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Structure Based Drug Design and AutoDock Study of Potential Protein Alanine Aminotransferase in The Treatment of PCOS and Uterine Cancer

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ABSTRACT

Polycystic ovary syndrome (PCOS) is a worldwide reproductive disorder that is surrounded by numerous health conditions together with an impact on several metabolic processes. The specific root cause for PCOS is not known. Uterine cancer is the most common cancer occurring within a woman's reproductive system. **T**he aim is to enhance confirmation for the protein as well as the ligand and the relative orientation among the protein and ligand so that the free energy of the whole system is reduced. The current research is carried out using molecular docking as protein-ligand interactions play an essential role in drug design. The 3D structure of the Alanine aminotransferase enzyme was procured from the Protein Data Bank and docked with the structure of Pyranopyridine derivatives compounds using the software that are AutoDock Tools and Discovery studio. The drug-likeness quality was examined by imposing Lipinski's rule of five on the Pyranopyridine derivatives compounds to check the activity. The docking results that were predicted by AutoDock Vina revealed that hydrogen bonds were formed between the proteins and the inhibitors used. The finest compound which showed development towards a new drug was chosen concerning binding energy. This research indicates that the chosen compounds can be further investigated and evaluated. These compounds have been found to show marked binding activity which can lead to the synthesis and pharmacological activity of pyranopyridine derivates as a drug.

1. INTRODUCTION: -

The polycystic ovary syndrome PCOS is the combination of excessive spreading of the male sex hormone and anovulation with enlarged ovaries. It is generally caused because of infertility due to anovulation. The eggs are produced by the ovaries which get released every month, but when diagnosed with PCOS, the egg might not develop the way it should or may not get released during the process of ovulation. PCOS is a hormonal imbalance that results in the skip of their menstrual cycle and eventually makes it hard for them to get pregnant. Women between the age of 15 to 44 or during their childbearing age are prone to have PCOS.

1.1 Causes of PCOS: -

The specific cause of PCOS is unknown. Yet, some doctors consider it may be due to the high level of male hormone which may cause the prohibition of the ovaries from producing eggs and the hormones normally. The factors that are associated with the excess production of androgen in the body are as follows: -

1) Genes: The study shows that PCOS may be hereditary. Although, there may be many genes, that contribute to PCOS.

2) Insulin resistance: Nearly 70% of women who are detected with PCOS also have insulin resistance. This proves that insulin is not utilized by their cells accurately. The pancreas produces the hormone insulin to guide the body to utilize the glucose for energy. The requirement for insulin will increase within the body while the cells are not capable to use it. To compensate for this necessity, the pancreas produces more insulin that is accountable for activating the ovaries to make more male hormones. Insulin governs the blood sugar level and if someone is suffering from PCOS, the body shall not respond to insulin the way it does.

3) Inflammation: Women with PCOS normally have swelled in the body. The reason can be because of being obese. A relationship has been observed between elevated androgen levels and excess inflammation.

4) Hormone levels: Variation of the insulin hormone and androgens that contribute to male hormones is testosterone. The characteristic of insulin in the body is to preserve the quantity of energy in the blood which gets increased after eating. This works by unbinding cells of the

body and by permitting the entry of glucose to pass from the blood in cells with results in the drop of the levels of energy in the blood.

Uterine cancer is the most common cancer occurring within a woman's reproductive system. At the point where the cancer growth starts in the uterus, it is known as uterine cancer. The shape of the uterus resembles a pear in a woman's pelvis. The uterus is likewise known as the womb, in which the child grows when a woman is pregnant. The most well-known kind of uterine cancer is referred to as endometrial cancer. It is commonly a disease of postmenopausal sufferers, 8-14% of those cancers are in sufferers earlier than forty-five years of age. The risk factors related to the reproductive and menstrual cycle include early menarche (earlier than 12 years), late menopause (after 55 years), extra lifetime menstrual cycle, infertility. There are two types of uterine cancer, Adenocarcinoma, and Sarcoma.

1.2 Causes of Uterine cancer: -

Several factors affect the risk of developing endometrial cancer, including: -

1) Obesity: - This is linked to hormone changes. Most of the estrogen is produced by a woman's ovaries before menopause. However, the fat tissue can change a different hormone (referred to as androgens) into estrogens. This can affect estrogen levels, mainly after menopause. More fat tissue can boom a woman's estrogen levels, which will increase her endometrial cancer risk.

2) Diet and exercise: - Diet complete with fats can grow the chance of many cancers, including endometrial cancer due to the fact fatty meals are also high-calorie foods, a high-fat food regimen can result in obesity, which is a famous endometrial cancer risk factor. Many scientists suppose that is the principal manner wherein a high-fat food regimen increases endometrial cancer risk. It is considered by a few scientists that fatty foods additionally may have a direct impact on how the body makes use of estrogen, which may tend to increase the endometrial cancer risk.

3) Hormonal factors: - The hormonal balance plays an important role in the improvement of endometrial cancers. Various dangerous elements for endometrial cancer influence estrogen levels. Before menopause, the ovaries are the primary supply of the twopredominantforms of female hormones are estrogen and progesterone. The stability among those hormones changes each month during the menstrual cycle. This results in the woman's monthly periods and

maintains the endometrium healthy. A shift in the stability of those hormones towards extra estrogen leads to an increase in a woman's risk for endometrial cancer. After menopause, the ovaries prevent making those hormones. However, a small quantity of estrogen remains made evidently in the fat tissue. Estrogen from the fat tissue has a larger effect after menopause than it does earlier than menopause.

4) Birth control pills: - by using birth control pills (oral contraceptives) the chance of endometrial cancer gets decreased. The hazard is lowest in those women who consume the pill for a prolonged period, and this protection lasts for a minimum of 10 years after a woman discontinues the consumption of the pill. However, it is critical to examine all the dangers and benefits while choosing a contraceptive method, the endometrial cancer risk is only one element to consider.

2. DOCKING: -

The molecular docking research enlightens about the computationally stimulating molecular identification procedure. The aim is to enhance confirmation for the protein as well as the ligand and the relative orientation among the protein and ligand so that the free energy of the whole system is reduced. One of the ways is to use the matching technique which narrates about the protein and the ligand as complementary surfaces. The next way encourages the real docking process where the ligand-protein pairwise interconnection energies are determined. The process is speedy to permit virtual screening of the ligand libraries consisting of 10,000 mixtures. The docking studies help inspect the purpose of the target and the virtual screening in which a wide range library of compounds can be docked and ranked and might be used in recognition of new inhibitors for the development of the drug.

2.1 Different Docking Software's: -

1. AUTODOCK
2. AUTODOCK VINA
3. RACOON2
4. GOLD (GENETIC OPTIMIZATION FOR LIGAND DOCKING)
5. FLExX

6. FRED (Fast Rigid Exhaustive docking)

1. AUTODOCK: -

AutoDock is a set of automatic docking tools, which is created in a way to indicate how small molecules, such as substrates or drug applicant sticks to a receptor to know the 3D. The ongoing division of autodock comprises two generations of software which are - AutoDock 4 and AutoDock Vina. The software AutoDock -4 contains two chief programs. AutoDock carries out the docking of ligand to a set of grids outlining the target protein. Auto grid pre evaluates these grids. Furthermore, docking is also used to visualize the atomic affinity grids. For instance, this may assist by guiding the organic synthetic chemists to make better binders. AutoDock is accessible for the systems which need additional methodological enhancement.

2. AUTODOCK VINA: -

AutoDock Vina is assembled and runs under Windows 10 Operating System. Every figure was produced with representation by using the Discovery Studio Visualizer. For docking, all water molecules are eliminated, and polar hydrogen atoms are attached to the purified model using AutoDock Tools (ADT). The prepared protein is then saved in PDBQT format. The ligands are downloaded from ChemSketch Database and converted to PDB file format by using Openbabel software. In Auto Dock Vina that pdbqt files for protein and ligands preparation and grid box creation are completed using Graphical User Interface program Auto Dock Tool. ADT allocates the polar hydrogens, united atom Kollman charges, solvation parameters, and fragmental volumes to the protein. AutoDock saves the prepared file in PDBQT format. AutoGrid is used for the composition of the grid map using a grid box. AutoDock Vina is a new generation docking software from the Molecular Graphics Lab. Remarkable development is attained in the average accuracy of the binding mode predictions. The scores shown by AutoDock Vina are mostly estimated with globular and symmetric hydrogen bond potentials, unstated hydrogens, and no electrostatic contribution. It is used to exhibit its performance with ligands of typical biological dimension and constitution. The AutoDock force field comprises of contributions based physically, which consists of two directional hydrogen-bonding terms with direct polar hydrogens, and electrostatics. It is extremely improved to carry out docking experiments by making use of proved and tested default techniques. AutoDock Vina is rapid and effective for nearly all procedures.

3. RACOON2: -

Virtual screening is swiftly turning out to be the main application of computational docking systems, with several victories in the establishment of new lead compounds for pharmaceutical development. The objective here is, to screen a huge library of easily accessible ligands for the identification of a minute subtype for purchase and experimental testing. Raccoon is a graphical user interface that is used to design to organize the steps for executing a virtual screening and scanning the results.

4. GOLD (GENETIC OPTIMIZATION FOR LIGAND DOCKING): -

To search the rotational flexibility of receptor hydrogens and ligand conformational flexibility the GOLD makes use of the hereditary algorithm. In GOLD docking takes place by using the wizard with default parameters population size (100); selection- pressure (1.1); the number of operations (10,000); the number of islands (1); niche size (2); and operator weights for migrating (0), mutate (100), and crossover (100) are applied. GOLD is used by a Gold Score fitness function. Gold Score is a molecular procedure-like function and is improved for the calculation of binding positions of ligand and to achieve high database enhancement.

