue some industry-oriented executive course being offered by many institutions. Such practice will definitely help them to impart practical knowledge to the students. Administration should create an open environment where students and faculty members can freely exchange their ideas and opinions. Discipline is very much necessary to bring the things in order

- **Limitations of the Study**

- There is a major constraint regarding the number of participants. Limited number of participants were included in the survey for the purpose of the study.

- In addition, industries, HEIs, industry professional, and students were taken for the study. But for the further study, some other stakeholders may also be taken.

- First, the sample size of the study could be large. Therefore, the results have to be evaluated in further research with a larger sample size. There are also limitations related to the measures that were used. The number of questions could be added in the length of the questionnaire.

Academia-industry collaboration has always been a topic of discussion in both the sides. And still no model exists that is widely used. Indeed, the collaboration, world over, is quite limited. This just shows the difficulty of the problem. In this article, we discuss the different types of collaboration that are possible, particularly in the Indian scenario.

Producer-Consumer Interaction

The importance on academia-industry partnership is not only important for academicians and industry only but it also traces the importance with regard to producers and consumers also. There is relationship between both of them. This relationship necessitates some collaboration as the consumer has to ensure that the output of the producer satisfies the needs to a large extent. Hence, one form of collaboration, which is more in the nature of a feedback loop, is for the industry for the purpose of providing inputs back to the HEIs regarding their perception or evaluation of their products. Interestingly, even this rather obvious kind of interaction does not occur in a structured manner, as both the sides maintain a distant relationship. Though there are many reasons for this (for example, the academia not taking kindly to the often self-serving suggestions of a company), the main reason is lack of suitable forums and platforms to facilitate this. Note that though general forums covering the issue at a broad level are useful, to implement this collaboration in any meaningful way, forums at institute level are necessary. As we know that in India, it is a great lacking of skilled and trained manpower. This lacking can be overcome by the way of collaboration with the industries. The findings of the study reveal that the present engineering education system is not an ideal shape and structure and it requires the structural changes and reforms. The higher education of the cannot be dependent only on government, private sector have to involve in it. Some companies and institutes have started some initiatives of their own on this front. But this seems like a very viable area for collaboration, where joint programs have a better chance of success. However, not much seems to be happening in this area, even though both sides can gain substantially from it.

Collaboration in Continuing Education

Teaching is the core competency of academic institutions. And many institutes engaged in education at high end, have the courseware and ability to provide training for high-end manpower development. There may be many areas and topics which may be relevant and important for the growth of the industry. Therefore, a natural collaboration possibility is for the academic faculty and institutes to conduct training in topics of interest for industry. This model has existed for long time and is reasonably well understood. This form of relationship is also beneficial to both. Typically, in this form of collaboration, continuing education programs are offered which are designed for industry participants. Or, short courses may be offered by some faculty in some company or some common place. The present study reveals that if we talk about the competence in technological uses and advancements in industries have increased substantially. Now the different kind of on the job training programs and workshops are being conducted by the institutions so that the dependency of the students on the theoretical models and theories can be reduced.

On the contrary the training programs are required to train the working professionals to enhance their efficiency and productivity. Programs for working professionals in management are now picking up in India. However, such programs for technology areas have not developed in any serious manner. This is one area that can be potentially developed, and it is best done if both sides collaborate.

Collaboration in Research

In today's world the intellectual property rights have become very important as the interest is dad by day is increasing. That is main reason that the significance and relevance of collaboration with the industry has substantially increased. For serving that purpose collaborations with the industries are being done by the academia and also faculties are getting involved in that process. The main aim of any kind of research is to find out the solution of an existing problem of to add some knowledge in the existing knowledge base. One this is to be understood that academicians are the researchers as well. As they are good enough or possess sufficient knowledge to conduct any research but they do not have the sufficient and adequate research facilities or equipment's. Therefore, for bridging that gap collaboration with industries is needed. Industry and academia will come together with folding hands. One will contribute their intellectual skill or technical expertise on the hand other will facilitate the physical art of infrastructure and will satisfy the financing needs.

