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# An Insilico Evaluation of Indole Benzimidazole Scaffolds As Antimicrobial and Anticancer Agents

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**ABSTRACT**

*In-silico* molecular modeling and ADME prediction of proposed Indole-benz-imidazole derivatives using softwares such as Molinspiration and PreADMET Software respectively. This helped to determine the drug likeness properties and various pharmacokinetic properties of proposed derivatives. These analogues undergone molecular docking studies with the help of Schrodinger Software. The ligands docked with bacterial, fungal and anticancer enzyme like DNA Gyrase subunit B (PDB ID: 3U2K), Lanosterol 14α-Demethylase 9 (PDB ID: 5TZ1) and Human Estrogen Receptor alpha (PDB ID: 1A52) respectively. From the obtained docking scores, it was found that the derivatives have good docking score than the standard drugs, of this the derivative JJ2 [2-(5-methyl-1H-indol-3-yl)-1H-benz-imidazole] have most promising action as antimicrobial and anticancer activity.

**KEYWORDS:** *Insilico* molecular modeling, ADME, benzimidazole, indole

## INTRODUCTION

Heterocyclic compounds play a critical role in drug development, offering structural diversity and potential for novel mechanisms of action. Among these, nitrogen-containing heterocycles are particularly significant due to their ability to form hydrogen bonds, facilitating selective protein binding. Benz-imidazole, a prominent nitrogen-containing heterocycle, is an aromatic bicyclic compound comprising a fused benzene and imidazole ring with the molecular formula Heterocyclic compounds play a critical role in drug development, offering structural diversity and potential for novel mechanisms of action. Benz-imidazole, a prominent nitrogen-containing heterocycle, is an aromatic bicyclic compound comprising a fused benzene and imidazole ring with the molecular formula $C_7H_6N_2$. It serves as a benzo derivative of the imidazole ring and is known for its extensive biological activity spectrum. The benz-imidazole [1] nucleus is a structural component in numerous bioactive compounds, demonstrating interactions with various enzymes and proteins. This structural versatility allows it to act as a scaffold in designing drugs with diverse pharmacological effects, including antibacterial [2], antifungal[3], antitubercular[4], antimalarial[5], anti-inflammatory[6], antiamoebic[7], antiulcerative[8], antihypertensive[9], antiproliferative[10], anti-kinase, and anti-HIV-1 properties antitumor[11].

Indole, or benzopyrrole, is a heterocyclic aromatic chemical having the formula $C_8H_7N$. A nitrogen-containing five-membered pyrrole ring is fused to a six-membered benzene ring. Indole's basicity and reactivity make it a useful building block in medicinal chemistry and drug creation due to its unique

structure. Indole [12] has less basicity than other amines owing to the nitrogen lone pair delocalisation within the aromatic ring's π-electron system. The nitrogen is less basic than conventional amines due to electron delocalisation, which decreases the lone pair for protonation. Thus, indole is protonated at the C-3 location of the pyrrole ring, not the nitrogen atom. The aromaticity of the indole ring structure makes C-3 protonation more thermodynamically stable. Indole's most reactive location, C-3, causes electrophilic substitution reactions and other chemical activities. Active pharmacophore of various indole analogues produces anti-inflammatory[13] antimicrobial[14] anti-tubercular[15] anticonvulsant[16] antidiabetic anticancer activities. Indole participates in a wide range of chemical reactions due to the reactivity of the C-3 position. Electrophilic substitution is one of the most common reactions, where an electrophile replaces a hydrogen atom at C-3. This reaction is crucial in the synthesis of indole derivatives, which have diverse biological activities. In addition to electrophilic substitution, indole also forms organometallic indole anion complexes, which are important intermediates in organic synthesis [17]. The C-3 position of indole is also involved in reactions such as carbon lithiation**,** oxidation**,** and cycloaddition. Both benzimidazole and indole having lot of similar pharmacological action, by mixing these two heterocyclic rings produces a synergistic action, this helps to develop more active molecules.

Major obstacles in traditional drug discovery is the high attrition rate throughout the research and development process. For every new drug that reaches the market, it is estimated that researchers must conduct over 100 screens to find viable drug leads. This screening process involves narrowing down tens of thousands of compounds to identify those with promising therapeutic potential. However, even after an initial lead compound is found, the drug discovery process remains lengthy and costly, with some estimates suggesting that it takes over five years and more than $200 million to discover a viable lead compound. This is in addition to the even greater time and financial investments required for subsequent drug development, including clinical trials. As a result, drug discovery and development are fraught with uncertainty, making the process both time-consuming and expensive. Approaches such as computational modeling, high-throughput screening, and target validation can help to increase the likelihood of success and minimize resource waste.