5. FLExX: -

FlexX (a part of LeadIT) is a flexible technique for docking that uses an Incremental Construction (IC) algorithm and a pure empirical scoring function alike to the one evolved by Bohm and coworkers to put the ligands into the active site. Initially, IC algorithms dissect individual molecule in a set of rigid fragments according to rotatable bonds, and then gradually assembles the fragments all over the binding pocket. For docking studies, the PDB files of ligands are transformed into an SYBYL mol2 file format and a ligands library is generated. Through the FlexX graphic interface, a receptor description file is developed.

6. FRED (Fast Rigid Exhaustive docking): -

A multi-conformer docking algorithm is used by FRED that individually creates a set of low-energy conformers, and carries docking rigidly for every conformer. FRED requires a correct receptor-prepared file with a ligand conformer library to bring precise docking. FRED with a Gaussian type fitting scoring function Chemgauss4 is used to dock ASMT with ligands conformer library towards achieving a potent inhibitor against ASMT.

3. AIM AND OBJECTIVE: -

3.1 AIM: -

Structure-based drug design and AutoDock study of potential protein Alanine aminotransferase in the treatment of PCOS and Uterine Cancer.

3.2 OBJECTIVE: -

Softwares such as Auto Dock Vina, Discovery Studio Visualizer, Chem Sketch, Open Babel, were used based on Drug Design and Development. In online mode, we have used Pyranopyridine derivatives as a novel synthetic compound. The main focus of the molecular docking technique is to recognize the best position for a substrate molecule to hold together a receptor molecule and anticipate the appropriate matching binding mode of a ligand to a Protein. The underlying principle in the drug design is to predict if a given molecule will stick to a target and how strongly if it does.

4. METHODS: -

Molecular docking is performed to analyze how two or more molecules, for instance, a drug and enzyme or protein are arranged together. In other words, docking can be defined as a molecular modeling technique that is used to estimate how a protein (enzyme) is associated with small molecules (ligands). 73 compounds of pyranopyridine derivatives were docked with a protein (1Xi9) to recognize the binding affinities. For Docking the foremost thing to be done is to take the base as the main moiety, further substituents we added by using the software called CHEMSKETCH. Lastly, every compound was individually saved as an MOL file.

4.1 CHEM SKETCH: -

ChemSketch is an application of a molecular modeling program that is used to produce and adjust images of chemicals. ChemSketch Freeware is software where you can draw different structures of chemicals together with organics, organometallics, polymers. Due to this application, it is feasible to write and produce chemical equations, diagrams, IUPAC names for numerous entities. Figure 1 depicts the ChemSketch software.

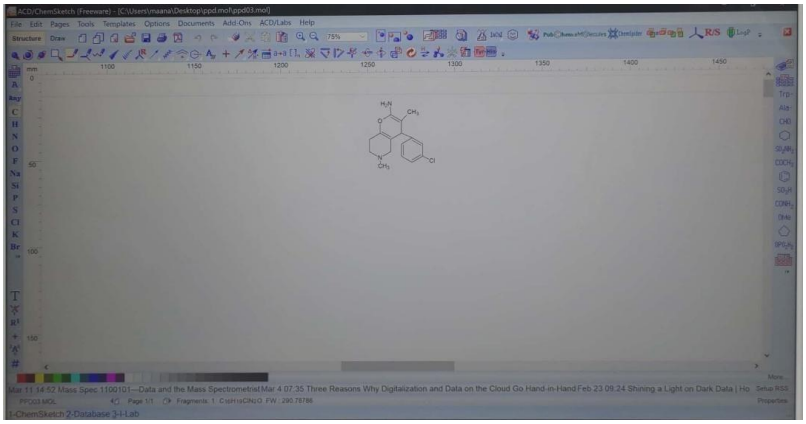


Figure 1: - Chemsketch

After drawing structures, the MOL files were converted to PDB format with the help of OPEN BABEL for further docking.

4.2 OPEN BABEL: -

Open Babel is a publicly accessible software in which the chemical toolbox expresses many languages of chemical data. Open Babel version 2.3 interchanges about 110 formats. Complete 111 chemical file formats are supported by Open Babel. It can read 82 formats and write 85 formats. These enclose the common formats used in Cheminformatics (SMILES, InChI, MOL, MOL2), input and output files from diverse computational chemistry. Open Babel recognizes all linear and ring substances in the molecule of lengths 1 to 7 (excluding the 1-atom subs C and N) and plots them in a sequence of bits. Figure 2 represents the open Babel software.

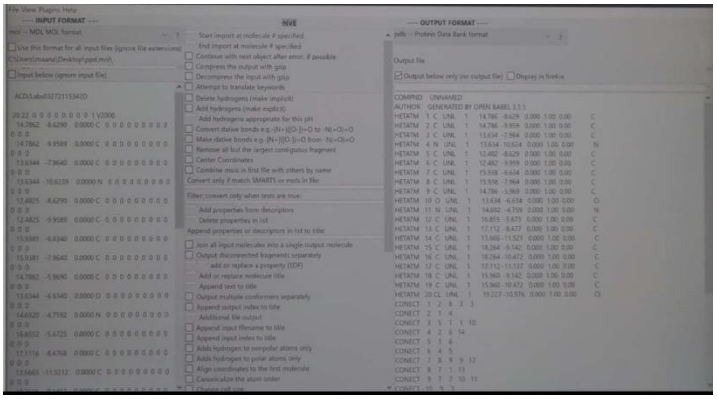


Figure 2: - Open Babel Conversion Of Mol To Pdb

After the conversion, the properties of compounds were observed (i.e. physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry friendliness.) The compounds that were chosen followed "Lipinski's rule of five" which states that an orally active drug should not show more than one violation.

4.3 SWISSADME (an online tool): -

SwissADME is a web tool that is freely accessible to the structures for determining the physicochemical properties, pharmacokinetics, drug-likeness, and medicinal chemistry friendliness. "Lipinski's rule of five" is used to calculate the drug-likeness of a chemical compound. It declares that an orally active drug should not show more than one violation of the following criteria:

a) less than 5 hydrogen-bond donors,

b) less than 10 hydrogen-bond acceptors,

c)a molecular mass less than 500 Da, and

d)log P not greater than 5.

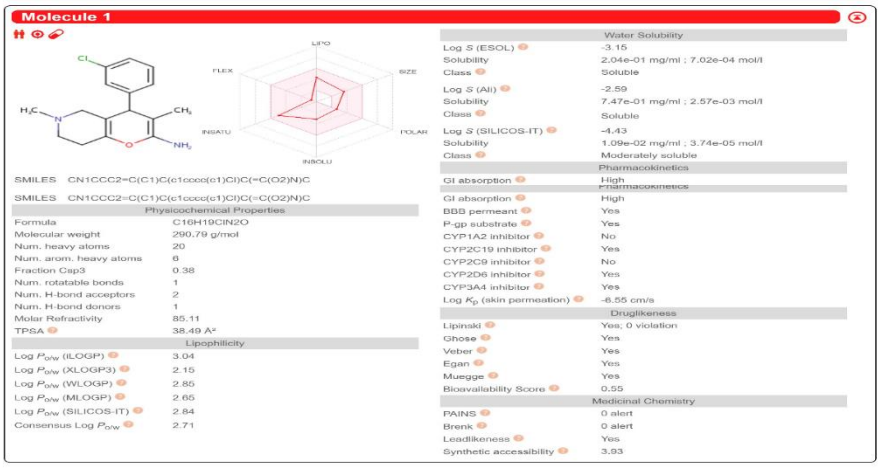


Figure 3: - Results obtained by Swiss ADME.

The ligands of the current search meet the condition of "Lipinski's rule of five". Figure 3 depicts the outcome obtained by Swiss ADME. Following the authorization of compounds from SwissADME, the protein was downloaded and named as shown in Table No.1. The proteins were downloaded from the following site: https://www.rcsb.org/ Figure 4 & Figure 5 exhibits proteins which are obtained from Protein Data Bank(PDB).

Figure 4: - Protein 1xi9

4.4 DISCOVERY STUDIO VISUALIZER: -

Discovery Studio is a software that is used for preparing protein for docking, viewing interactions of ligand and protein, replicating the design of small molecule and macromolecule, and the validation by Dassault System BIOVIA.

4.5 AUTODOCK TOOLS: -

Molecular modeling is an investigated technique to a great extent to observe the potent compounds in the absence of unnecessary efforts and investment in the research. AutoDock Tool ADT 1.5.6 is software used to look over the activity in terms of binding affinity (Kcal/mol), and the results are compared subsequently in binding affinity score for finest docked conformation. The outcomes of results get examined by AutoDock Vina result due to which close contact, hydrogen bond, hydrophilic, and hydrophobic interactions get disclosed. By using ADT we can effortlessly discover the affinity of their compound with protein. Figure 5 explains the ligand view in the AutoDock image. In figure 6 Docking result is obtained by command prompt.

