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INSILICO MOLECULAR DOCKING STUDIES OF CHALCONE BASED TETRALONE DERIVATIVES FOR ANTIMICROBIAL ACTIVITIES

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ABSTRACT

The increasing resistance to existing antimicrobial agent as created an urgent need of new chemo therapeutic agents. In these study a series of chalcone base tetralone derivative were evaluated for their antimicrobial potential through Insilico molecular docking against the bacterial target DNA gyrase B (PDB id – 1RA1). The design derivatives were optimized and subjected to docking analysis to evaluate their binding affinity and molecular evaluation. Compound (SC-97,SC-102 and SC-81) show superior docking score compare to reference ligand showing strong hydrogen bonding and hydrophobic interactions with key active sides. These results indicate that chalcone tetralone hybrid poses significant potential as lead candidates for further antimicrobial drug development.

KEYWORDS: Chalcone, tetralone, Insilico studies, Antimicrobial.

INTRODUCTION

Antimicrobial resistance has become critical challenge become worldwide, reducing the effectiveness of existing of antibiotics and increasing the need for novel structural frame works with promising biological activity[1] computational drug design tools particularly molecular docking, play an essential role in identifying potential drug candidates by priding binding affinity and interaction profiles with biological targets.[15]

Chalcones, which consist of an αβ unsaturated carbonyl system, have been widely reported for their antimicrobial, antiviral, anti-inflammatory and anticancer activities[2,11] tetralone derivatives also exhibit diverse pharmacological properties and serves as important precursors in medicinal chemistry.

Combining these two molecules into chalcone based tetralone hybridize May enhance biological activity through synergistic interaction and favorable structural features.

DNA gyrase B, a component of bacterial type II is responsible topo isomerize, is responsible for ATP dependent DNA negative super coling and is considered a validated target for antibacterial drug development.[3,14] Inhibiting its ATP binding pockets effectively suppresses bacterial growth.

This study investigates the molecular interaction of chalcone tetralone derivative with DNA gyrase B using Insilico molecular docking techniques.

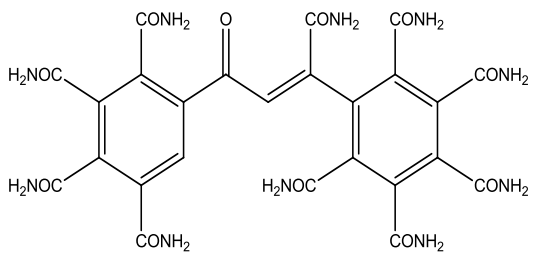
In silico studies

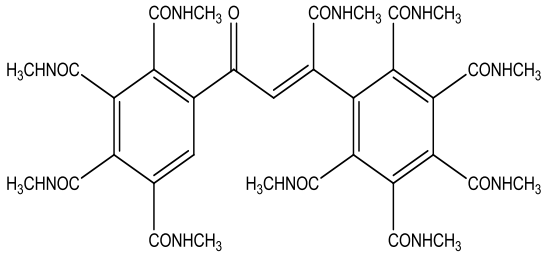
In these in silico study, essential molecular properties Such as log p, molecular weight, no of hydrogen bond donors and acceptors, and rotatable bonds were calculated using standard online computational tool to evaluate the drug- likeness of the designed derivatives. Key ADME parameters, including solubility, permeability metabolism and excretion behavior were predicated, using established computational approaches. The compounds were further screened for toxicity risk such as hepatotoxicity, mutagenicity; only molecules exhibiting acceptable drug- likeness, low predicated toxicity were selected for molecular docking studies.[4,5,6,7]