Computer-Aided Drug Design (CADD) serves as an essential instrument in contemporary drug discovery, facilitating the anticipation of interactions between small molecules and biological targets. A fundamental aspect of CADD is its ability to evaluate the probability of a molecule binding to a target and, if binding occurs, the strength of that interaction. This forecast is essential for identifying potential drug candidates that demonstrate high specificity and efficacy. CADD employs computational techniques to optimise the drug discovery process, minimising the reliance on extensive experimental trials and improving the accuracy of therapeutic interventions [18].

## METHODOLOGY

### Protein Preparation

The protein production wizard in the Schrodinger program's graphical user interface MaestroV 12.8 was used to build the protein structure (PDB ID: 3U2K, 5TZ1, 1A52). By removing the substrate cofactor, changing the bond ordering, deleting metal ions and crystallographically visible water molecules (water without H bonds), fixing mistakes in the PDB dataset, and optimizing hydrogen bonds, the protein underwent independent preprocessing[19].

### Ligand Preparation

A series of indole benzimidazole derivatives were generated using Maestro's workspace and subsequently

converted to a three-dimensional format for docking studies. All ligands were constructed utilising the Maestro build panel. The ligands were prepared using 'LigPrep'. The 'LigPrep' process involves a sequence of steps that execute conversions, apply structural corrections, generate structural variations, eliminate undesired structures, and optimise the resulting structures. Following the conversion of structures to Maestro format, hydrogen atoms were incorporated using the Hydrogen Treatment panel in Maestro. Then unwanted molecules like water and salt were removed and neutralize charged atoms by neutralizer which add or remove hydrogen ion.

**ADME/T Studies**

The prepared ligands were neutralized and analyzed for their ADME/T properties using the QikProp software (Version 12.8, 2021). QikProp is a computational tool widely used in drug discovery to predict pharmacokinetics and pharmacodynamics by evaluating drug-like properties of molecules. This analysis provides crucial insights into the absorption, distribution, metabolism, excretion, and toxicity (ADME/T) characteristics of the ligands, aiding in the selection of candidates with optimal properties for further development. Significant ADME/T properties were predicted to assess the drug-likeness of the ligands.

## DOCKING

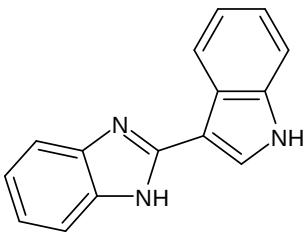
**Receptor Grid Generation**

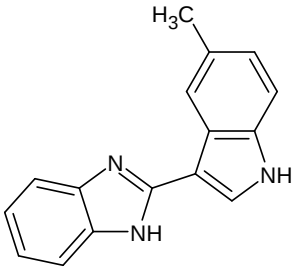
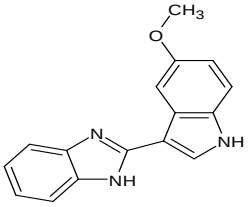
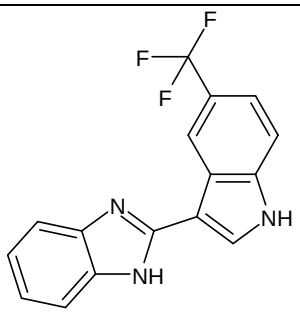
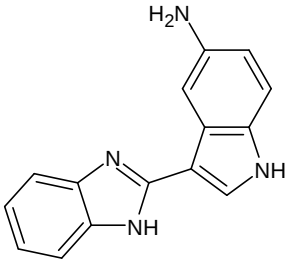
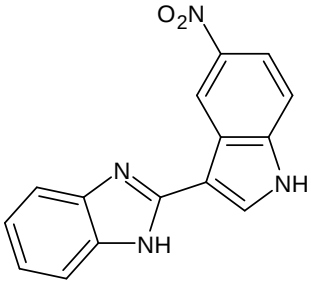
Receptor grids were calculated for prepared proteins so that various ligand poses might bind within the expected active site during docking[20]. The OPLS 2001 force field was applied while grids were generated in Glide with the default charge cutoff 0.25 and van der Waals scaling factor 1.00. SP Flexible ligand docking was used in Schrödinger-Maestro V12.8 2021. All the docking and scoring calculations were executed by the Glide version 6.9. All ligands were docked with the protein grid (PDB ID: 3U2K, 5TZ1, 1A52) using ligand docking application of Glide version 6.9 in Schrodinger Maestro version 12.8.Glide Extra Precision (XP) flexible ligand docking was carried out in Glide of Schrödinger Maestro v12.8.