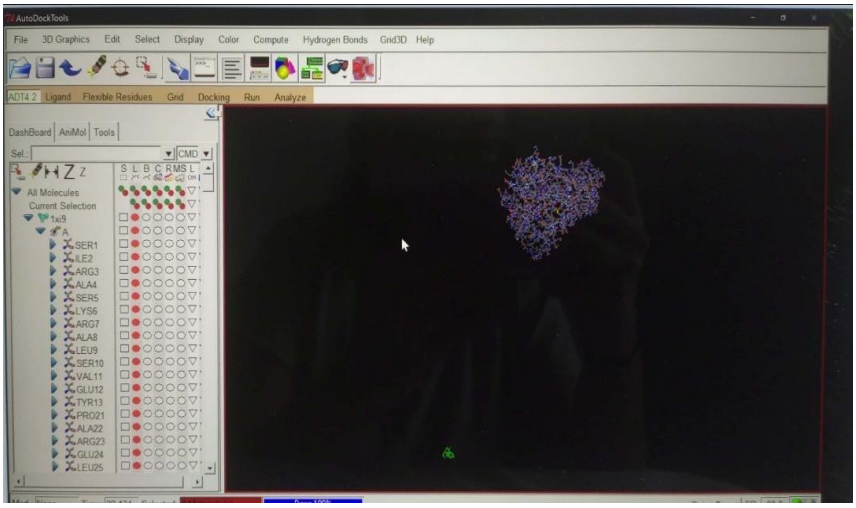


FIGURE 5: - LIGAND VIEW IN AUTODOCK

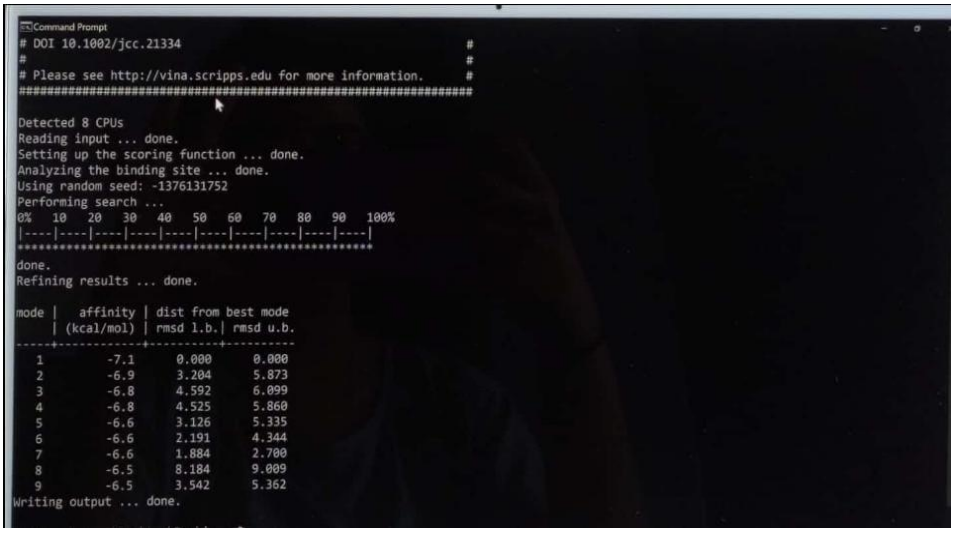


FIGURE 6: - DOCKING RESULTS OBTAINTED BY COMMAND PROMPT

5. RESULTS AND DISCUSSION: -

We have designed the novel synthetic compounds from pyranopyridine derivatives based on the drug design and development to find out its activity. It was considered satisfying to perform molecular docking studies, hence viewing the compounds, and inculcating the results. Considering Alanine aminotransferase as the enzyme, which was obtained from Protein Data Bank by X-ray diffraction method of resolution 2.33 Å, docking studies with the newly synthesized structure were performed to determine the best conformation. The software used in the docking program was Autodock Vina. Docking compounds into the binding site of a receptor and evaluating the binding affinity of the compound is an essential part of the

structure drug design process. With the newly synthesized ligands, the docking of the receptor exhibited a well-established bond with more than one amino acid in the receptor active pocket. These compounds followed Lipinski's rule of five without any violation concerning molecular weight (≤500). This is very crucial for the determination of a compound for appropriate drug design. On docking pyranopyridine derivatives formed at least 1 Hydrogen bond with the targeted protein. ARG, TYR, THR, PRO, GLY, PLP, LYS, LEU, ASP, ILE VAL, PHE, ASN, were found to be common amino acids interacting residues in the target protein for ligands. Higher docking scores, it represents strong protein-ligand binding affinity concerning the lower docking score values. It was observed that in pyranopyridine derivatives, the structure below in the diagram, showed the best affinity score of -10.2 with the formation of 5-H bonds with GLY38, TYR328, ARG371, ARG371, THR103, PLP501, TYR13, TYR127, VAL11, TYR13, TYR13 amino acids, and 6 hydrophobic interactions, due to hexahydrospiro and amine groups present in the structure.

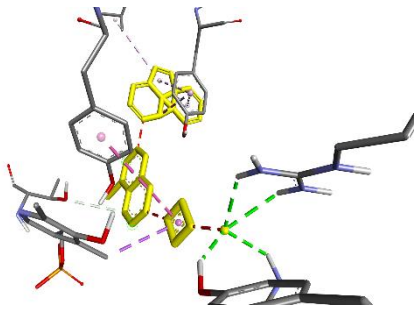


FIGURE 7

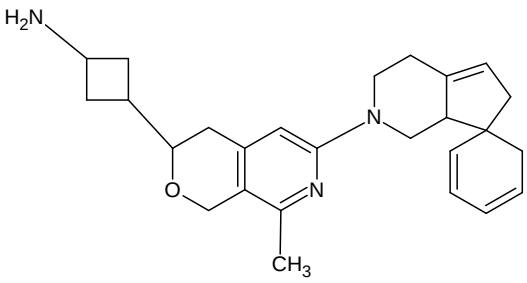
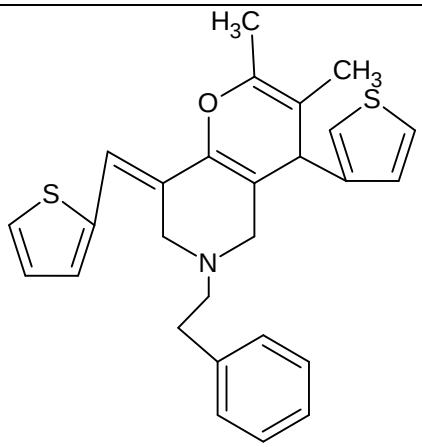
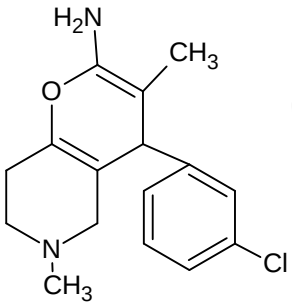
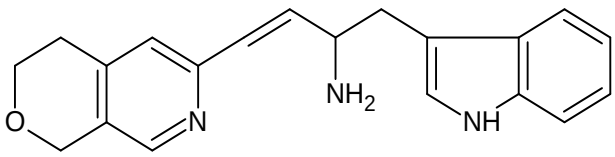


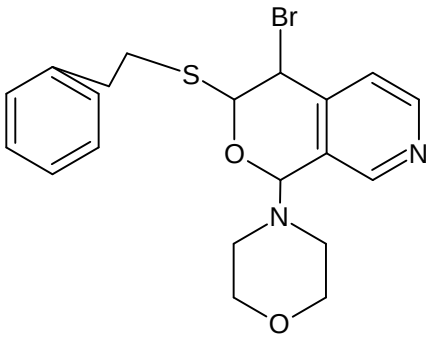
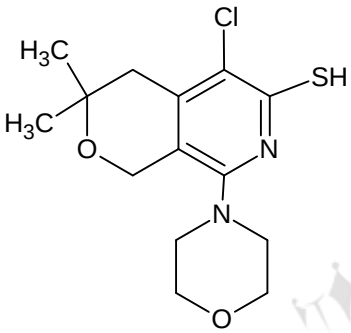
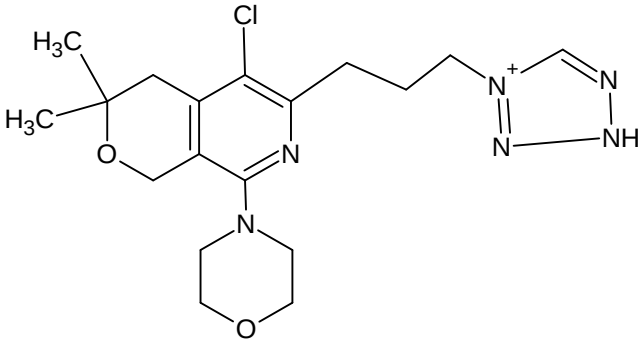
FIGURE 8

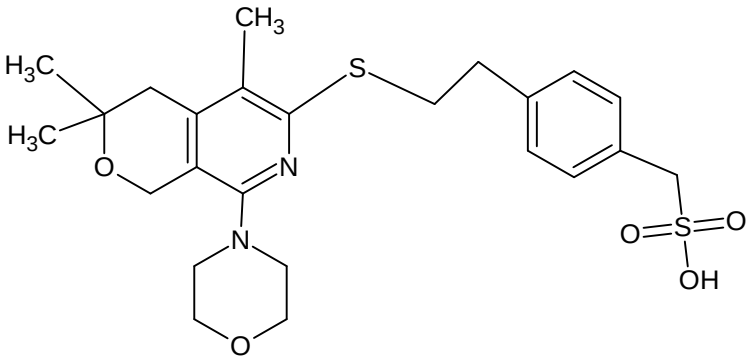
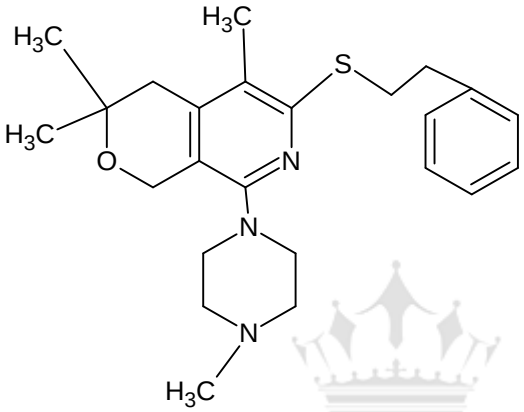
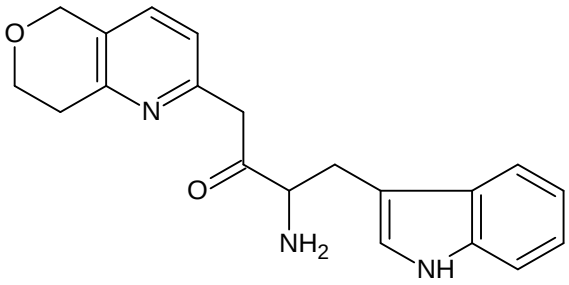
In total seventy-two structures have been docked with a good range of binding affinities. The ligand enzyme complex is stabilized mainly by hydrogen bonds and hydrophobic interactions. Out of seventy-two compounds, three structures showed scores above 10, the next good

