RESEARCH ARTICLE

In-silico ADME Evaluation and Molecular Docking of a Novel Compound' 2-(4-Allylpiperazin-1-Yl)-1-(1-(4-Nitrophenyl)-1h-Tetrazol-5-Yl) Ethanone' as Potential Antimicrobial Agents

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ABSTRACT

Molecular docking serves as a pivotal tool in comprehending drug-receptor interactions within modern-day drug design. In a previous report, new compounds 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1H-tetrazol-5-yl) etalons were analyzed. Among these compounds, '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' was singled for molecular docking as it shows dual antibacterial and antifungal studies. Docking investigations revealed promising binding affinity of the compound towards *Escherichia coli* (1KZN), exhibiting significant antibacterial activity of docking grade -5.53 Kcal/mol, indicative of a fortified binding interaction. Conversely, the compound exhibited weaker binding affinity towards *Candida albicans* (1AI9) with a docking grade of -0.72 Kcal/mol. Negative binding energy signifies a robust alignment between the ligand and target protein, suggesting potential therapeutic efficacy against microbial activity. Moreover, *in-silico* ADMET calculations were conducted, and the synthesized compound confirms the drug-likeness within the defined parameters: molecular weight between 150 to 500 g/mol, TPSA polarity between 20 to 130 Å^2, lipophilicity ranging between -0.7 to +5.0 Log S not exceeding 6, flexibility not exceeding 9, and saturation not inferior to 0.25. The compound demonstrated compliance with these criteria, suggesting favorable *in-vivo* drug absorption and permeation characteristics.

Keywords: Molecular docking, Lipinski's rule of five, Binding affinity, Antimicrobial, Swiss ADME.

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INTRODUCTION

Molecular docking is an essential process that elucidates the optimal alignment, often referred to as the 'best fit', linking a ligand and its target protein, thereby facilitating the prediction of intermolecular complexes. Widely employed in modern drug design, molecular docking enables a profound understanding of drug-receptor interactions.[1] By predicting the binding affinity of these interactions, molecular docking serves as a crucial tool in drug development, providing insights into the binding orientation of drugs and their target proteins ultimately aiding in the prediction of affinity.[2] In the context of a world where human populations face continual exposure to pathogens, microbial infections pose significant challenges, particularly among immunocompromised individuals. The urgent need for novel antimicrobial agents has spurred extensive research efforts aimed at combating life-threatening infections. To address the escalating threat of antimicrobial resistance, there is a pressing demand for antimicrobial agents that are not only more precise and potent but also less harmful than current medications.[3]

A novel series of 2-(4-allylpiperazin-1-yl)-1-(1-aryl-1H-tetrazol-5-yl) etalons were synthesized via the reaction of triethylamine and allyl bromide with 1-(1-aryl-1H-tetrazol-5-yl)-2-(piperazin-1-yl) ethanones in acetonitrile environment[4]. Among these compounds, '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' was specifically chosen for further investigation since it showed good activity. This compound, synthesized in the laboratory, exhibited potent inhibition against *E. coli*, attributed to the presence of nitro group. Notably, nitro-substituted compounds displayed excellent antibacterial properties. Additionally, the compound demonstrated significant inhibitory effects against *Candida*

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albicans, due to the existence of the group nitro, as observed in antifungal studies.[4]

To explore its antimicrobial potential further, molecular docking of the compound was conducted using the Maestro molecular platform by Schrödinger in the present study. Currently, computational methods play a crucial part in anticipating the ADME properties of drugs, providing valuable data alongside experimental results. These computational models offer insights into pharmacokinetics, physiochemical attributes, and medicinal properties of compounds.[5,6] Among these resources, Swiss ADME stands out as a prominent platform operated by the Swiss Institute for Bioinformatics, which facilitates the analysis of ADME parameters for drug molecules, aiding in decision-making for drug discovery. It enables the evaluation of Lipinski's concept of 5, a key criterion for evaluating oral bio-availability and drug-likeness.[7]

Drug-likeness encompasses a range of characteristics, including molecular flexibility, hydrophobicity, distribution of electrons, molecular weight, and hydrogen bonding properties. Swiss ADME's features extend to BOILED-Egg evaluation,[8] predicting efflux/retention by glycoprotein and gastrointestinal absorption. Moreover, it offers predictions on Cytochrome P450 enzyme substrate inhibition and blood-brain barrier penetration, addressing pseudo-affirmative results often combat in biochemical assessment with an impartial grade of accuracy.[6,9]

In this epoch study, the synthesized compound underwent *in-silico* ADME assessment through the Swiss ADME website. The objective of this screening was to assess various ADME behaviors, such as pharmacokinetics, lipophilicity, physiochemical characteristics, water solubility, medicinal chemistry, and drug-likeness of the synthesized compounds.