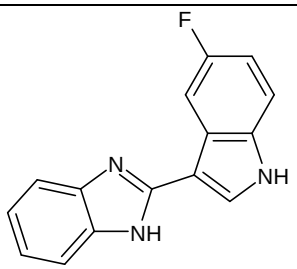
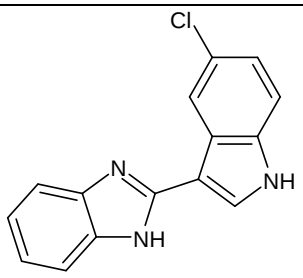
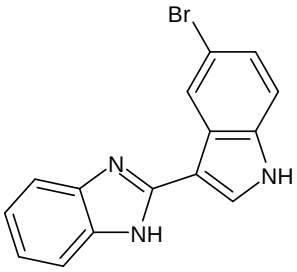
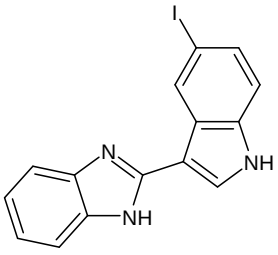
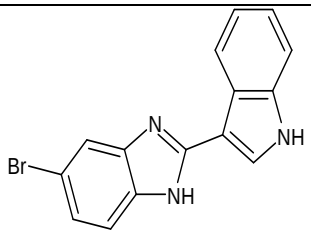
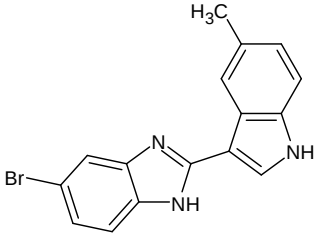
## RESULTS AND DISCUSSION

*In silico* screening of the proposed compounds was conducted successfully using a combination of commercially available and freely downloadable software tools. This hybrid approach facilitated an efficient, systematic evaluation of the molecular properties and interactions of the compounds, providing critical insights into their potential applications.

**TABLE 1: STRUCTURE, IUPAC NAME AND SMILE NOTATION OF PROPOSED INDOLE-BENZ-IMIDAZOLE DERIVATIVES**

| COMPD CODE | IUPAC NAME | STRUCTURE | SMILE NOTATION |
|---|---|---|---|
| JJ1 | 2. (1 H-indol-3-yl)-1 H-benzimidazole |  | c1cccc2[NH]c(nc12)c1c[NH]c2ccccc21 |

| | | | |
|---|---|---|---|
| JJ2 | 2- (5-methyl-1*H* indol-3-yl)-1*H*-benz-imidazole |  | Cc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ3 | 2(5-methoxy-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | COc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ4 | 2- [5-(trifluoromethyl)-1 *H*-indol-3-yl]-1 *H*-benz-imidazole |  | FC(F)(F)c1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ5 | 3- (1 *H*-benzimidazol-2-yl)-1 *H*-indol-5-amine |  | Nc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ6 | 2- (5-nitro-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | [O-][N+](=O)c1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ7 | 2- (5-fluoro-1 *H*-indol-3-yl)-1 *H*-benz-imidazole | | Fc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |

| | | | |
|---|---|---|---|
| | |  | |
| JJ8 | 2- (5-chloro-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | Clc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ9 | 2- (5-bromo-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | Brc1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ10 | 2- (5-iodo-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | Ic1ccc2[NH]cc(c3nc4ccccc4[NH]3)c2c1 |
| JJ11 | 5-bromo-2-(1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | Brc1cc2nc([NH]c2cc1)c1c[NH]c2cccc21 |
| JJ12 | 5-bromo-2- (5-methyl-1 *H*-indol-3-yl)-1 *H*-benz-imidazole |  | Cc1ccc2[NH]cc(c3nc4cc(Br)ccc4[NH]3)c2c1 |

The table above gives a clear representation of the proposed indole-benz-imidazole derivatives. These include the molecular structure, IUPAC names, and SMILE (Simplified Molecular Input Line Entry System) notations. This is important to understand and convey the chemical identity and properties of the compounds.

## LIPINSKI RULE ANALYSIS OF PROPOSED DERIVATIVES

Physicochemical parameters of proposed indole-benz-imidazole derivatives (JJ1 to JJ16) were systematically determined using Molinspiration Software. This comprehensive computational analysis provided valuable insights into key molecular properties essential for evaluating the drug-likeness and potential pharmacological efficacy of the derivatives.