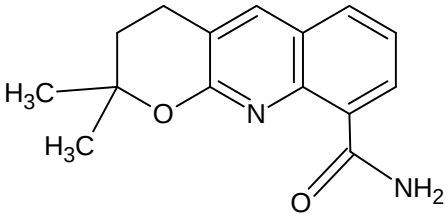
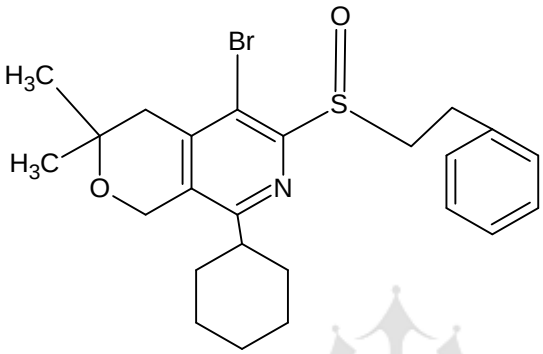
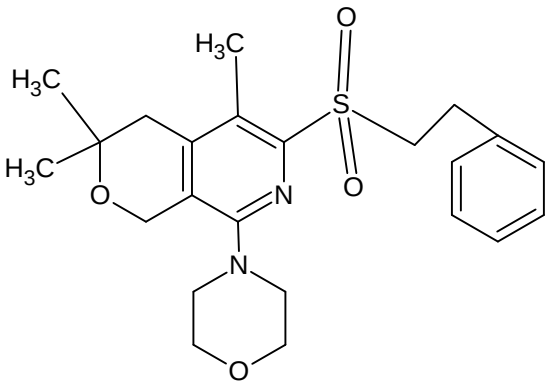
affinity was shown by fifteen structures of the score between 9 to 10, followed by twenty-four structures showing the range of 8 to 9, the score from 7 to 8 was depicted by twenty structures. 8 structures were shown for affinity 6 to 7 and 1 structure of score of 5.5. It forms hydrogen bonds, hydrophobic and ionic interactions. The docked pose with the least binding energy has the highest affinity and hence is the best-docked conformation.

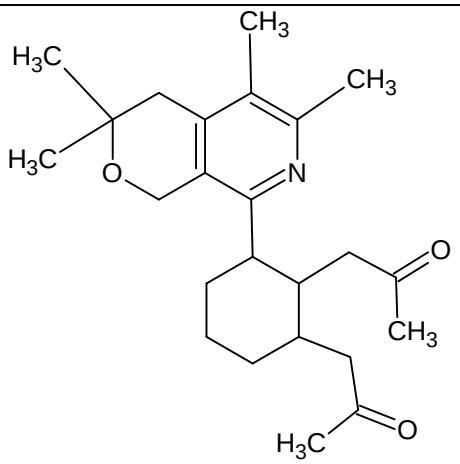
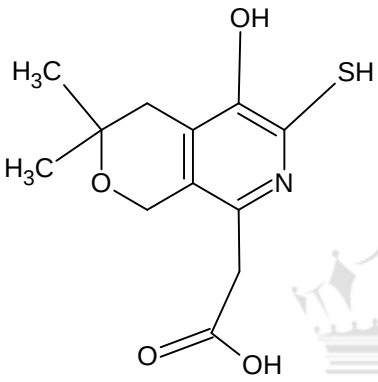
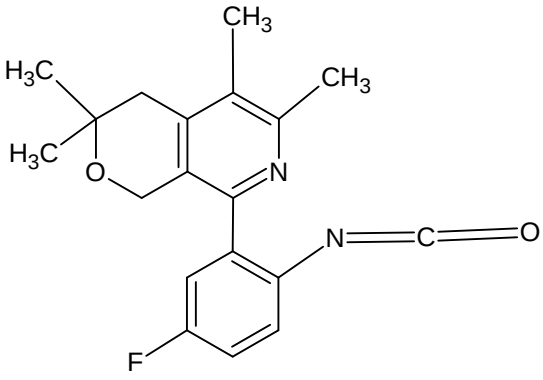
5.1 Table no 01: - Docking score of the ligands concerning proteins: -

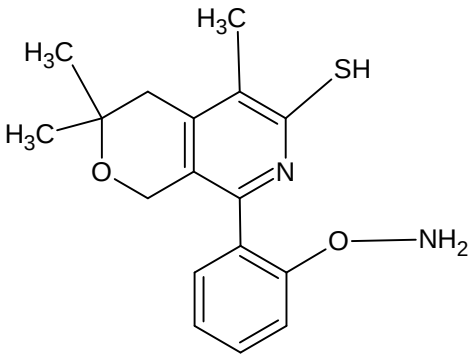
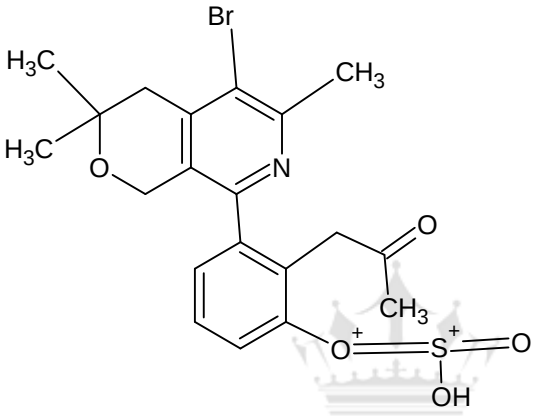
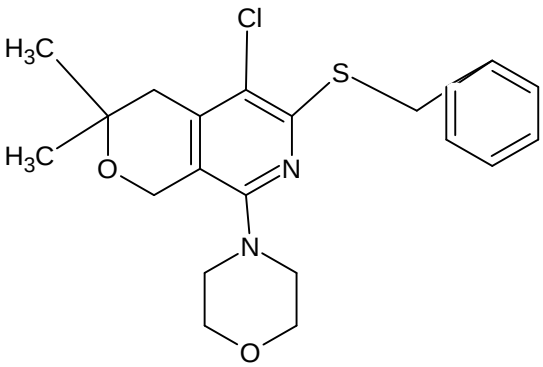
SR NO	.MOL	STRUCTURE	
1	Ppd02.mol		logo:- 4.94 XLOGP3:-5.15 WLOGP:-6.62 MLOGP:-4.57 SILICOS-IT:-8.16 Consensus logP O/W:-5.89
	IUPAC	(8E)-2,3-dimethyl-6-(2-phenylethyl)-8-[(thiophen-2-yl)methylidiene]-4-(thiophen-3-yl)-4H,5H,6H,7H,8H-pyrano[3,2-c]pyridine	
2	Ppd03.mol		iLOGP:- 3.04 XLOGP3:-2.15 WLOGP:-2.85 MLOGP:-2.65 SILICOS-IT:-2.84 Consensus logP O/W:-2.71
	IUPAC	4-(3-chlorophenyl)-3,6-dimethyl-4H,5H,6H,7H,8H-pyrano[3,2-c]pyridine-2-amine	
3	Ppd04.mol		iLOGP:- 2.88 XLOGP3:-2.19 WLOGP:-2.96 MLOGP:-1.77 SILICOS-IT:-4.52 Consensus logP O/W:-2.86
	IUPAC	1-(1H-indol-3-yl)-4-{1H,3H,4H-pyrano[3,4-c]pyridine-6-yl}but-3-en-2-amine	