MATERIAL AND METHODS

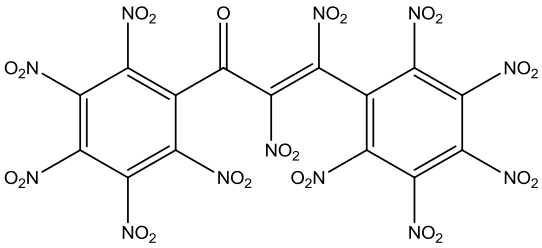
Preparation of ligands

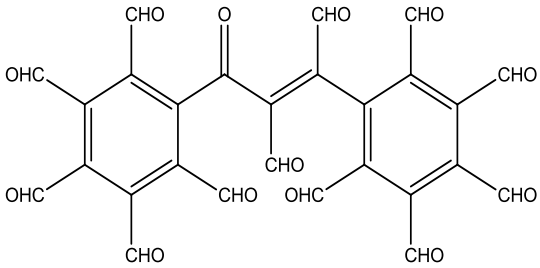
The chemical structures of the design ligands where first drawn using the ChemDraw ultra software. These 2D structures were then transfer to the Chem 3D ultra environment, were their 3D confirmations were generated and optimized using the MOPAC-based energy minimization protocol. The ligand confirmation displacing the lowest energy was considered the most stable and was selected for subsequent docking studies at the target protein active side.



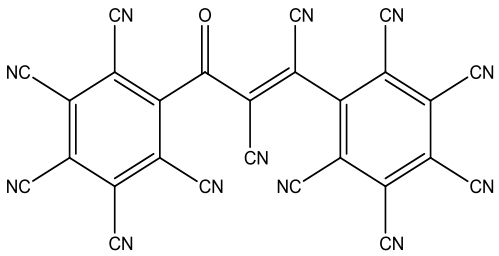


Chalcone derivative 97 (SC97) Chalcone derivative 102 (SC102)





Chalcone derivative 81 (SC81) Chalcone derivative 100 (SC100)

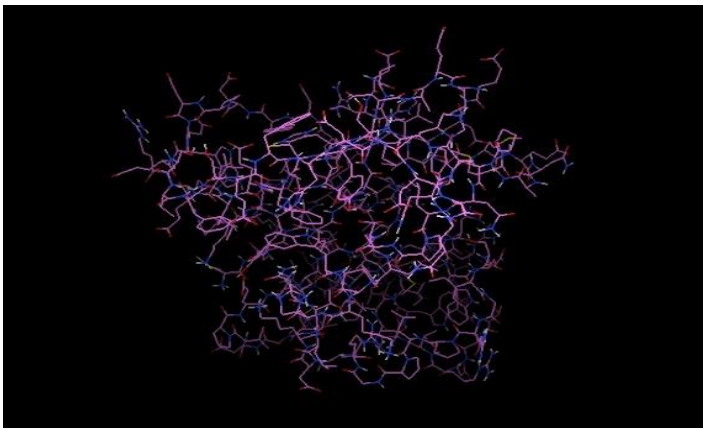


Chalcone derivative 98 (SC98)

Energy minimization of ligands – ChemDraw ultra 3D was used with the MM2 job to minimize energy. By ensuring that every ligand confirmation was in its lowest energy state, this step increased the precision of docking. The Pdb format was used to store the reduced ligand.

Protein preparation

The crystal structures of DNA gyrase (PDB id – 1RA1) were retrieved from protein data bank.[10] All the water molecule and co crystallized were removed, while essential cofactor required for structure stability was retained. The protein structure was than clean to eliminate any unwanted confirmations and the active binding reason was carefully examine. Finally the protein was prepared and optimized according to specification of the adopted molecular docking protocol.



Prepared Protein

Receptor grid generation - To identify the target protein's active site region for molecular docking experiment .Grid box generation was carried out. The coordinates Center_x = 14.987, center_y = 18.200 and center_z = 12.425 were used to center the grid box at the active site. To guarantee full coverage of the binding site and provide enough room for ligand flexibility, the grid box dimension were adjusted to size_x = 40 Å, size_y = 40 Å and size_z = 40 Å. AutoDock Vina docking trials were conducted with these adjusted grid parameters.

Molecular docking- AutoDock Vina was used for the docking process.[9] Using a fixed grid box surrounding the ligand- binding site, each ligand was docked into 1RA1. Each ligand had ten binding poses produced by docking simulations; the optimal pose was chosen based on the lowest binding energy.