**TABLE 2: Analysis of Lipinski Rule of Five of Proposed Indole-Benz-Imidazole Derivatives**

| Sl. No. | CPD Code | n atoms | MW | n ON | n OHNH | mi log P | n violations | n rotb |
|---|---|---|---|---|---|---|---|---|
| 1 | JJ1 | 18 | 233.27 | 3 | 2 | 3.69 | 0 | 1 |
| 2 | JJ2 | 19 | 247.3 | 3 | 2 | 4.12 | 0 | 1 |
| 3 | JJ3 | 20 | 263.3 | 4 | 2 | 3.73 | 0 | 2 |
| 4 | JJ4 | 22 | 301.27 | 3 | 2 | 4.57 | 0 | 2 |
| 5 | JJ5 | 19 | 248.29 | 4 | 4 | 2.75 | 0 | 1 |
| 6 | JJ6 | 21 | 278.27 | 6 | 2 | 3.63 | 0 | 2 |
| 7 | JJ7 | 19 | 251.26 | 3 | 2 | 3.83 | 0 | 1 |
| 8 | JJ8 | 19 | 267.72 | 3 | 2 | 4.35 | 0 | 1 |
| 9 | JJ9 | 19 | 312.17 | 3 | 2 | 4.48 | 0 | 1 |
| 10 | JJ10 | 19 | 359.17 | 3 | 2 | 4.75 | 0 | 1 |
| 11 | JJ11 | 19 | 312.17 | 3 | 2 | 4.48 | 0 | 1 |
| 12 | JJ12 | 20 | 326.2 | 3 | 2 | 4.91 | 0 | 1 |
| 13 | JJ13 | 21 | 342.2 | 4 | 2 | 4.51 | 0 | 2 |
| 14 | JJ14 | 20 | 327.19 | 4 | 4 | 3.53 | 0 | 1 |
| 15 | JJ15 | 22 | 357.17 | 6 | 2 | 4.42 | 0 | 2 |
| 16 | JJ16 | 20 | 330.16 | 3 | 2 | 4.62 | 0 | 1 |

The synthesized indole-benz-imidazole derivatives were evaluated for their compliance with Lipinski's Rule of Five to predict their drug-likeness and oral bioavailability. No violations of the rule were observed, with all parameters falling within the acceptable range.

**ADME PREDICTION OF PROPOSED DERIVATIVES**

ADME properties of the 16 proposed indole-benz-imidazole derivatives (JJ1 to JJ16) were thoroughly assessed using PreADMET software, providing a comprehensive evaluation of their absorption, distribution, metabolism, and excretion profiles. These parameters are crucial for understanding the compounds' drug-likeness and potential pharmacokinetic behavior, offering insights into their suitability for therapeutic applications.

**TABLE 3: ADME Propertied of Proposed Indole-Benz-Imidazole Derivatives**

| Sl. No. | CPD Code | BBB Penetration | Caco2 cell permeability | Absorption in Human Intestine (HIA) | Plasma Protein Binding (PPB) | Skin Permeability |
|---|---|---|---|---|---|---|
| 1 | JJ1 | 7.7874 | 41.9212 | 92.3387 | 87.6952 | -4.0075 |
| 2 | JJ2 | 9.1041 | 34.6685 | 92.4896 | 82.9690 | -3.9325 |
| 3 | JJ3 | 5.4908 | 53.8587 | 91.8023 | 84.8753 | -4.3329 |
| 4 | JJ4 | 10.4648 | 24.562 | 92.5052 | 95.2330 | -2.9409 |
| 5 | JJ5 | 2.6887 | 16.2245 | 90.3840 | 82.4632 | -4.2873 |
| 6 | JJ6 | 0.1830 | 13.253 | 88.2856 | 94.2089 | -4.6136 |
| 7 | JJ7 | 8.3404 | 46.4386 | 92.3420 | 85.7880 | -4.2959 |
| 8 | JJ8 | 9.5376 | 36.1141 | 93.1023 | 91.6472 | -4.0948 |
| 9 | JJ9 | 5.0025 | 35.6308 | 93.3064 | 86.4058 | -4.3677 |
| 10 | JJ10 | 9.3266 | 35.0756 | 94.6520 | 89.1164 | -4.0479 |
| 11 | JJ11 | 9.7340 | 36.4485 | 93.4992 | 96.8431 | -3.9876 |
| 12 | JJ12 | 11.1319 | 42.0702 | 93.5890 | 91.0361 | -3.9220 |
| 13 | JJ13 | 7.7077 | 41.061 | 93.1953 | 90.8951 | -4.3022 |

| | | | | | | |
|---|---|---|---|---|---|---|
| 14 | JJ14 | 3.9831 | 17.2598 | 92.3233 | 89.3993 | -4.2548 |
| 15 | JJ15 | 1.1095 | 17.492 | 90.4101 | 97.4382 | -4.2476 |
| 16 | JJ16 | 10.2331 | 38.8099 | 93.5028 | 91.5583 | -4.2675 |

These ADME results highlight the favorable pharmacokinetic properties of the synthesized derivatives, making them viable candidates for further development in antibacterial, antifungal and anticancer therapeutic applications.