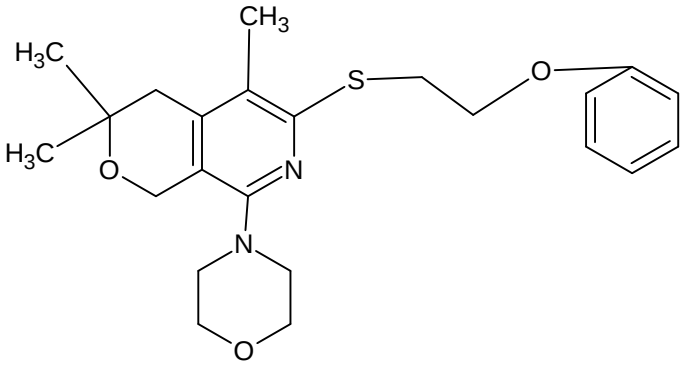
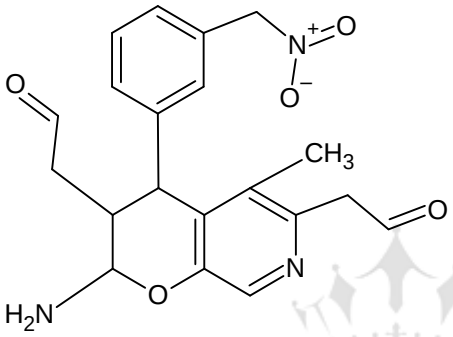
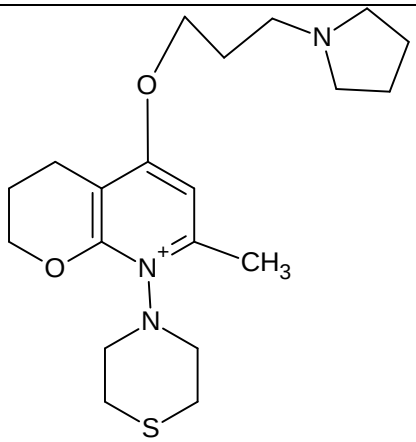
4	Ppd05.mol		iLOGP:- 3.37 XLOGP3:-3.43 WLOGP:-3.15 MLOGP:-2.74 SILICOS-IT:-3.86 Consensus logP O/W:-3.31
	IUPAC	4-{4-bromo-3-[(2-phenylethyl)sulfanyl]-1H,3H,4H-pyrano[3,4-c]pyridine-1-yl}morpholine	
5	Ppd06.mol		iLOGP:- 3.18 XLOGP3:-2.35 WLOGP:-2.18 MLOGP:-2.01 SILICOS-IT:-3.54 Consensus logP O/W:-2.65
	IUPAC	5-chloro-3,3-dimethyl-8-(morpholin-4-yl)-1H,3H,4H-pyrano[3,4-c]pyridine-6-thiol	
6	Ppd07.mol		iLOGP:- -1.44 XLOGP3:-2.41 WLOGP:-0.93 MLOGP:-2.10 SILICOS-IT:-2.97 Consensus logP O/W:-1.39
	IUPAC	4-{3-[5-chloro-3,3-dimethyl-8-(morpholin-4-yl)-1H,3H,4H-pyrano[3,4-c]pyridine-6-yl]propyl}-2H-1,2,3,4-tetrazol-4-ium	

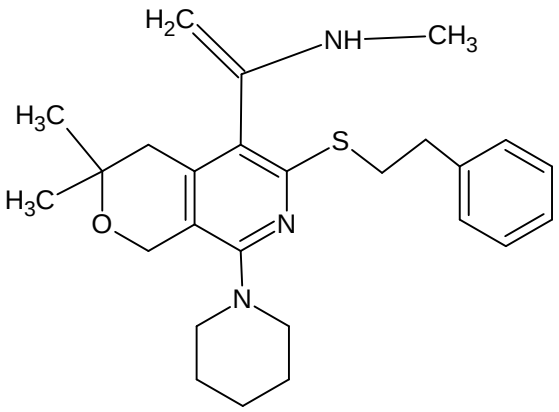
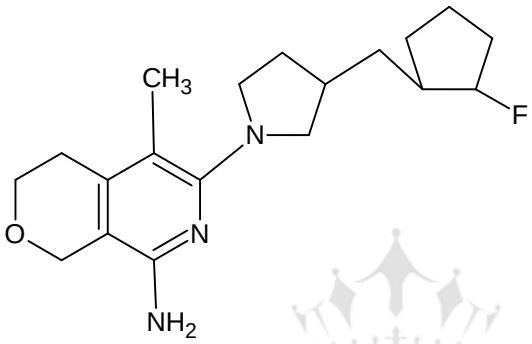
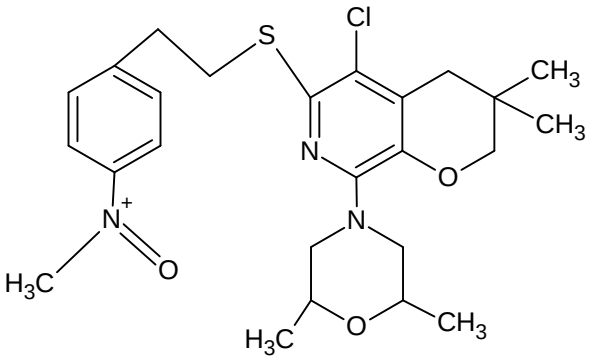
7	Ppd08.mol		iLOGP:- 3.30 XLOGP3:-3.09 WLOGP:-4.20 MLOGP:-2.57 SILICOS-IT:-4.29 Consensus logP O/W:-3.49
	IUPAC	[4-(2-{[3,3,5-trimethyl-8-(morphine-4-yl)-1H,3H,4H-pyrano[3,4-c]pyridin-6-yl]sulfanyl}ethyl)phenyl]methanesulfonic acid	
8	Ppd09.mol		iLOGP:- 4.17 XLOGP3:-4.59 WLOGP:-3.41 MLOGP:-3.55 SILICOS-IT:-5.17 Consensus logP O/W:-4.18
	IUPAC	1-methyl-4-{3,3,5-trimethyl-6-[2-phenylethyl)sulfanyl]-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}piperazine	
9	Ppd10.mol		iLOGP:- 2.00 XLOGP3:-1.44 WLOGP:-2.17 MLOGP:-0.94 SILICOS-IT:-4.24 Consensus logP O/W:-2.16
	IUPAC	3-amino-4-(1H-indol-3-yl)-1-{5H,7H,8H-pyrano[4,3-b]pyridin-2-yl}butan-2-one	

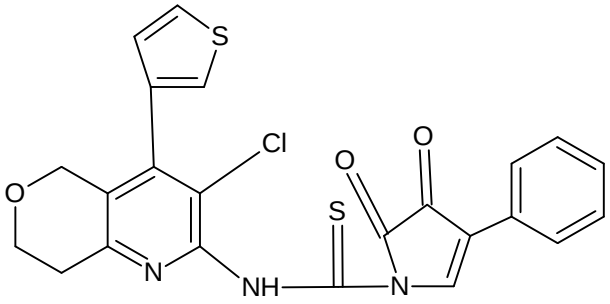
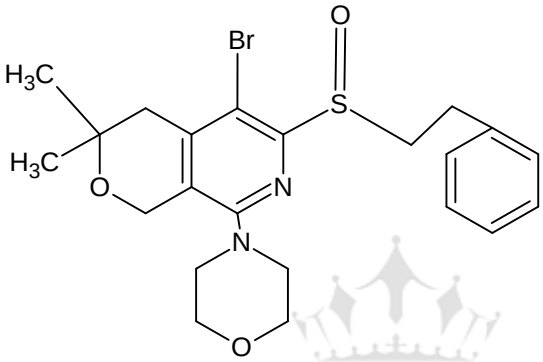
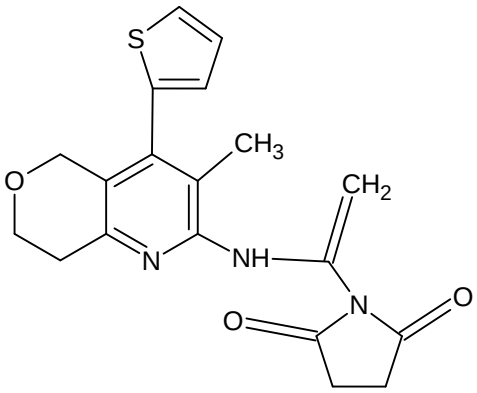
10	Ppd11.mol		iLOGP:- 1.65 XLOGP3:-2.38 WLOGP:-2.44 MLOGP:-2.12 SILICOS-IT:-2.88 Consensus logP O/W:-2.29
	IUPAC	2,2-dimethy-2H,3H,4H-pyrano[2,3-b]quinoline-9-carboximide	
11	Ppd12.mol		iLOGP:- 3.80 XLOGP3:-5.39 WLOGP:-6.81 MLOGP:-4.22 SILICOS-IT:-6.13 Consensus logP O/W:-5.27
	IUPAC	5-bromo-8-cyclohexyl-3,3-dimethyl-6-(2-phenylethanesulfinyl)-1H,3H,4H-pyrano[3,4-c]pyridine	
12	Ppd13.mol		iLOGP:- 3.79 XLOGP3:-3.13 WLOGP:-3.64 MLOGP:-2.35 SILICOS-IT:-4.27 Consensus logP O/W:-3.44
	IUPAC	4-[3,3,5-trimethyl-6-92-phenylethanesulfonyl0-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]morpholine	