3. RESULT

Energy Minimization of Ligands – table 1 summarizes the final total energy values that required from each chemical following reduction. The energy is expressed as Kcal/mol. These reduced structures were then utilized as input for the DNA gyrase B (1RA1) docking experiments.

Table 1: Energy minimization results of chalcone, chalcone derivatives and Ciprofloxacin.

Compound ID	Ligand Name	Substituent Group	Final Energy (Kcal/mol)
SC97	Carboxamide derivative	$–CONH_2$	-79.3942
SC102	N-Methylcarboxamide derivative	$–CONHCH_3$	-64.7843
SC81	Nitro derivative	$–NO_2$	None
SC100	Aldehyde derivative	–CHO	-8.1646
SC98	Carboxylic acid derivative	–COOH	-45.3854
Chalcone	Chalcone	NO	3.0835
CP	Reference drug (Ciprofloxacin)	NO	120.1759

Docking studies data

Table 2: Docking Affinity Results of Compound SC-97 with DNA Gyrase B (1RA1).

Pose ID	Binding Energy (kcal·mol⁻¹)	RMSD Lower Bound (Å)	RMSD Upper Bound (Å)
1	–14.8	0.000	0.000
2	–14.6	0.842	3.482
3	–14.4	1.021	4.892
4	–14.3	1.346	3.962
5	–14.1	1.527	3.835
6	–14.0	1.683	4.521
7	–13.9	1.752	2.591
8	–13.8	1.893	2.389
9	–13.7	1.947	3.902
10	–13.6	1.998	9.422

Table 3: Docking Poses of SC-102 with DNA Gyrase B (1RA1)

Docking mode	Binding Energy (kcal·mol⁻¹)	RMSD Lower Bound (Å)	RMSD upper Bound (Å)
1	–13.8	0.000	0.000
2	–13.5	3.437	9.160
3	–13.2	3.407	9.250
4	–13.0	3.652	9.210
5	–12.8	3.219	10.092
6	–12.6	3.423	9.072
7	–12.6	1.936	10.063
8	–12.6	3.630	8.783
9	–12.6	1.966	10.088
10	–12.6	2.191	9.992

Table 4: Docking Poses of SC-81 with DNA Gyrase B (1RA1)

Docking mode	Binding Energy (kcal·mol⁻¹)	RMSD Lower Bound (Å)	RMSD upper Bound (Å)
1	–12.0	0.000	0.000
2	–11.3	1.656	4.648
3	–11.0	1.635	3.723
4	–10.8	1.506	8.766
5	–10.8	3.482	5.768
6	–10.5	2.055	3.707
7	–10.5	2.326	2.631
8	–10.4	6.274	11.788
9	–10.3	2.279	2.939
10	–10.3	0.456	2.872

Table 5: Docking Poses of SC-100 with DNA Gyrase B (1RA1).

Docking mode	Binding Energy (kcal·mol⁻¹)	RMSD Lower Bound (Å)	RMSD upper Bound (Å)
1	–11.7	0.000	0.000
2	–11.7	0.062	2.836
3	–11.6	0.380	4.025
4	–11.6	0.337	2.855
5	–11.1	2.811	5.183
6	–11.0	2.769	8.911
7	–10.9	2.912	4.891
8	–10.8	2.798	9.021
9	–10.8	3.010	6.427
10	–10.7	2.911	8.592

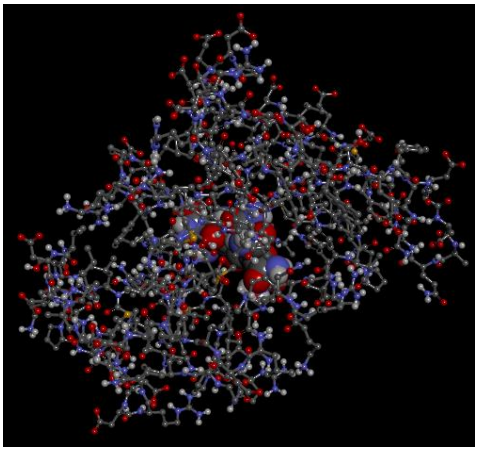
Table 6: Docking Poses of SC-98 with DNA Gyrase B (1RA1).