## MOLECULAR DOCKING

Indole-benz-imidazole derivatives were evaluated by performing molecular docking studies against antibacterial, antifungal, and anticancer enzyme targets using the Schrodinger Software.

### Antibacterial Activity

For antibacterial activity, the derivatives were docked with DNA Gyrase Subunit B, a critical enzyme in bacterial DNA replication, using PDB ID 3U2K.

**TABLE 4: Docking Scores of Proposed Indole-Benz-Imidazole Derivatives with 3U2K (DNA Gyrase Subunit B)**

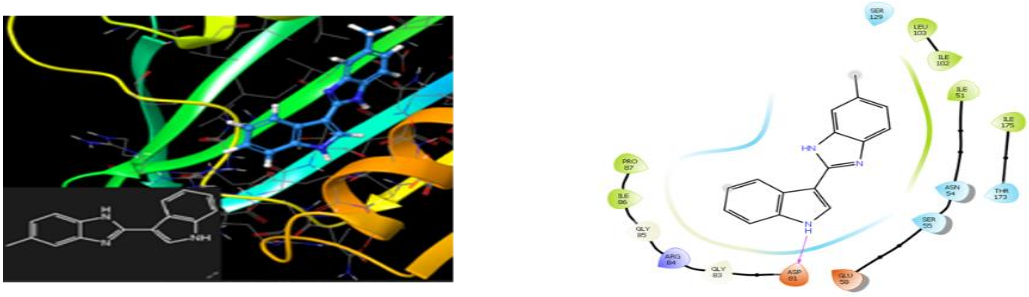
| Sl. No. | Compound Code | Dock Score (K. cal/mol) |
|---|---|---|
| 1 | **JJ1** | **-7.5** |
| 2 | **JJ2** | **-8.1** |
| 3 | JJ3 | -4.8 |
| 4 | JJ4 | -4.8 |
| 5 | JJ5 | -4.9 |
| 6 | JJ6 | -4.5 |
| 7 | JJ7 | -4.5 |
| 8 | JJ8 | -4.6 |
| 9 | JJ9 | -4.8 |
| 10 | JJ10 | -4.8 |

| | | |
|---|---|---|
| 11 | JJ11 | -6.6 |
| 12 | JJ12 | **-7.2** |
| 13 | JJ13 | -5.0 |
| 14 | JJ14 | -5.0 |
| 15 | JJ15 | -5.0 |
| 16 | JJ16 | **-7.1** |

The proposed indole-benz-imidazole derivatives were screened for docking against 3U2K-DNA gyrase subunit B. The compounds JJ1, JJ2, JJ12, and JJ16 showed the best docking scores among all the molecules, with a highest negative score, indicating strong affinity of these derivatives for the target protein.

**Hydrogen Bond Interaction of JJ2 with 3U2K**

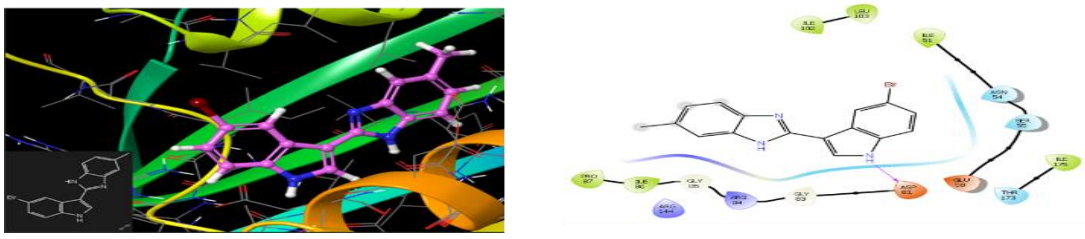
**Figure no.1: Docked image of ligand (JJ2) with the protein (3U2K) and the ligand interaction.**



The nitrogen atom in the Indole moiety of JJ2 has Hydrogen bond interaction with with aspartic acid 81 of 3U2K enzyme