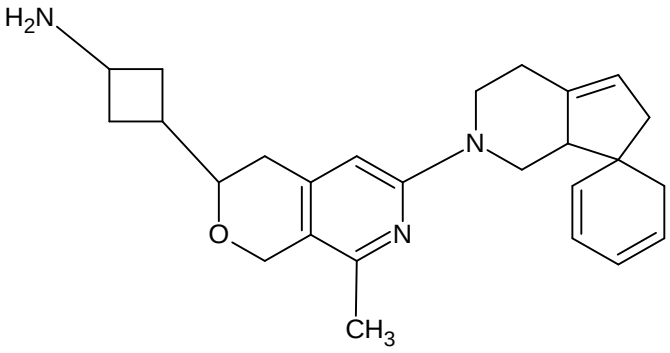
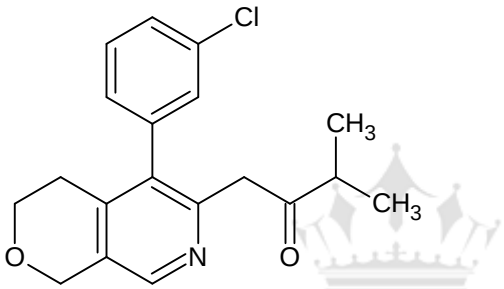
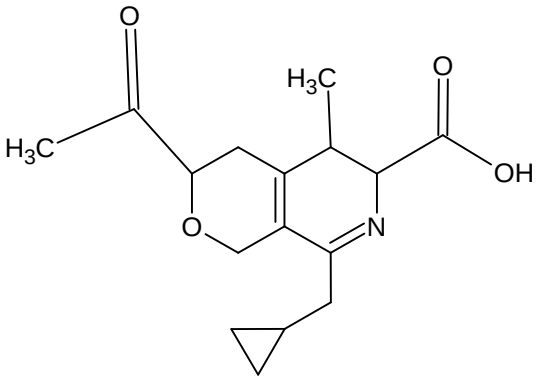
13	Ppd14.mol		iLOGP:- 3.73 XLOGP3:-3.05 WLOGP:-4.86 MLOGP:-2.69 SILICOS-IT:-6.23 Consensus logP O/W:-4.11
	IUPAC	1-[2-(2-oxopropyl)-6-{3,3,5,6-tetramethyl-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl}cyclohexyl]propane-2-one	
14	Ppd15.mol		iLOGP:- 1.81 XLOGP3:-0.78 WLOGP:-1.40 MLOGP:-0.44 SILICOS-IT:-2.22 Consensus logP O/W:-1.33
	IUPAC	2-{5-hydroxy-3,3-dimethyl-6-sulfanyl-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}acetic acid	
15	Ppd16.mol		iLOGP:- 3.50 XLOGP3:-4.48 WLOGP:-4.59 MLOGP:-2.81 SILICOS-IT:-5.90 Consensus logP O/W:-4.26
	IUPAC	8-(5-fluro-2-isocyanatophenyl)-3,3,5,6-tetramethyl-1H,3H,4H-pyrano[3,4-c]pyridine	

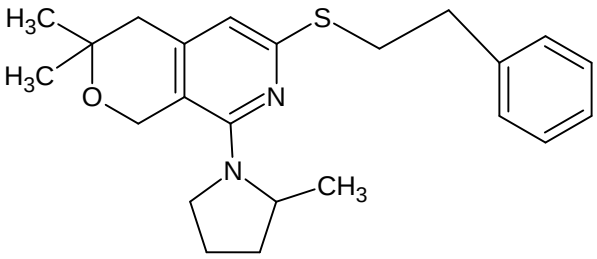
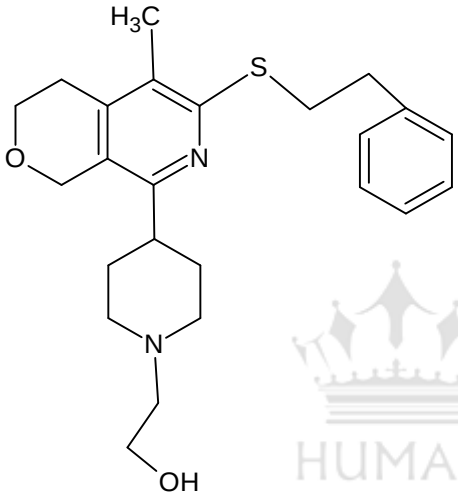
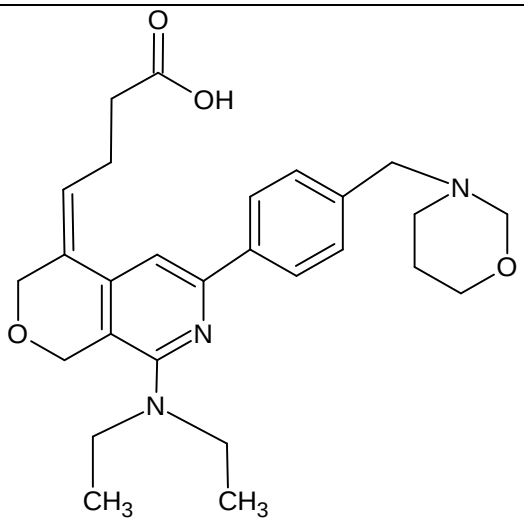
16	Ppd17.mol		iLOGP:- 3.06 XLOGP3:-2.89 WLOGP:-3.30 MLOGP:-2.39 SILICOS-IT:-3.84 Consensus logP O/W:-3.09
	IUPAC	8-[2-(aminooxy)phenyl]-3,3,5-trimethyl-1H,3H,4H-pyrano[3,4-c]pyridine-6-thiol	
17	Ppd18.mol		iLOGP:- 0.00 XLOGP3:-2.17 WLOGP:-4.68 MLOGP:-2.35 SILICOS-IT:-3.54 Consensus logP O/W:-2.55
	IUPAC	[(3-{5-bromo-3,3,6-trimethyl-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}-2-(2-oxoppropyl)phenyl)oxidaniumylidiene](hydroxy)oxo-6-sulfanylium	
18	Ppd19.mol		iLOGP:- 3.98 XLOGP3:-4.20 WLOGP:-4.03 MLOGP:-3.39 SILICOS-IT:-5.27 Consensus logP O/W:-4.17
	IUPAC	4-[6-(benzylsulfinyl)-5-chloro-3,3-dimethyl-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]morpholine	

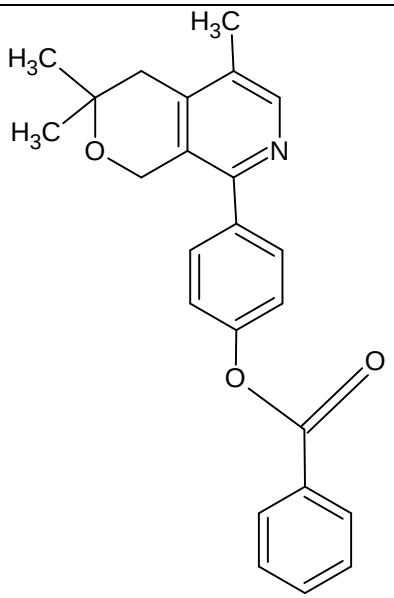
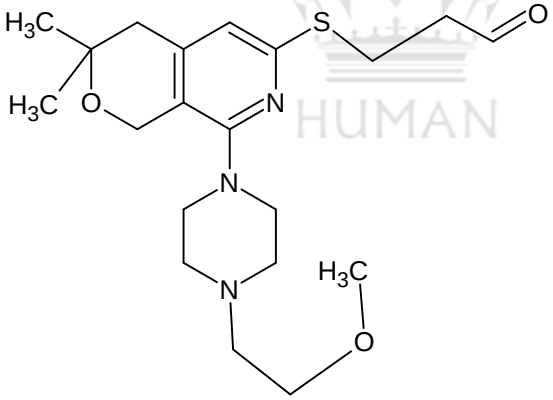
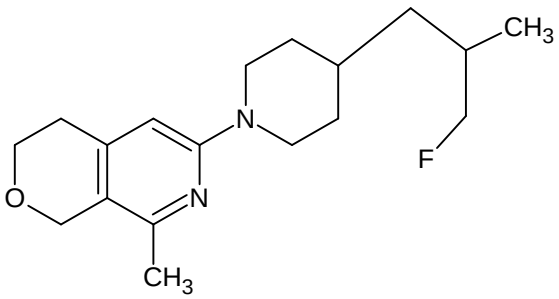
19	Ppd20.mol		iLOGP:- 3.59 XLOGP3:-4.11 WLOGP:-3.72 MLOGP:-2.77 SILICOS-IT:-5.08 Consensus logP O/W:-3.85
	IUPAC	4-{3,3,5-trimethyl-6-[2-phenoxyethyl)sulfanyl]-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}morpholine	
20	Ppd21.mol		iLOGP:- 1.23 XLOGP3:-0.79 WLOGP:-1.77 MLOGP:-0.23 SILICOS-IT:-1.61 Consensus logP O/W:-1.13
	IUPAC	2-{2-amino-5-methyl-4-[3-(nitromethyl)phenyl]-3-(2-oxoethyl)-2H,3H,4H-pyrano[2,3-c]pyridine-6-yl}acetaldehyde	
21	Ppd22.mol		iLOGP:- 1.12 XLOGP3:-3.91 WLOGP:-1.40 MLOGP:-3.19 SILICOS-IT:-3.26 Consensus logP O/W:-2.57
	IUPAC	7-methyl-5-[3-(pyrrolidine-1-yl)propoxy-8-(thiomorpholine-4-yl)-2H,3H,4H-8H-5-pyrano[2,3-b]pyridine-8-ylium	