MATERIALS AND METHODS

The antimicrobial property of the compound' 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' was examined by performing docking studies with target protein *E. coli* (1KZN) and *C. albicans* (1AI9). Ciprofloxacin and fluconazole are the control ligands used for docking studies. Molecular docking was conducted using the commercially licensed Maestro molecular platform by Schrödinger.[5,10]

Protein Preparation

The protein underwent minimization and refinement as a step in the protein preparation procedure via the "Protein Preparation Wizard" of the Schrödinger suite.[11] Premier tool is employed to determine and fill in any lacking side chains and H-atoms.[7,12]

Generation of Receptor Grid

The receptor grid describes the area of communication between the ligand and the protein. This was done in Maestro, which shows the zone around the active site in position of coordinates x, y, and z. The protein *E. coli* (1KZN) and *C. albicans* (1AI9) underwent energy minimization by applying the OPLS4 unit field to achieve their almost stable energy states. To facilitate the creation of a grid and hold all structural amino acid residues affiliated with specified grid dimensions, a cubicle grid around the active region of the proteins.

Grid information (x, y, z grid points)

1KZN (grid dimensions) = 19.0209587765, 29.6323681529, 34.7413308118

1AI9 (grid dimensions) = 28.1039892297, -7.24288459459, 12.1995197162

Preparation of Ligand

The LigPrep program was utilized to create the lowest energy 3D structures for ligand optimization using the OPLS4 force field. The ligand was prepared, tautomers were produced, and default settings were chosen.[13,14]

Molecular Docking

The molecular docking investigations employed the Glide ligand docking tool, which considers prepared ligands and screens them against the receptor grid using the extra precision (XP) method. This method incorporates various functional features and ligand-specific modifications. GLIDE score and docking score were generated for the foremost docked point of a ligand. These scores help in determining the relative binding energies of receptors, individual ligands, and complex structures, thereby contributing to the total binding energies.

Swiss ADME

It was utilized to evaluate the respective ADME characteristics of the compound. The software features a chemical sketcher powered by ChemAxon's Marvin JS, enabling us to sketch and alter 2D chemical structures conveniently. Subsequently, the structures of the synthesized compounds were regenerated to the canonical format of SMILES and submitted for calculation.[15]

Structure and Bioavailability Radar

The bioavailability radar offers an initial glimpse into the molecule's drug-likeness under scrutiny. Within this radar, the pink region represents the ideal physicochemical space where properties conducive to oral bioavailability are predicted to reside. Six key physicochemical characteristics are considered: POLAR, LIPO, INSOLU, SIZE, FLEX, and INSATU. This visualization aids in assessing the potential oral bioavailability of the molecules based on their alignment with these crucial properties.[16]

Physiochemical Characteristics

It provides in-depth characteristics encompassing the molecular weight, molecular formula, no. of heavy and aromatic heavy atoms, no. of H-bond donors and acceptors, molar refractivity, no. of rotatable bonds, csp3 hybridization, and topological polar surface area. These values were computed, ensuring accuracy and reliability in the analysis of the compounds' properties.[16,17]

Lipophilicity

In drug designing and the discovery of medicinal chemistry, lipophilicity[18] serves as a complementary factor among the crucial physiochemical attributes.[19,20] Swiss ADME offers 5 available, accessible models for assessing the lipophilicity

profile of a composite, *i.e.,* iLOGP, MLOGP, XLOGP3, WLOGP and SILICOS-IT. All these methods give a value of Consensus log Po/w by the arithmetic mean, offering a comprehensive assessment of the compound's lipophilicity.[16]

Water Solubility

On the basis of permeability and solubility, drugs are categorized into four classes-highly permeable and highly soluble 2) Highly permeable and low soluble 3) Low permeable and highly soluble 4) Low permeable and low soluble.[21] The Swiss ADME tool incorporates two methods for evaluating the solubility of water. Firstly, it utilizes the ESOL model, and secondly, it employs the Ali model.[22] These methods diverge from the basic general solubility equation.[23] Additionally, Swiss ADME incorporates a third predictor developed by SILICOS-IT. In this predictor, the linear coefficient is adjusted by molecular weight, resulting in an improved correlation coefficient of R2 = 0.75.