**Hydrogen Bond Interaction of JJ12 WITH 3U2K**

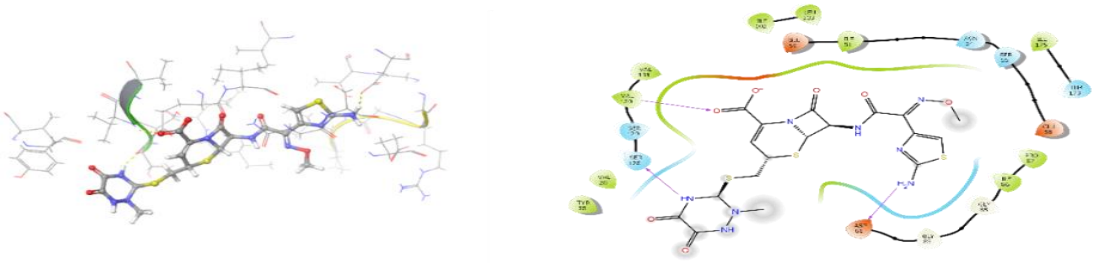
**Figure no.2: Docked image of ligand (JJ12) with the protein (3U2K) and the ligand interaction.**



The nitrogen atom in the Indole moiety of JJ12 has strong Hydrogen bond interaction with with aspartic acid 81 of 3U2K enzyme.

**Standard Drug Ceftriaxone on PDB ID 3U2K**

**Figure no.3: Molecular visualization of the standard drug** ceftriaxone **bound to the DNA gyrase subunit B (PDB ID: 3U2K) and ligand interaction of ceftriaxone**



It highlights the interactions between ceftriaxone and the protein, with details of the binding site and molecular interactions, including hydrogen bonds and hydrophobic contacts. The 3D structure of ceftriaxone is depicted, showing its molecular components, while protein's secondary structures such as alpha helices and beta sheets, are also visible. From the above docked data, it is found that standard drug **(**ceftriaxone) was less potent than synthesized compounds.

**Antifungal Activity**

The antifungal activity was screened by docking compounds with Lanosterol 14α-demethylase, an enzyme of significant importance in the fungal sterol biosynthesis pathway, using PDB ID 5TZ1.

**TABLE 5: Docking Scores of Proposed Indole-Benz-Imidazole Derivatives with 5TZ1**

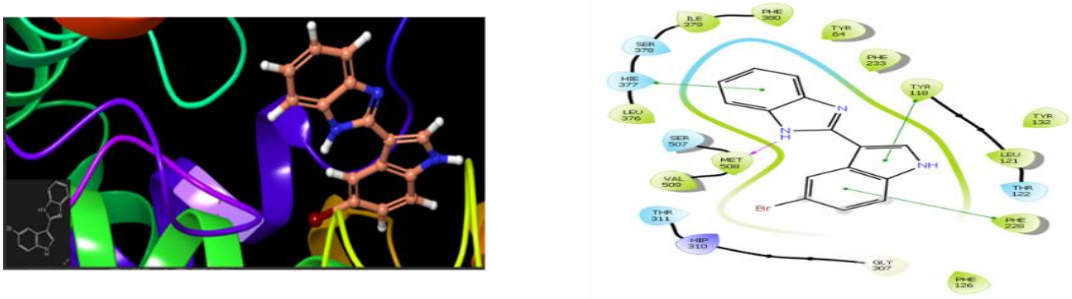
| **Sl. No.** | **Compound Code** | **Dock Score (K. cal/mol)** |
|---|---|---|
| 1 | **JJ1** | **-8.4** |
| 2 | **JJ2** | **-8.2** |
| 3 | JJ3 | -7.1 |
| 4 | JJ4 | -7.1 |
| 5 | JJ5 | -6.8 |
| 6 | JJ6 | -6.3 |
| 7 | JJ7 | -6.2 |
| 8 | JJ8 | -7.7 |
| 9 | JJ9 | -6.3 |

| | | |
|---|---|---|
| 10 | JJ10 | -7.0 |
| 11 | **JJ11** | **-8.7** |
| 12 | **JJ12** | **-8.0** |
| 13 | JJ13 | -5.0 |
| 14 | JJ14 | -7.4 |
| 15 | JJ15 | -6.9 |
| 16 | JJ16 | -6.9 |

The proposed indole-benz-imidazole derivatives were screened for docking against PDB ID 5TZ1-Lanosterol 14α-demethylase. The compounds JJ1, JJ2, JJ11, and JJ12 showed the best docking scores among all the molecules, with a highest negative score, indicating strong affinity of these derivatives for the target protein.

