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MOLECULAR DOCKING STUDIES ON THE FUNCTION OF TETRACYCLINE AND CHLORAMPHENICOL PYRANOCHALCONES ON A *PSEUDOMONAS* TRANSCRIPTIONAL REGULATOR ENZYME

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ABSTRACT

This study shows the docking outcomes of two existing Pyrano-chaalcones like tetracycline and chloramphenicol on the transcriptional regulator enzyme, that is the main effluence drive called TtgABC in the *Pseudomonas putida* which is a Gram- negative bacteria as a receptor. Transcriptional regulator enzyme is the multidrug required protein and controls the main processes of the antibiotic's confrontation by dynamic swelling of toxic complexes over the membrane that is destined to effluence impels. While a microbes show endurance in contradiction of a number of the antibiotic, two pyranochalcones, tetracycline and chloramphenicol have been described as the energetic contrary to it. While occurrence of alkoxy mediety in fragrant cross component of the pyranochaalcones appears to be active in fastening.

Keywords: Molecular dockage, tetracycline, *pseudomonas,* pyranochalcones, chloramphenicol.

INTRODUCTION

This increasing in antibiotic confrontation straining of the bacteria has now turn out to be one of the main disinfectants that is a consequence of 3 key approaches specifically enzymetic deactivation of a drug, alteration of the marked positions and gibbosity by effluence. While the dynamic effluence of poisonous complexes is the communal procedures used by microorganisms to defend them in contradiction of harmful outcomes of poisonous particles they come across with the atmosphere. The strain called DOT-T1E is fascinating used for its mostly more confrontation with the lethal biological diluents and 3 RND effluence impels which are Ttgabc, TtgDEE, and TtgHGI, discovered are important for this process of confrontation. Pyranochalcones include chloramphenicol and tetracycline are extensively dispersed naturally existing flavonoid compounds encounters as focused in the research field in the drug proposal or in finding. A large amount of pyranochalcones have been described to display ant mutagenic, disinfectant, and anticancer activities. The pyranochalcones I had secluded from *Taphrosia deflexea*, and this is revealed with antiseptic movement in contradiction of the bacteria called *Pseudomonas putida*. While this extensive variety of organic characteristics has encouraged awareness in the formation of existing pyranochaalcones. The study on the collaboration of diverse existing pyrnochalcones on the TtgR of *pseudomonas putida* that were approved by the writers, as this enzyme appears to be most significant constituent in detection. While the active exclusion of substances poisonous to a bacterium, that is stated in current study.

MATERIAL AND METHODS

Software Requirements

- Discovery studio
- Pay mole
- Auto dock
- Vina
- MedChem

The Substratum

The TtgR enzyme (from PDB) in *pseudomonas* was occupied as a substratum for docking analysis. The substrates were selected as enzyme TtgR required protein that suppresses the transcript of enzyme Ttgabc. It activates the impelling out of poisonous ingredients manufacturing the creature unaffected to antibiotic, diluents and the lethal plant's secondary materials. Explorations of PDB files informed TtgR to fix with plant derivative naturally occurring flavonoids, quericetin and remarkably, pyranochaalcones have the basic characteristics of both the quercetins, tetracycline, chloramphenicol and plant antimicrobial.

Protein Preparation

Protein is downloaded from protein data bank and then remove the ligand from protein in discovery studio and save the in pdb. And convert the pdb in pdbqt in auto dock and made the grid box .in the auto dock water molecule is removed and hydrogen is added and save in pdbqt.

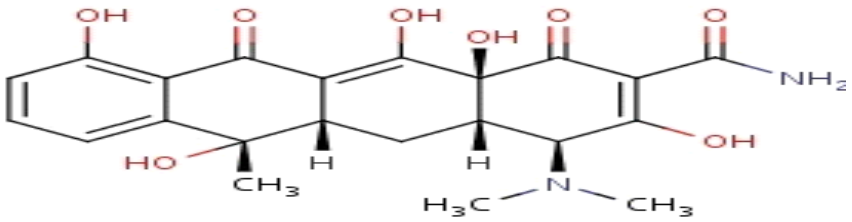
Ligand

P. putida is resistant to poisonous substance or antibiotics, so far, the pyranochalcones showed inhibitory outcome. Having this in observance, huge amount of instinctive and artificial

pyranochaalcones described in numerous books believed as the ligands. There are several ligands of *P. putida*. There are various types of ligands but here we use two ligands of chloramphenicol and tetracycline. The 3D structure of ligand is obtained from protein PubChem ID. And ligands convert in the pdb file and by auto docking ligands are converted into pdbqt.