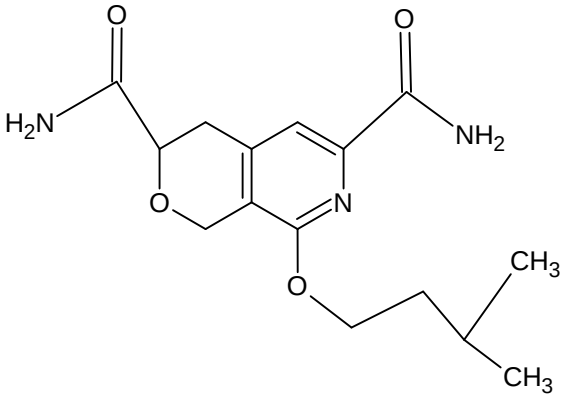
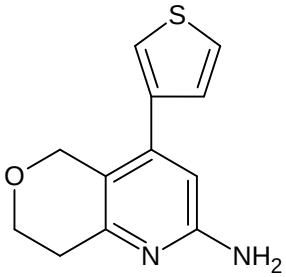
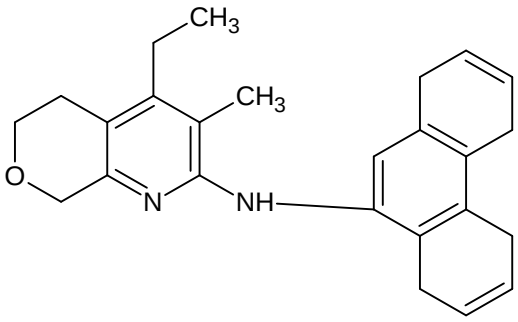
22	Ppd23.mol		iLOGP:- 4.29 XLOGP3:-5.81 WLOGP:-4.92 MLOGP:-3.88 SILICOS-IT:-6.03 Consensus logP O/W:-4.99
	IUPAC	(1-{3,3-dimethyl-6-[(2-phenylethyl)sulfanyl]-8-(piperidin-1-yl)-1H,3H,4H-pyrano[3,4-c]pyridine-5-yl}ethenyl)(methyl)amine	
23	Ppd24.mol		iLOGP:- 3.25 XLOGP3:-3.27 WLOGP:-3.30 MLOGP:-2.82 SILICOS-IT:-3.61 Consensus logP O/W:-3.25
	IUPAC	6-{3-[2-fluorocyclopentyl)methyl]pyrrolidine-1-yl}-5-methyl-1H,3H,4H-pyrano[3,4-c]pyridine-8-amine	
24	Ppd26.mol		iLOGP:- 2.46 XLOGP3:-5.71 WLOGP:-5.30 MLOGP:-3.85 SILICOS-IT:-4.72 Consensus logP O/W:-3.43
	IUPAC	4-(2-{[5-chloro-8-(2,6-dimethylmorpholin-4-yl)-3,3-dimethyl-2H,3H,4H-pyrano[2,3-c]pyridine-6-yl]sulfanyl}ethyl)-N-oxoanilinium	

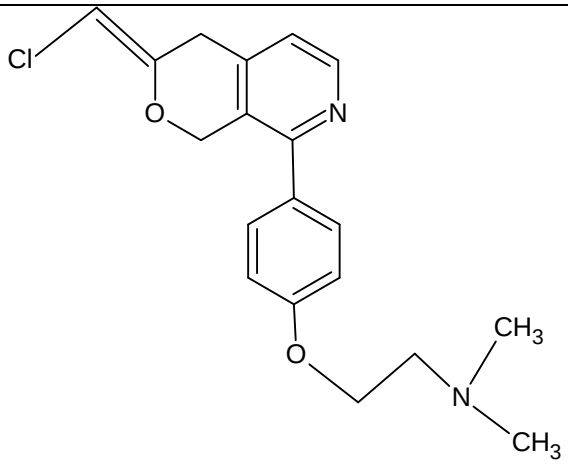
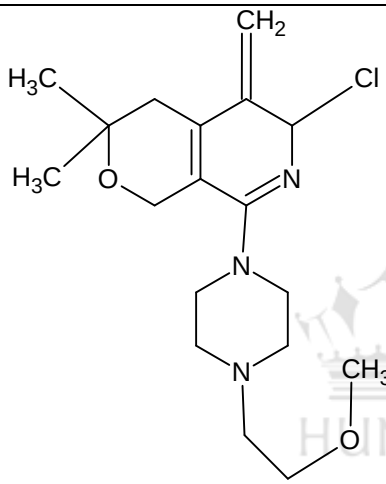
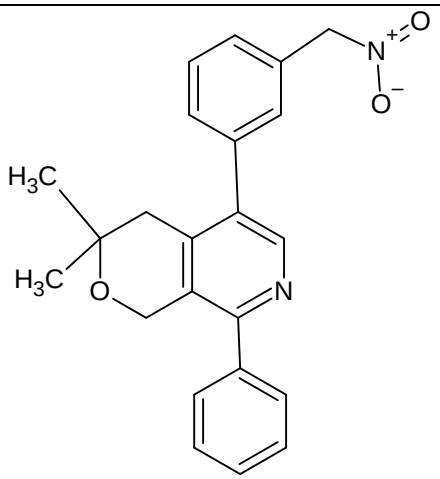
25	Ppd27.mol		iLOGP:-3.43 XLOGP3:-3.80 WLOGP:-3.96 MLOGP:-1.82 SILICOS-IT:-6.32 Consensus logP O/W:-3.87
	IUPAC	N-[3-chloro-6-ethyl-5-(hydroxymethyl)-4-(thiophen-3-yl)pyridine-2-yl]-2,3-dioxo-4-phenyl-2,3-dihydro-1H-pyrrole-1-carbothioamide	
26	Ppd28.mol		iLOGP:-3.36 XLOGP3:-3.28 WLOGP:-4.22 MLOGP:-2.80 SILICOS-IT:-4.37 Consensus logP O/W:-3.60
	IUPAC	4-[5-bromo-3,3-dimethyl-6-(2-phenylethanesulfinyl)-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]morpholine	
27	Ppd29.mol		iLOGP:-2.82 XLOGP3:-2.08 WLOGP:-2.50 MLOGP:-1.16 SILICOS-IT:-4.31 Consensus logP O/W:-2.57
	IUPAC	1-(1-{[3-methyl-4-(thiophen-2-yl)-5H,7H,8H-pyrano[4,3-b]pyridine-2-yl]amino}ethenyl)pyrrolidine-2,5-dione	

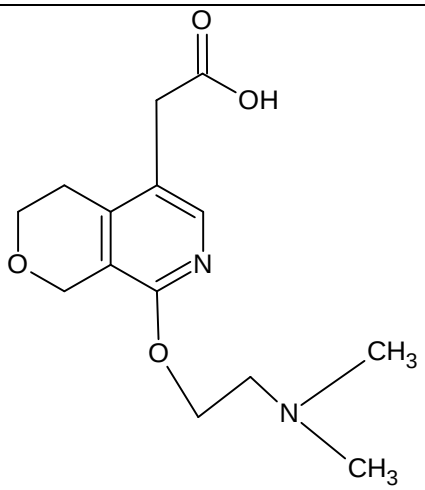
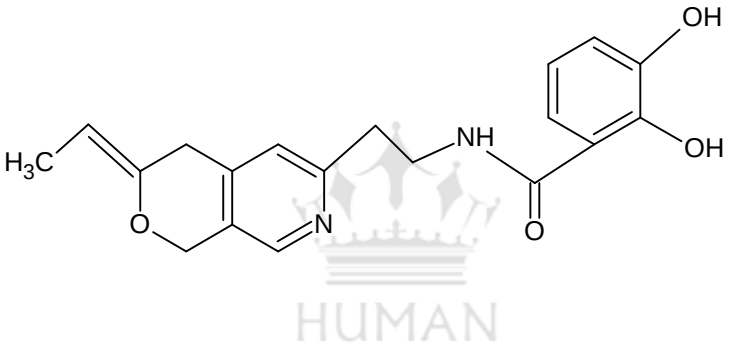
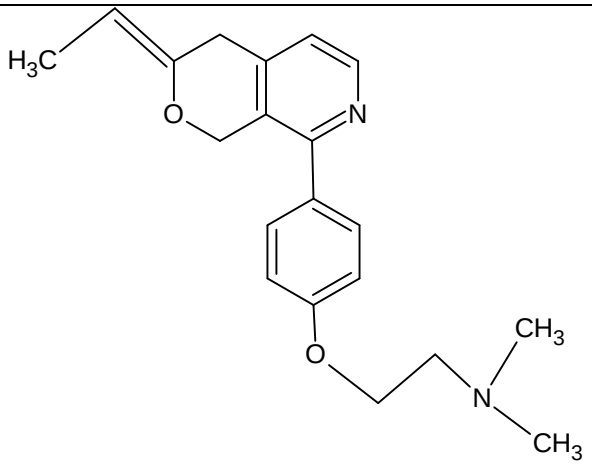
28	Ppd30.mol		iLOGP:-3.98 XLOGP3:-3.61 WLOGP:-3.69 MLOGP:-3.69 SILICOS-IT:-3.42 Consensus logP O/W:-3.68
	IUPAC	3-(6-{1’,2’,3’,4’,6’,7’a-hexahydrospiro[cyclohexane-1,7’-cyclopenta[c]pyridine]-2,4-dien-2’yl}-8-methyl-1H,3H,4H-pyrano[3,4-c]pyridine-3-yl)cyclobutan-1-amine	
29	Ppd31.mol		iLOGP:-2.85 XLOGP3:-3.49 WLOGP:-4.09 MLOGP:-2.78 SILICOS-IT:-5.69 Consensus logP O/W:-3.78
	IUPAC	1-[5-(3-chlorophenyl)-1H,3H,4H-pyrano[3,4-c]pyridine-6-yl]-3-methylbutan-2-one	
30	Ppd32.mol		iLOGP:-1.82 XLOGP3:-0.72 WLOGP:-1.56 MLOGP:-0.95 SILICOS-IT:-2.85 Consensus logP O/W:-1.58
	IUPAC	3-acetyl-8-(cyclopropylmethyl)-5-methyl-1H,3H,4H,5H,6H-pyrano[3,4-c]pyridine-6-carboxylic acid	