**Hydrogen Bond Interaction of JJ11 with 5TZ1**

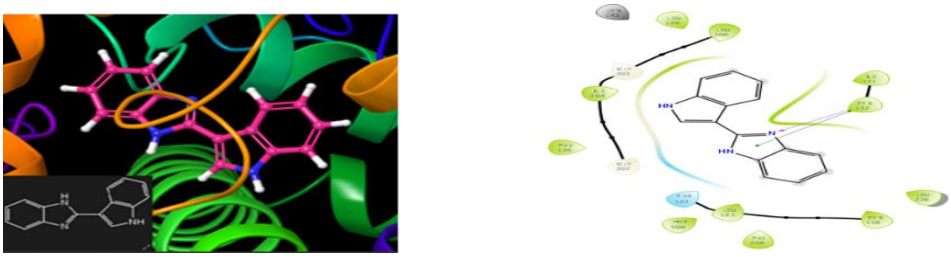
**Figure no.4: Docked image of ligand (JJ11) with the protein (5TZ1) and the ligand interaction.**



The Nitrogen atom of benz-imidazole moiety in JJ11 has hydrogen bond with methionine 508 of enzyme 5TZ1. Also there are three pi-pi stacking interactions, two of them are with phenyl alanine 228 and tyrosine 118. These two are generating from indole moiety. Third pi-pi stacking is between benz-imidazole moiety and histidine 377.

**Hydrogen Bond Interaction of JJ1 with 5TZ1**

**Figure no.5: Docked image of ligand (JJ1) with the protein (5TZ1) and the ligand interaction.**



The JJ1 has hydrogen bond interaction between benz-imidazole moiety and tyrosine 132. Also has pi-pi stacking interaction with the same amino acid.

**Docking Image of Standard Antifungal Drug Fluconazole Against 5TZ1**

**Figure no. 6: Docked image of fluconazole against the PDB 5TZ1 and ligand interaction**

structure reveals the binding interactions between fluconazole and the protein, illustrating key molecular interactions and potential binding sites.

Fluconazole is a standard antifungal drug known for its efficacy against a broad spectrum of fungal infections. However, our docking studies revealed that fluconazole exhibited a lower docking score compared to our synthesized derivatives. The higher docking scores of the derivatives suggest a stronger interaction with the target protein, indicating their superior potential as antifungal agents. These findings are particularly significant given the rising concern over antifungal resistance, emphasizing the need for more potent and reliable therapeutic alternatives.

**Anticancer Activity**

For anticancer activity, the derivatives were docked with the estrogen receptor, an important target in hormone-dependent cancers, using PDB ID 1A52.

**TABLE 6: Docking Scores of Proposed Indole-Benz-Imidazole Derivatives with 1A52**

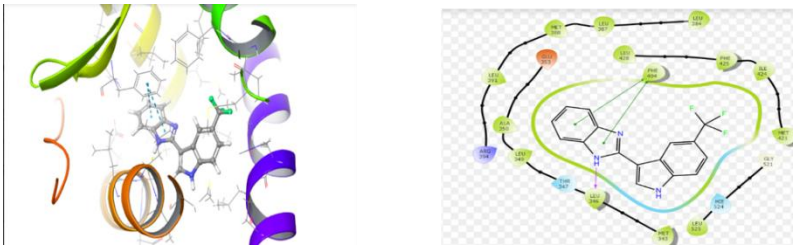
| Sl. No. | Compound Code | Dock Score (K. cal/mol) |
|---|---|---|
| 1 | **JJ1** | **-8.38** |
| 2 | **JJ2** | **-8.56** |
| 3 | JJ3 | -7.92 |
| 4 | **JJ4** | **-9.04** |
| 5 | JJ5 | -7.79 |
| 6 | JJ6 | -7.72 |
| 7 | **JJ7** | **-8.31** |
| 8 | JJ8 | -7.76 |
| 9 | JJ9 | -8.23 |

| | | |
|---|---|---|
| 10 | JJ10 | -7.72 |
| 11 | JJ11 | -7.02 |
| 12 | JJ12 | -7.54 |
| 13 | JJ13 | -7.14 |
| 14 | JJ14 | -6.64 |
| 15 | JJ15 | -7.02 |
| 16 | JJ16 | -5.67 |

The table above highlights the docking scores of proposed indole-benz-imidazole derivatives with the estrogen receptor 1A52, revealing JJ4, JJ1, JJ2, and JJ7 as the top-performing compounds. These derivatives exhibited the highest negative docking scores, indicating their strong binding affinity with the receptor.