Biological Source of Tetracycline

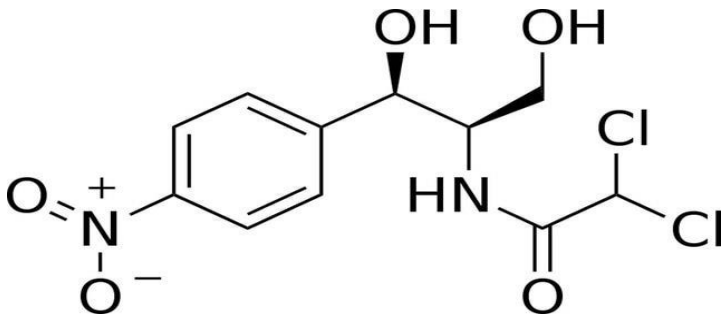
INN that is a broad-spectrum polyketide antibiotic formed by spectromyces species of antibacterial shown for use in contrast to many bacterial contaminations it is a protein synthesis suppressor. It is generally used to cure acne and additional recently acne rosacea and it is factually important in dropping the number of losses from the cholera disorder.



Tetracycline

Biological Source of Chloramphenicol

INN is an antibiotic beneficial for the cure of number of bacterial diseases. It is thought a classical wide spectrum antibiotic together with the tetracycline and as it is both inexpensive and informal to production. It is commonly an antibiotic of optimal in emerging world it is recognized as clarithromycin is dynamic against extensive diversity of gram positive bacteria and grams negative microorganisms. As well as most anaerobic animals due to confrontation and safety are tumorous. It is no lengthier a first –line negotiator for any contamination in established nations with distinguished exception of interesting handling of contagions.



Chloramphenicol

Autodocking

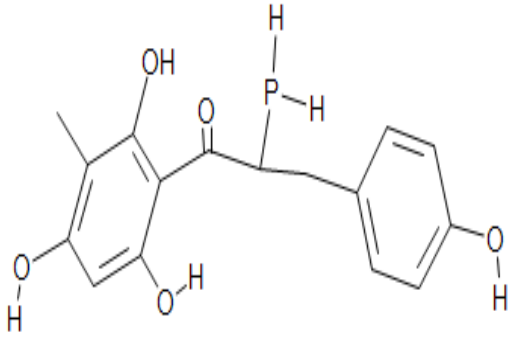
I downloaded the sdf files of the ligand I selected then I opened them in discovery studio 4and then I modified the ligands as follows. In auto docking we change the ligands in this paper; these ligands are quercetin, Naringenin, phloretin, chloramphenicol, tetracycline etc. But here we use only two ligand and by discovery studio 4 modified them. These two ligands are tetracycline and chloramphenicol. During modification in Naringenin H-30 attach with C then c-30 and add hydrogen to complete the valency .and the H-27 is attached with N and changed in the N-27 and hydrogen atom is added to complete the valency. In the quercetin the H-25 is attaches with nitrogen atom and then N-25 and then hydrogen is added, H-29 is attaches with c and the C-29 is formed and hydrogen atom is added and the H-28 is changed in to the O-28 by attaching with oxygen and then hydrogen is added.

The tetracycline is modified by changing there the H-55 is changed in the P-55 by attaching with p and hydrogen is added. the H-56 IS changed in the N-56 by attaching with nitrogen then the water is added to complete the valency the H-53 is changed in the C-53 and the hydrogen is added and in chloramphenicol the H-27 is changed in the O-27 by attaching with O and the hydrogen is added. The H30 is changed in the p30 by replacing the p and the hydrogen is added for the completion of valency. the H-29 is changed in the C-29 by attaching with c and the hydrogen is added in discovery studio 4. then I opened in auto-dock software and saved as pdbqt file , pdbqt file of ligands and protein are copy in vina folder which take place in program file the I gave the command to proceed the docking .

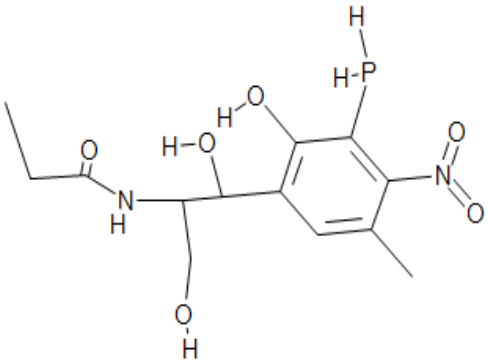
RESULTS

For docking I have used two ligands first used them without modification and then modified them and found better results. The ligands which I have used are phloretin and chloramphenicol.