Docking mode	Binding Energy (kcal·mol⁻¹)	RMSD Lower Bound (Å)	RMSD upper Bound (Å)
1	–11.4	0.000	0.000
2	–11.3	1.650	4.120
3	–11.3	2.288	4.351
4	–11.2	1.503	4.109
5	–11.1	1.427	4.818
6	–10.9	2.227	9.208
7	–10.8	3.570	5.783
8	–10.7	1.969	9.264
9	–10.7	1.982	4.259
10	–10.6	2.010	4.310

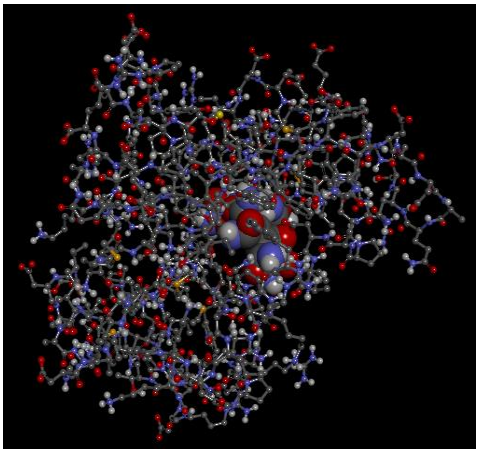
Comparative analysis of SC97 to Chalcone with Reference drug – All the design molecules were successfully docked into the active pocket of DNA gyrase B. the SC97,SC102,SC81,SC100 and SC98 are higher affinity compare to the reference ligand.

Table 7: Comparative Docking Result of Compounds SC97-Chalcone with Reference drug (Ciprofloxacin).

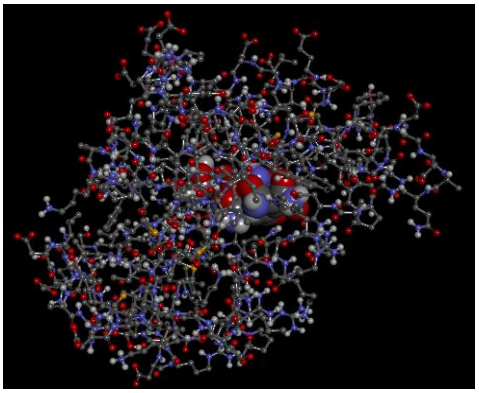
Compound	Binding energy (Kcal/mol)	Key interactions
SC 97	-14.8	H-bond with TYR A100,ALA A7,ILE A94 Π- donor H-bond with SER A49
SC 102	-13.8	H-bond with TRP A22,SER A49 Π-σ bond with LEU A28
SC 81	-12.0	Attractive charge with ASP A27 Π-alkyl with ILE A14
SC 100	-11.7	Π-σ bond with ILE A50 H-bond with THR A46
SC 98	-11.4	Unfavorable donar-donar bond with THR A123 C-H bond with HIS A45,SER A49
Chalcone	-7.9	Vander wall with LEUA54 & PHEA31 Π-alkyl with ILEA28 & LYSA28
CP	-7.8	H-bond with GLYA27 Π-alkyl with ILEA14 C-H bond with GLYA96



Pose 1



Pose 2



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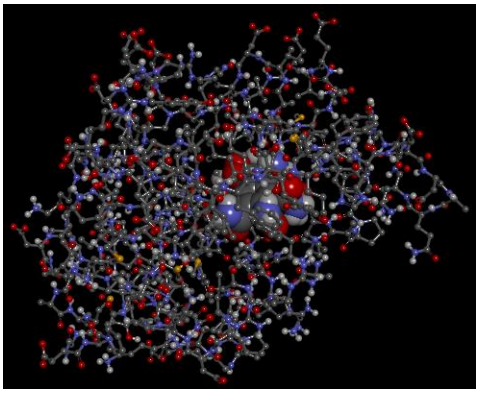