**Hydrogen Bond Interaction of JJ4 with 1A52**

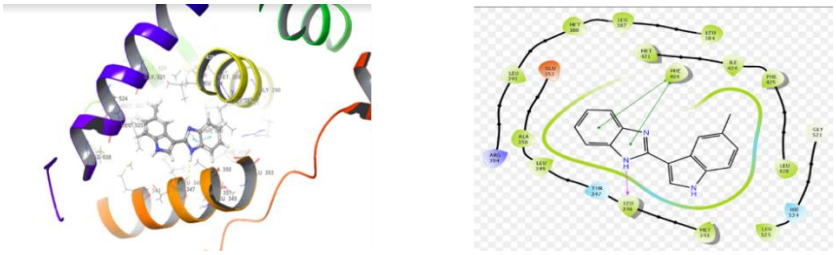
**Figure no. 7: Docked image of ligand (JJ4) with the protein (1A52) and the ligand interaction**



The Nitrogen atom of benz-imidazole moiety in JJ4 has hydrogen bond with leucine 346 of enzyme 1A52. Also there are two pi-pi stacking interactions, both with amino acid phenylalanine 404 with benz-imidazole moiety.

**Hydrogen Bond Interaction of JJ2 with 1A52**

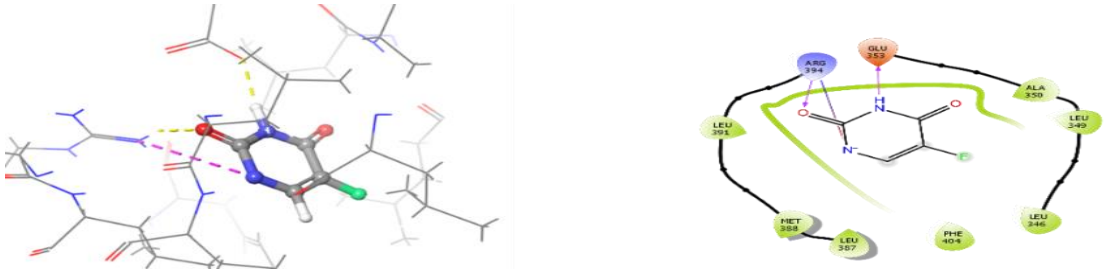
**Figure no. 8: Docked image of ligand (JJ2) with the protein (1A52) and the ligand interaction.**



The Nitrogen atom of benz-imidazole moiety in JJ2 has hydrogen bond with leucine 346 of enzyme 1A52. Also there are two pi-pi stacking interactions, both with amino acid phenylalanine 404 with benz-imidazole moiety.

**Hydrogen Bond Interaction of 5 Flurouracil with 1A52**

**Figure no. 9: Hydrogen bond interaction of 5-fluorouracil with the 1A52 protein and its ligand interaction**



5-Fluorouracil (5-FU) is an established chemotherapeutic agent widely used for treating various cancers. In our docking analysis, the derivatives demonstrated higher docking scores compared to 5-FU, indicating stronger binding affinities to the target protein. This suggests that the derivatives may exhibit enhanced anticancer properties, offering a promising avenue for the development of novel cancer therapies with potentially improved efficacy and reduced side effects compared to existing treatment.

## CONCLUSION

This research work was aimed to develop novel antimicrobial and anticancer drugs with significant activity in the era of increasing antimicrobial resistance. Among the heterocyclic rings Indole and Benz-imidazole are most promising nitrogen containing scaffolds with different biological activities. The discovery of antimicrobial and anticancer drugs with Indole and benz-imidazole moieties will represent a significant milestone in the field of drug discovery. By companying these two moieties produce synergistic action.

The research involves the *In-silico* molecular modeling and ADME prediction of proposed Indole-benz-imidazole derivatives using softwares such as Molinspiration and PreADMET Software respectively. This helped to determine the drug likeness properties and various pharmacokinetic properties of proposed derivatives. These analogues undergone molecular docking studies with the help of Schrodinger Software. The ligands docked with bacterial, fungal and anticancer enzyme like DNA Gyrase subunit B (PDB ID: 3U2K), Lanosterol 14α-Demethylase 9 (PDB ID: 5TZ1) and Human Estrogen Receptor alpha (PDB ID: 1A52) respectively. From the obtained docking scores, it was found that the derivatives have good docking score than the standard drugs, of this the derivative JJ2 [2-(5-methyl-1H-indol-3-yl)-1H-benz-imidazole] have most promising action as antimicrobial and anticancer activity.

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