Ligand structures



Ligand 1: Phloretin



Ligand 2: Chloramphenicol

Docking Structures

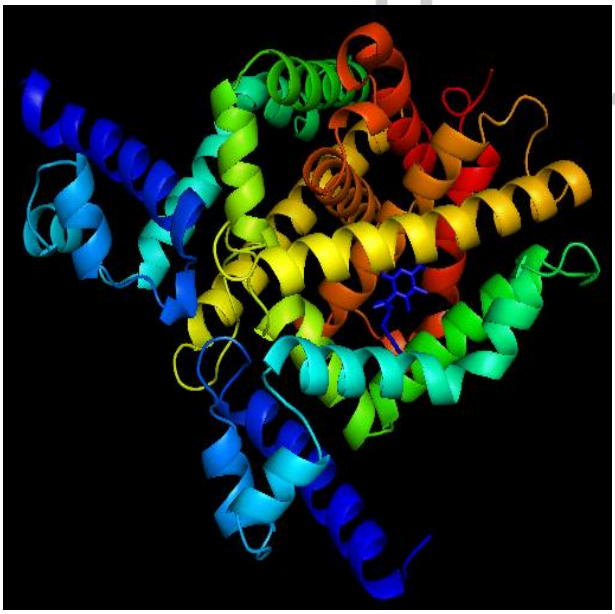


Fig.1: Phloretin

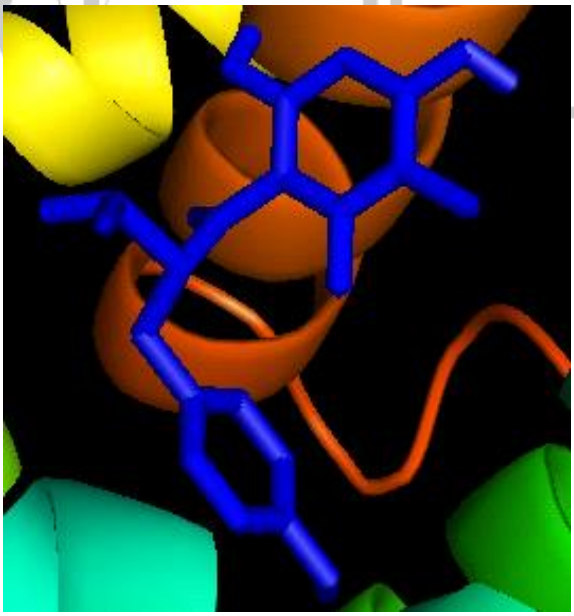


Fig.2: Docking of Phloretin

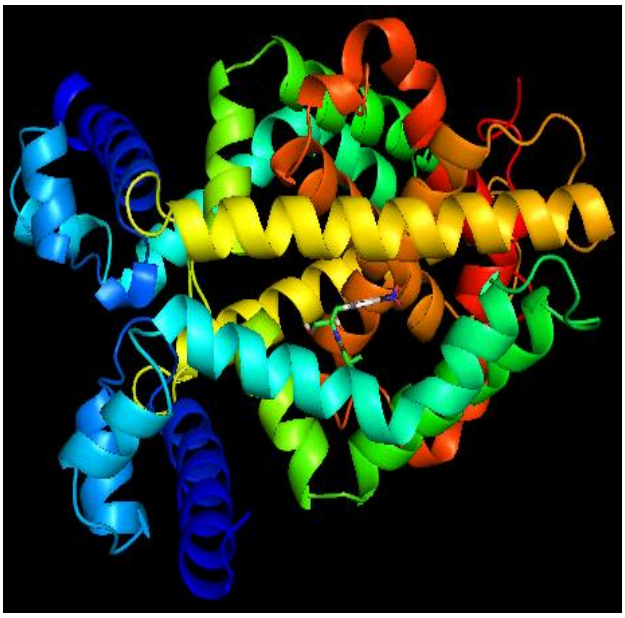


Fig.3: Chloramphenicol

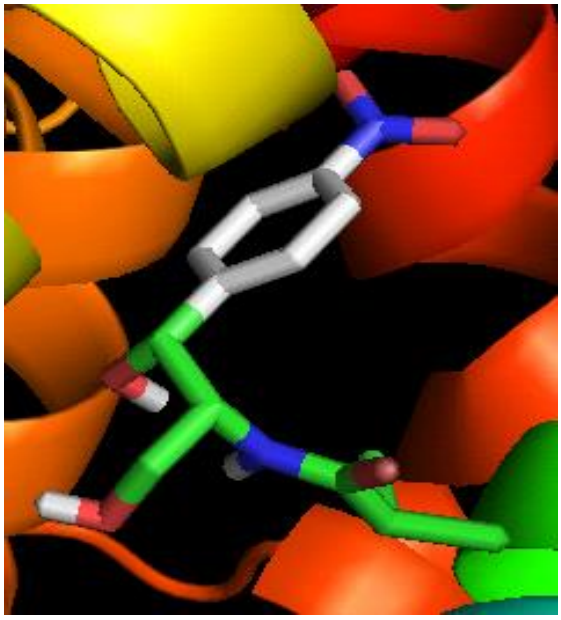


Fig.4: Docking of Chloramphenicol

Modified Sites table

Table 1: Original ligands showing modification

Ligand Name	Original Ligand	Modifications
Ligand 1	Phloretin	CH3, O, NH3
Ligand 2	Chloramphenicol	NH3, CH3, NH3

Docking Results

Table 2: Binding affinity values of ligands

Ligands	1	2	3	4	5	6	7	8	9
Ligand 1	-7.6	-7.3	-7.2	-7.2	-7.1	-7.1	-7.1	-7.0	-7.0
Phloretin	-7.5	-7.2	-7.2	-7.0	-7.0	-7.0	-6.9	-6.9	-6.9
Ligand 2	-7.2	-7.2	-6.8	-7.0	-6.9	-6.8	-6.7	-6.7	-6.5
Chloramphenicol	-6.3	-6.1	-6.0	-6.0	-6.0	-6.0	-5.9	-5.9	-5.8

ADMET

A set of test categories including Absorption, distribution, metabolism, excretion, toxicity used collectively in drug development to offer vision into how a therapeutic drug interrelates with the entire body.

Table 3: ADMET properties of Ligand compounds

Structure Name	MlogP	S+logP	S+logD	Ruleof5	MWt	M_NO	T_PSA	HBDH
Chloramphenicol (Modified)	1.259	2.823	2.824	0.000	330.279	8.000	135.610	4.000
Chloramphenicol (Unmodified)	0.956	0.311	0.311	0.000	268.271	7.000	115.380	3.000
phloretin (Modified)	2.091	1.817	1.242	0.000	320.284	5.000	97.990	4.000
phloretin (Unmodified)	1.842	2.437	1.605	0.000	274.275	5.000	97.990	4.000

Scoring

Scoring of new modified ligand were done through DSX online (server) and table given bellow:

Table 4: Modified ligands scoring values

Ligand Name	Rmsd	Rank(score)	score
Chloramphenicol (Un Modified)	None	1	-13
Chloramphenicol (Modified)	None	1	-98
Phloretin (Un Modified)	None	1	-13
Phloretin (Modified)	None	1	-115