Pharmacokinetics

ALOGP vs PSA are the two computed descriptors that show a distinct delineation emerges within a range of favorable characteristics for gastrointestinal absorption. Within this delineated area, commonly referred to as the Egan egg, molecules that are well absorbed tend to cluster in an elliptical pattern. For evaluating the prognostic capability of models for access to the brain via passive diffusion and GI absorption, Egan egg serves as a serviceable tool. This concept led to the development of the Brain or Intestinal Estimate D penetration prognostic model (BOILED-egg).[8,16,24-26] Cytochrome P450 isoenzymes show a crucial function in the biotransformation of a significant portion ranging from 50 to 90% of therapeutic molecules. This process predominantly involves five major isozymes: CYP2D6, CYP3A4, CYP2C9, CYP1A2, and CYP2C196.[27] SVM is particularly employed for databases containing noted substrates or non-substrates, facilitating binary categorization tasks essential for understanding drug metabolism and interactions.

Drug-likeness

It evaluates the amount of a compound regarding its bioavailability for becoming a drug candidate for oral-bioavailability.[16] The Lipinski model, developed by Pfizer, serves as the pioneering rule of 5 for characterizing tiny compounds dependent on physicochemical properties. These properties view a molecular weight < 500 Da, a calculated partition coefficient (MLOGP) of ≤ 4.157.

Medicinal Chemistry

This objective is to inspire and support medicinal chemists in the discovery of drugs. Pan Assay INterference compounds (PAINS) are the unit that pretense potent responses in the study regardless of the target proteins involved[28]. In a different approach, Brenk et al. focus on compounds that are a little hydrophobic[7], with respect to expanding possibilities for lead optimization.[29-31]

RESULTS AND DISCUSSION

Molecular Docking

The purpose of this investigation is to identify the possible antimicrobial compounds dependent on molecular docking on the protein target of *E. coli* (1KZN) and *Candida albicans* (1AI9). 1KZN is a promising target for antibacterial drugs and 1AI9 for antifungal drugs. Therefore, targeting this protein to discover antimicrobial compounds from natural sources is a good strategy.

The molecular binding indicates the binding conformation of the ligand to the protein on the basis of shape, and electrostatic interconnection between ligand and protein. The docking grade is stated in a negative value which represents a stronger binding between the protein and ligands.

The docking result of the chemical, co-crystallized ligand fluconazole (Figure 1[a]), ciprofloxacin (Figure 1[b]), and the compound (Figure 1[c]) with target protein *E. coli* (1KZN) was given in Table 1. The higher negative grade represents a stronger interaction between the target protein and the ligand. The docking grade of fluconazole was -5.56 Kcal/mol, ciprofloxacin was -3.94 Kcal/mol, and the synthesized compound showed -5.53 Kcal/mol with the lowest interacting energy. The glide score is a function that shows the ligand binding free energy. The glide g score of fluconazole was -5.56 Kcal/mol, ciprofloxacin was -5.04 Kcal/mol, and the compound showed -5.54 Kcal/mol.

The docking result of the ligand fluconazole (Figure 2[a]), ciprofloxacin (Figure 2[b]), and the compound (Figure 2[c]) with target protein *C. albicans* (1AI9) was given in Table 1. The docking grade of fluconazole was -5.87 Kcal/mol, ciprofloxacin was -4.99 Kcal/mol, and the compound showed -0.72 Kcal/mol with the lowest interacting energy. The glide g score of fluconazole was -5.87 Kcal/mol, ciprofloxacin was -6.09 Kcal/mol and the compound showed -3.69 Kcal/mol.