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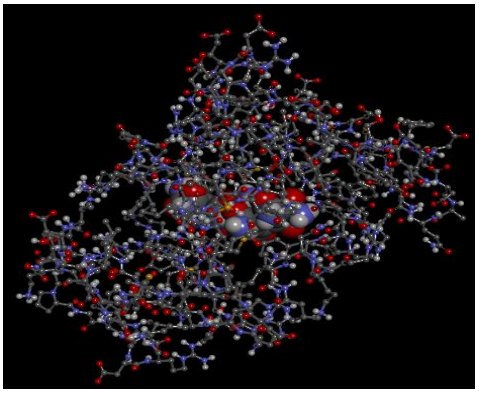
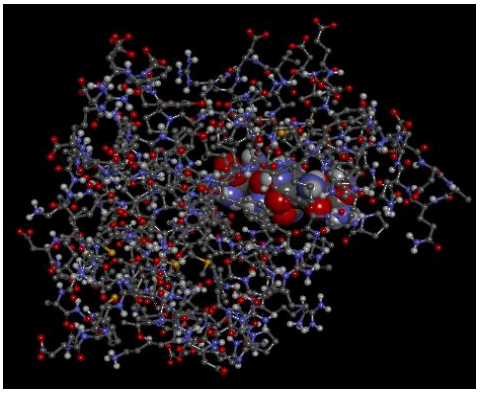
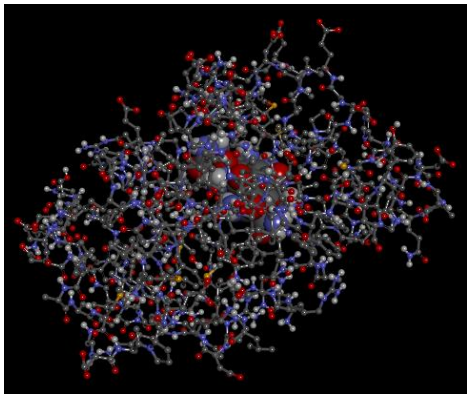


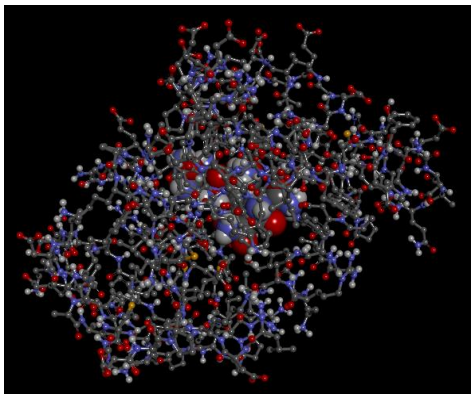
Pose 5



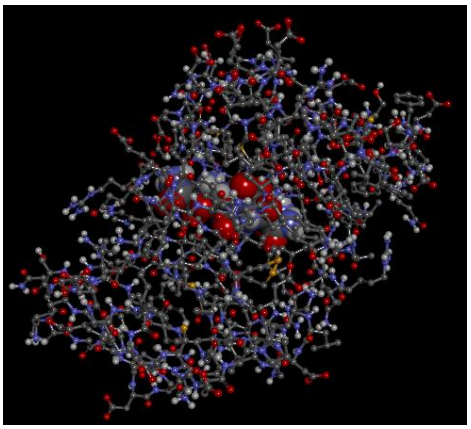
Pose 6



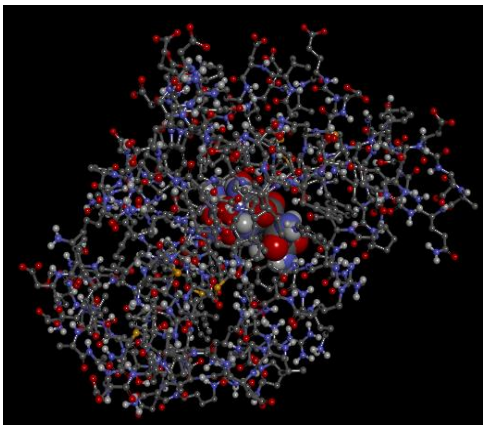
Pose 7



Pose 8



Pose 9



Pose 10

Interaction summary – The best scoring ligands show hydrogen bonding with amino acids