DISCUSSION

The increasing number of the antibiotics resistant straining of the microorganisms now became one of a main antimicrobics is as the consequence of 3 key approaches specifically enzymetic deactivation of a remedy, alteration of marked positions and gibbosity by effluence. A large amount of pyranochalcones have been described to display ant mutagenic, disinfectant, and anticancer activities. Pyranochalcones include chloramphenicol and tetracycline are extensively dispersed naturally existing flavonoid compounds encounters as focused in the research field in the drug proposal or in finding. While this extensive variety of organic characteristics has encouraged awareness in the formation of existing pyranochaalcones. The pyranochalcones tetracycline and chloramphenicol and were expected as effective in contradiction of the multidrug resilient straining of the microorganisms. The outcomes got will be useful in manipulation of newfangled sequence of the drug particularly to the antibiotics resistive microbes. Effort is in improvement to find relation to unusual artificial pyranochaalcones to this bacterial specie.

CONCLUSION

In this process of research, molecular docking has been operated with 2 naturally existing Pyranochalcones on the transcriptional regulator enzyme (TtgR) of bacteria pseudomonas putida. The pyranochalcones tetracycline and chloramphenicol and were expected as effective in contradiction of the multidrug resilient straining of the microorganisms. The outcomes got will be useful in manipulation of newfangled sequence of the drug particularly to the antibiotic's resistive microbes. Effort is in improvement to find relation to unusual artificial pyranochaalcones to this bacterial specie.

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