Interaction Profiling of Proteins and Ligands

The mechanism of interaction of fluconazole, ciprofloxacin, and the compound with target protein *E. coli* (1KZN) is shown in Figure 3. The quality of these chemical bonds based on the chemical properties of both the ligand's active site and the amino acid residues within the enzyme's active site. The amino acid residue of fluconazole shows amino acid residues ASP49, GLU50, ALA47, VAL43, GLY77, ARG76, ILE78, and PRO79. The active site shows a pi-pi stacking with a chain of rings with ASP49, while a hydroxyl is being donated from ASN46 at the operational site to the hydroxyl group represented in Figure 3(a). The amino acid residue of ciprofloxacin shows amino acid residues ASP73, ARG76, GLY77, ILE78, and PRO79. The active site shows a stacking with the ketone group linked to ASP73, while a hydroxyl is being donated from conserve THR165 at the site to the hydroxyl group given in Figure 3(b).[32] The amino acid residue of the compound shows amino acid residues ASP73, VAL71, GLN72, ARG76, ILE78, and PRO79. The active site shows a stacking with the nitro group linked

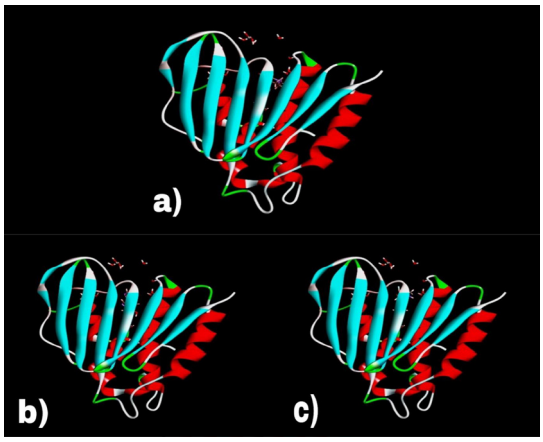

Figure 1: Ribbon presentation [3D] of a) 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethenone; b) Fluconazole; c) Ciprofloxacin with target protein *E. coli* (1KZN)

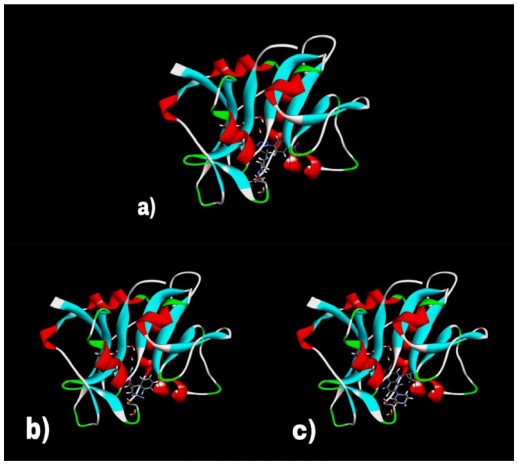

Figure 2: Ribbon presentation [3D] of a) 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone; b) Fluconazole; c) Ciprofloxacin with target protein *Candida Albicans* (1AI9)

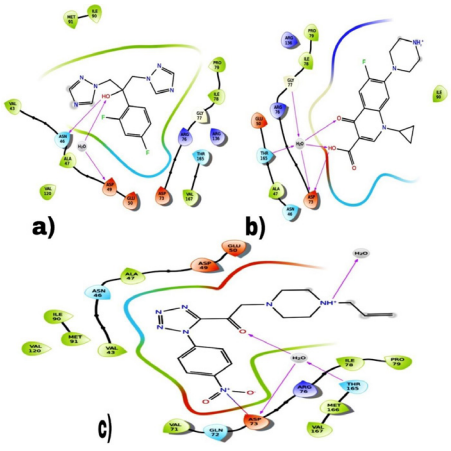

Figure 3: Protein ligands interaction [2D] profile of a) Fluconazole with target protein *E. coli* (1KZN); b) Ciprofloxacin with target protein *E. coli* (1KZN); c) '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl) ethanone'with target protein *E. coli* (1KZN)

to ASP73 and the oxygen group to THR165, represented in Figure 3(c).