- **Hydrogen bonds with** THR A46, THR A123, MET A16, ASP A27
- **Hydrophobic interaction** with HIS A45, LEU A28
- **Vander walls interaction** with MET A20, LEU A28, SER A49, ILE A50

CONCLUSION

These Insilico molecular docking studies indicate that chalcone based tetralone derivative exhibited strong binding potential toward DNA gyrase B. SC97,SC102,SC81,SC100 and SC98 higher binding affinity then the Ciprofloxacin due to stable hydrogen bonding, aromatic stacking and hydrophobic interactions. These findings support there potential as lead compound for novel antimicrobial drug development. Further synthesis biological evaluation and ADMET analysis are recommended.

REFERENCES

1. Ventola CL. The antibiotic resistance crisis: causes and threats. Pharmacy and Therapeutics, 2015; 40(4): 277–283.
2. Zhuang C, Zhang W, Sheng C, Zhang W, Xing C, Miao Z. Chalcone: a privileged structure in medicinal chemistry. Chemical Reviews, 2017; 117(12): 7762–7810.
3. Bax BD, Chan PF, Eggleston DS, Fosberry A, Gentry DR, Gorrec F, et al. Type IIA topoisomerase inhibition by a new class of antibacterial agents. Nature, 2010; 466(7309): 935–940.
4. Lipinski CA, Lombardo F, Dominy BW, Feeney PJ. Experimental and computational approaches to estimate solubility and permeability in drug discovery and development settings. Advanced Drug Delivery Reviews, 2001; 46(1–3): 3–26.
5. Veber DF, Johnson SR, Cheng HY, Smith BR, Ward KW, Kopple KD. Molecular properties that influence the oral bioavailability of drug candidates. Journal of Medicinal Chemistry, 2002; 45(12): 2615–2623.
6. Egan WJ, Merz KM Jr, Baldwin JJ. Prediction of drug absorption using multivariate statistics. Journal of Medicinal Chemistry, 2000; 43(21): 3867–3877.
7. Gleeson MP. Generation of a set of simple, interpretable ADMET rules of thumb. Journal of Medicinal Chemistry, 2008; 51(4): 817–834.
8. Morris GM, Huey R, Lindstrom W, Sanner MF, Belew RK, Goodsell DS, Olson AJ. AutoDock4 and AutoDockTools4: automated docking with selective receptor flexibility. Journal of Computational Chemistry, 2009; 30(16): 2785–2791.
9. Trott O, Olson AJ. AutoDock Vina: improving the speed and accuracy of docking with a new scoring function, efficient optimization, and multithreading. Journal of Computational Chemistry, 2010; 31(2): 455–461.
10. Berman HM, Westbrook J, Feng Z, Gilliland G, Bhat TN, Weissig H, et al. The Protein Data Bank. Nucleic Acids Research, 2000; 28(1): 235–242.

11. Singh P, Anand A, Kumar V. Recent developments in biological activities of chalcones: A mini review. European Journal of Medicinal Chemistry, 2014; 85: 758–777.
12. Sharma R, Kumar R, Kodwani R, Kapoor S. Design, synthesis and antimicrobial evaluation of novel chalcone derivatives. Bioorganic & Medicinal Chemistry Letters, 2016; 26(23): 5652–5656.
13. Ghosh AK, Samanta I, Mandal A. Molecular docking studies of flavonoid derivatives as DNA gyrase inhibitors. Computational Biology and Chemistry, 2019; 80: 69–78.
14. Silver LL. Challenges of antibacterial discovery. Clinical Microbiology Reviews, 2011; 24(1): 71–109.
15. Sliwoski G, Kothiwale S, Meiler J, Lowe EW Jr. Computational methods in drug discovery. Pharmacological Reviews, 2014; 66(1): 334–395.