A technocrat professional one whose business depends on pushing technological advancements for developing new technologies that it can then use to bring out newer products in the market place. Though there were no technology driven companies in the country before, there are some that are now coming up. Even a services company can benefit from research, particularly if it is a large player. Research can enhance the ability of a company to adapt to changes and the readiness for absorbing changes in technology. It can also help the company build a leadership position in leveraging the new technology for offering higher value. Research can help service the constant demand for improvement quality, lowering costs, and creating more value. And can also help develop new approaches for solving problems, as engineers and managers may not be able to do this – engineers work for using existing knowledge to provide a solution, and managers stick to proven methods to reduce risks. There are other areas like dealing with scale, providing inputs to consulting practices, etc. where research inputs are useful. Besides these company-specific reasons, there is a general industry-wide reason as well for increasing research in companies. So far, most of the research has been done in the west as their businesses needed the innovation. It is clear that the business like the software services are shifting to India and in future this work will shrink further in the west. As a business shifts, the investments in research related to that business will reduce. That is, Indian companies which relied on knowledge from the west may find the ready flow of new knowledge reducing. In other words, as the work shifts to India, there is a need for R&D to also shift, so the innovation does not suffer and research becomes more aligned to the needs of the dominant business model of outsourcing. So, we can safely say that need for research in Indian companies is increasing. Lets look at the nature of research. Research can be basic or applied. Applied research is where the knowledge is being created with the intent that it will be used for commercial gains. Earlier, academics often were engaged in basic research. But now both applied and basic research is being done in academic institutions. Companies, by their nature, are generally interested in applied research. As academic institutions also now engage in this area, there is some convergence of interests. Academic research is driven by the impact it will have on the global research community, and the measures of success are largely based on publications. Research in a company, on the other hand, is driven by the impact it will have on the company, and the measures of success are largely based on the long and short term value it creates for the company. Though these two objectives seem quite at odd with each other, in practice they are not so. Though publications are often not the objective in a company, many companies have also found that often it is hard to evaluate the work without subjecting it to the reviews and eyes of other researchers. Due to this, often companies do publish parts of their work (after camouflaging the confidential parts). This brings in commonality of goals among the academic and industry researchers. With this alignment of goals and nature of research, there is a clear possibility of collaboration between academicians and industry. But there is a gap. Often academics are involved in academic or pure research which may not have applied aspect to it. With time the academicians tend to become too conceptual and too far removed from the real problems that the industry might be facing. And academicians realize that, leading to an underlying belief that the work they do is not useful for industry. This statement, in itself, is true. However, what it seems to imply is not. That is, the work the academician is doing may not be useful, but that does not mean that there is no common ground for common work. Academicians have a very strong ability to abstract from the problem and conceptualize and then solve it in the conceptual domain. This is an expertise that is woefully lacking in the industry, which is faced with down-to-earth problems day-in and day-out, often not letting the conceptualization skill to develop. And without proper conceptualization, there can really be no research, as research always tries to address a general problem (engineering on the other hand, may deal with a specific problem.) So, there is a natural synergy between the academic and the industry researcher – academician can lend the conceptualization and generalization skills and the industry can provide the practical reality in which the conceptualization can be rooted. What both sides have to realize is that bringing the two together requires a great deal of solid interaction as communication gaps exist. And there is no easy way to bridge this gap – both sides must simply spend time together to understand each other's context and develop a common language. Industry in India often looks for "consultants" in academic community – basically experts who can guide them in solving their problems. This model assumes that the academic is already working on those problems. As discussed, this is often not the case. Only after considerable time together can common issues be identified which may be addressable by joint research. Hence a main hurdle today is lack of structures and mechanisms to have researchers from two sides spend time together. One practical way to bridge this gap is to have industry to invite academics who may have an interest in their problems to spend time at their facility, interacting with researchers and practitioners. And this should be done without a defined outcome or result of this visit. That is, initial visits will be to set the stage for further collaboration, which, incidentally, may or may not materialize. Perhaps due to these uncertainties, there are no real models to invite faculty to just spend time at their facility. But research is unpredictable and we have to learn to appreciate it. So, in the end, it is very necessary to have the impetus, interaction is mandatory. For the purpose of drawing inferences and conclusions, all the concerned stakeholders must be taken into consideration. That is one of the best this done and contributed by the hosting faculty while their visit during summer and winter times. At that time it can be ensure that there must be an adequate interaction between the stakeholders. Not only inviting the guest faculties is important but also the visitors can also be get involved in such process. Such random visits can assist the academician also at large. This initiative with regard to collaboration with the industry is necessary for improving the overall personality of the graduates. Visitors having the expertise of their own area can facilitate the academicians and students both. Research and other academic involvement is a collective activity and cannot be performed in isolation.

MAHIPAL SINGH

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