The mechanism of interaction of fluconazole, ciprofloxacin, and the compound with the target protein *Candida albicans* (1AI9) is given in Figure 4. The amino acid residue of Fluconazole shows amino acid residues ILE9, VAL10, ALA11, ILE112, GLY113, GLY114, ALA115, TYR118, ILE19, GLY20, GLY21, LYS24, MET25, AND TRP27. The active site shows stacking with a nitro group with ALA115 and ALA11 represented in Figure 4(a). The amino acid residue of ciprofloxacin shows amino acid residues ILE19, GLY20, GLY23, LYS24, MET25, LYS57, THR58, and SER61. The active site shows a stacking with the hydroxyl group linked to ASP73, though a hydroxyl is being given from ALA11 at the site to the C group shown in Figure 4(b). The amino acid residue of compound shows amino acid residues ALA115, TYR118, PRO26, MET25, LYS24, GLY23, LYS22, TYR21, and ILE19 shown in figure 4(c).

The binding pocket of superimposed fluconazole, ciprofloxacin, and compound into the binding site of *E. coli* (1KZN) and *Candida albicans* (1AI9) is shown in Figures 5 and 6. From the research, it may be resolved that the compound may produce active drugs against microbial activity. The synthesized compound possesses a good antibacterial activity than antifungal activity against microorganisms, and a molecular docking analysis discovered an approving binding contact with the target bacteria *E. coli* (1KZN).

In-silico ADME Analysis

Swiss ADME web tool was used to study physiochemical characteristics, lipophilicity, and water solubility parameters (Table 2), pharmacokinetic characters, drug-likeness & bioavailability score and medicinal chemistry characteristics (Table 3), the bioavailability radar for drug-likeness of compound (Figure 7), respectively.

Lipinski *et al.*[7] serves as a guideline for identifying drug-like properties in the tiny molecules and the synthesized compound fully agrees with it. According to the reference, the compound has less than 10 rotatable bonds, H-bond donors <5, molecular weight fewer than 500 Da, H-bond acceptors <10, and topological surface area <140 Å², indicating sufficient molecular flexibility and the compound meets these criteria as represented in Table 2.

Lipophilicity, an essential property for molecular discovery, is quantitatively represented by the logP of a unit between water and n-octanol.[33,34] The compound's lipophilicity, estimated as the consensus Log P, should be less than 5 for favorable oral activity. The synthesized compound meets this criterion, indicating its potential as an orally active medicine.

Additionally, the compound exhibits moderate solubility in the ESOL and Ali models and complete solubility in the SILICOS-IT model (Table 2), further supporting its suitability for development as an oral drug candidate. These research findings conjointly hint that the compound shows desirable drug-like properties and holds promise for further development in medicinal chemistry.

Table 1: Docking results of the compound' 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' and control ligand Fluconazole and Ciprofloxacin with target protein *E. coli* (1KZN) and *Candida Albicans* (1AI9)

Ligand	*Docking score*	*Glide g score*	*Lipophilic EvdW*	*H Bond*	*Sitemap*
TARGET PROTEIN E.Coli (1KZN)					
Fluconazole	-5.56	-5.56	-2.6	-1.29	-1.16
Ciprofloxacin	-3.94	-5.04	-2.47	-1.6	-0.27
2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethenone	-5.53	-5.54	-3.11	-0.45	-0.45
TARGET PROTEIN Candida Albicans (1AI9)					
Fluconazole	-5.87	-5.87	-2.63	-0.81	-1.06
Ciprofloxacin	-4.99	-6.09	-3.74	-1.2	-0.61
2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethenone	-0.72	-3.43	-3.69	0	-0.55

Table 2: Physiochemical, lipophilicity characteristics and water solubility of the compound '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone'

Compound	*Canonical SMILES*	*Physiochemical characteristics*		*Lipophilicity*		*Water solubility*	
'2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl) ethanone'	[O-][N+](=O) C1=CC=C(C=C1) N1N=NN=C1C(=O) CN1CCN(CC=C)CC1	Molecular formula	$C_{16}H_{19}N_7O_3$	iLOGP	2.37	ESOL	
		Molecular weight	357.37 g/mol	XLOGP3	1.59	Log S	-2.91
		Num. Heavy atoms	26	WLOGP	-0.20	Solubility	4.41e-01 mg/ml ; 1.23 e-03 mol/l
		Num. arom. heavy atoms	11	MLOGP	1.30	Class	Soluble
		Fraction Csp3	0.38	SILICOS-IT	-1.28	Ali	
		Num. rotable bonds	7	Consensus Log $P_{o/w}$	0.76	Log S	-3.57
		Num. H-bond acceptors	8			Solubility	9.54e-02 mg/ml ; 2.67e-04 mol/l
		Num. H-bond donors	0			Class	Soluble
		Molar refractivity	102.85			SILICOS-IT	
		TPSA	112.97Å^2			Log S	-2.50
						Solubility	1.12e+00 mg/ml ; 3.13e-03 mol/l
						Class	Soluble

Num- Number, H-bond-Hydrogen bond, Arom.-Aromatic, TPSA-Topological Polar Surface Area

The drug-likeness and pharmacokinetic assessments conducted by Swiss ADME indicate an advanced level of gastrointestinal absorption for the compound. Additionally, Swiss ADME provides insights into the compound's likelihood of stating a substrate/non-substrate of P-glycoprotein and its inhibition potential against various Cytochrome P450 isoforms.

The compound is identified as Cytochrome P1A2 inhibitor listed. Furthermore, the skin permeability coefficient, *i.e.,* Log Kp is calculated to be -7.35 cm/s, representing relatively inferior skin permeability (Table 3).

Swiss ADME provides access to 5 different rule-dependent models, considering Egan, Lipinski, Ghose, Veber, and Muegge methods. The compound complies with the rules defined by these filters, with zero violations reported. Additionally, the compound receives a positive score from all five filters, with a bioavailability score, i.e., 0.55. These findings suggest the compound exhibits favorable drug-like characteristics according to Swiss ADME's assessments.

The Swiss ADME analysis did not flag any PAINS alerts for any of the molecules under consideration. However, according to Brenk's guidelines, three alerts were identified in the compound: the presence of a nitro group in ring form, an oxygen-nitrogen single bond, and an isolated alkene. Additionally, the lead-likeness analysis revealed two violations in the compound: molecular weight (MW) exceeding 350 and XLOGP3 value less than 3.5, as indicated in Table 3. These

Table 3: Pharmacokinetics, Drug-likeness rule, Bioavailability score and Medicina Chemistry of the compound 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone

Compound	*Pharmacokinetics*		*Drug likeness & Bioavailability score*		*Medicinal chemistry*	
2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone	GI absorption	High	Lipinski	Yes; 0 violation	PAINS	0 alert
	BBB permeant	No	Ghose	Yes	Brenk	3 alerts: isolated_alkene, nitro_group, oxygen-nitrogen_single_bond
	P-gp substrate	No	Veber	Yes	Leadlikeness	No; 1 violations: MW>350
	CYP1A2 inhibitor	Yes	Egan	Yes	Synthetic accessibility	3.00
	CYP2C19 inhibitor	No	Muegge	Yes		
	CYP2C9 inhibitor	No	Bioavailability Score	0.55		
	CYP2D6 inhibitor	No				
	CYP3A4 inhibitor	No				
	Log K_p (skin permeation)	-7.35 cm/s				

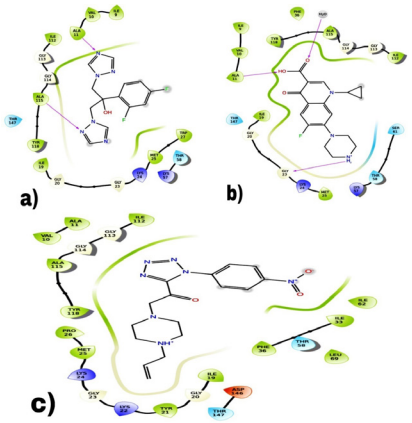

Figure 4: Protein ligands interaction [2D] profile of - a) Fluconazole with target protein *Candida Albicans* (1AI9); b) Ciprofloxacin with target protein *Candida Albicans* (1AI9); c) '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl) ethanone'with target protein *Candida Albicans* (1AI9)

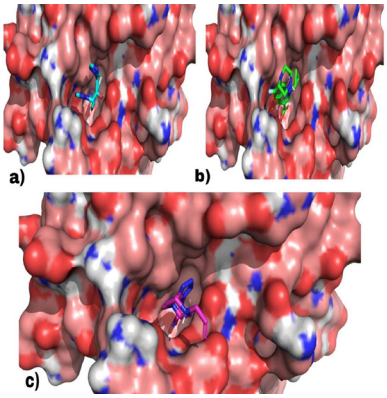

Figure 5: The binding pocket of superimposed a) Fluconazole into the binding site of *E. coli* (1KZN); b) Ciprofloxacin into the binding site of *E. coli* (1KZN); c) '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' into the binding site of *E. coli* (1KZN)

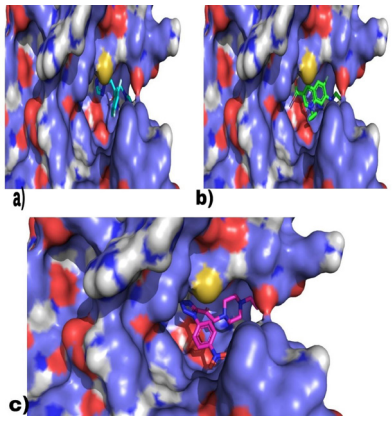

Figure 6: The binding pocket of superimposed; a) Fluconazole into the binding site of *Candida Albicans* (1AI9); b) Ciprofloxacin into the binding site of *Candida Albicans* (1AI9); c) '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone' into the binding site of *Candida Albicans* (1AI9)

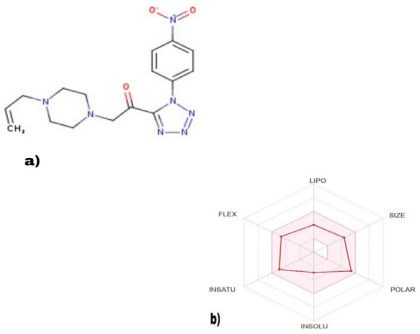

Figure 7: a) Molecular structure of the compound' 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone'; b) Schematic diagram of Bioavailability Radar for Drug likeness of the compound '2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl) ethanone'.

findings provide valuable insights for further refinement and optimization of the compound to enhance its drug-like properties.

The bioavailability radar evaluated the molecule's drug likeness. Within this radar chart, the pink area denotes the optimum reach for various characteristics crucial for drug development. The drug-likeness of any compound is evaluated based on the respective criteria:

Lipophilicity (XLOGP3) within the range of -0.7 to +5.0.
Polarity (TPSA) between 20 to 130 Å2.
Solubility (log S) not more than 6.
Molecular weight ranging 150 and 500 Da.
Flexibility not exceeding 9 rotatable bonds.
saturation not lesser than 0.25.

Meeting this criterion helps assess the likelihood of 2-(4-allylpiperazin-1-yl)-1-(1-(4-nitrophenyl)-1H-tetrazol-5-yl)ethanone being suitable for development of drugs indicating favorable *in-vivo* drug absorption and permeation characteristics.[35,36]

The *in-silico* ADME prediction analysis results corroborate with the computational assessment, affirming the pharmacologically active framework of the synthesized compound. This alignment underscores the viability of advancing further with potential hits identified through the evaluation process.[37,38]

CONCLUSION

The docking results indicate that the compound exhibited notable binding affinity towards *E. coli* (1KZN). Fluconazole showed a docking grade of -5.56 and ciprofloxacin showed -3.94 Kcal/mol. The compound demonstrated a compelling score of -5.53 Kcal/mol, reflecting the lowest binding energy in the molecular docking analyses. Moreover, the glide score further corroborated these findings, with fluconazole registering -5.56 Kcal/mol, ciprofloxacin recording -5.04, and the compound displaying -5.54 Kcal/mol. The negative binding signifies a robust binding relation between the target protein and the ligand. Based on these results, it can be inferred that the compound holds potential as a drug candidate against microbial activity. The interactions with the target molecule and gaining in-depth knowledge of the binding model, molecular docking analyses were conducted, yielding favorable binding interactions. Notably, the compound exhibited stronger antibacterial activity compared to antifungal activity. Furthermore, an assessment of ADME properties revealed that the synthesized compound possesses essential physicochemical and pharmacokinetic profiles, positioning it as a viable candidate for drug development. This study underscores how our technique facilitates the discovery of novel, promising structures. In conclusion, it summarizes the implications of the findings regarding the potential of the new compounds as antibacterial drugs.

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