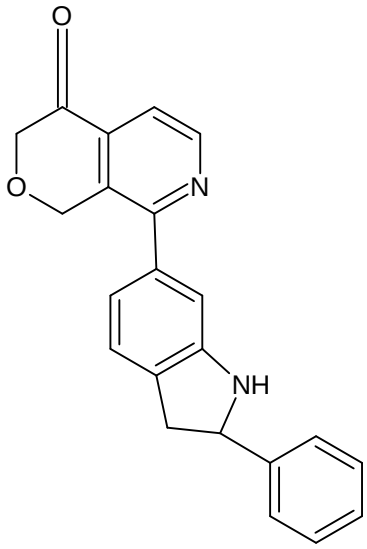
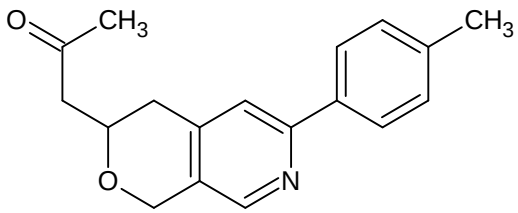
31	Ppd33.mol		iLOGP:-4.28 XLOGP3:-5.33 WLOGP:-4.72 MLOGP:-4.19 SILICOS-IT:-5.53 Consensus logP O/W:-4.81
	IUPAC	1-{3,3-dimethyl-6-[2-phenylethyl)sulfanyl]-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}-2-methylpyrroline	
32	Ppd34.mol		iLOGP:-3.95 XLOGP3:-3.63 WLOGP:-3.44 MLOGP:-2.87 SILICOS-IT:-5.46 Consensus logP O/W:-3.87
	IUPAC	2-(4-{5-methyl-6-[(2-phenylethyl)sulfanyl]-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl}piperidin-1-yl)ethan-1-ol	
33	Ppd35.mol		iLOGP:-3.71 XLOGP3:-0.59 WLOGP:-3.87 MLOGP:-2.51 SILICOS-IT:-4.74 Consensus logP O/W:-3.08
	IUPAC	4-[(4E)-8-(diethylamino)-6-{4-[(1,3-oxoazinan-3-yl)methyl]phenyl}-1H,3H,4H-pyrano[3,4-c]pyridine-4-	

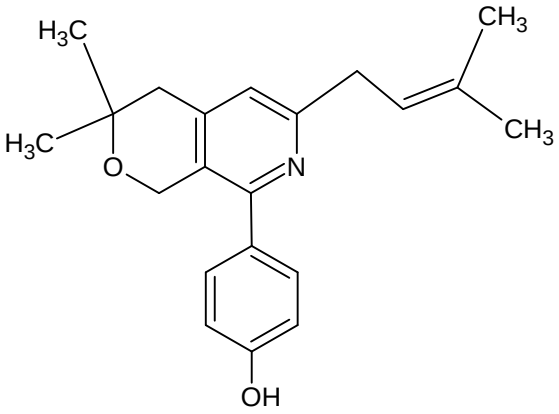
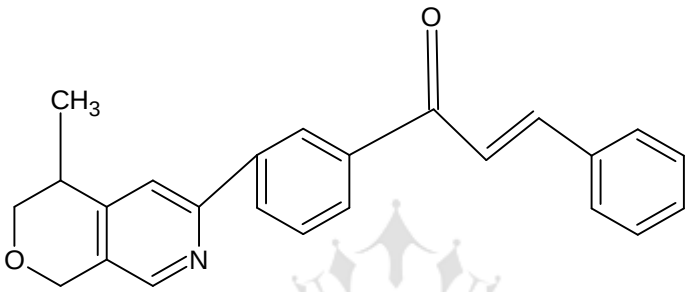
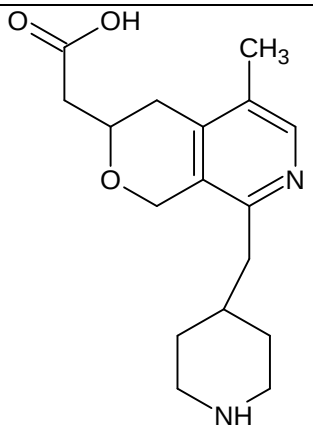
		yldiene]butanoic acid	
34	Ppd36.mol		iLOGP:-3.85 XLOGP3:-4.59 WLOGP:-4.98 MLOGP:-3.64 SILICOS-IT:-5.79 Consensus logP O/W:-4.57
	IUPAC	4-{3,3,5-trimethyl-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl}phenyl benzoate	
35	Ppd37.mol		iLOGP:-3.66 XLOGP3:-1.55 WLOGP:-1.47 MLOGP:-1.20 SILICOS-IT:-3.60 Consensus logP O/W:-2.30
	IUPAC	3-({8-[4-(2-methoxyethyl)piperazin-1-yl]-3,3-dimethyl-1H,3H,4H-pyrano[3,4-c]pyridine-6-yl}sulfanyl)propanal	
36	Ppd38.mol		iLOGP:-3.32 XLOGP3:-3.63 WLOGP:-3.56 MLOGP:-3.18 SILICOS-IT:-4.50 Consensus logP

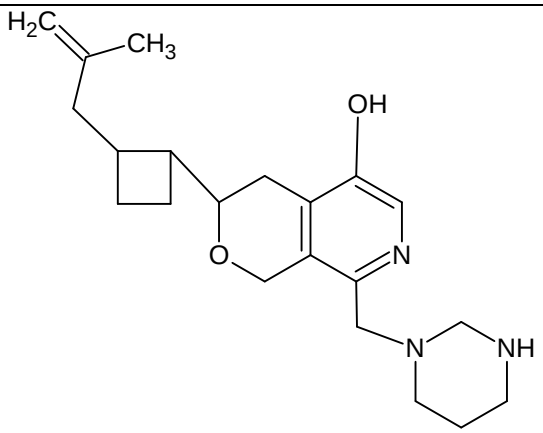
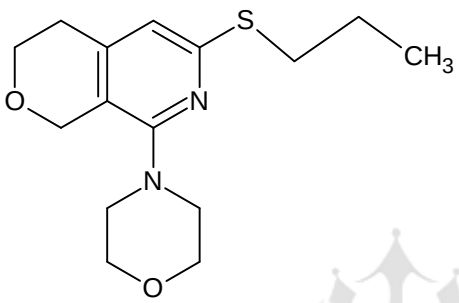
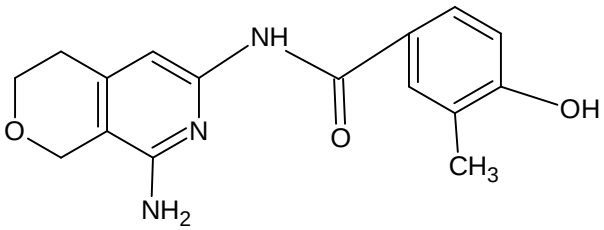
			O/W:-3.64
	IUPAC	4-(3-fluro-2-methylpropyl)-1-{8-methyl-1H,3H,4H-pyrano[3,4-c]pyridine-6-yl}piperidine	
37	Ppd39.mol		iLOGP:-2.09 XLOGP3:-0.72 WLOGP:-0.38 MLOGP:-0.06 SILICOS-IT:-1.42 Consensus logP O/W:-0.91
	IUPAC	8-(3-methylbutoxy)-1H,3H,4H-pyrano[3,4-c]pyridine-3,6-dicarboxamide	
38	Ppd40.mol		iLOGP:-2.13 XLOGP3:-1.53 WLOGP:-2.32 MLOGP:--1.32 SILICOS-IT:-3.68 Consensus logP O/W:-2.20
	IUPAC	4-(thiophen-3-yl)-5H,7H,8H-pyrano[4,3-b]pyridin-2-amine	
39	Ppd41.mol		iLOGP:-3.95 XLOGP3:-5.78 WLOGP:-4.93 MLOGP:-4.95 SILICOS-IT:-6.21 Consensus logP O/W:-5.06
	IUAPC	4-ethyl-3-methyl-N-(1,4,5,8-tetrahydrophenanthren-9-yl)-5H,6H,8H-pyrano[3,4-b]pyridine-2-amine	

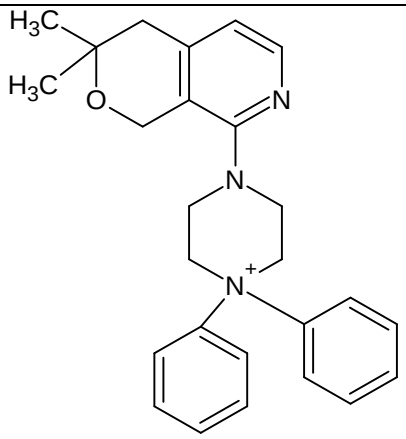
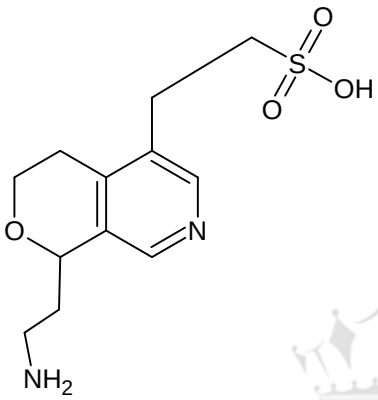
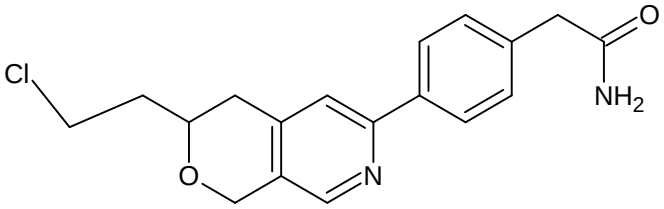
40	Ppd42.mol		iLOGP:-3.66 XLOGP3:-3.21 WLOGP:-3.69 MLOGP:-1.92 SILICOS-IT:-4.31 Consensus logP O/W:-3.36
	IUPAC	(2-{4-[(3Z)-3-(chloromethylidene)-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]phenoxy}ethyl)dimethylamine	
41	Ppd43.mol		iLOGP:-3.72 XLOGP3:-0.55 WLOGP:-1.14 MLOGP:-1.75 SILICOS-IT:-3.42 Consensus logP O/W:-2.12
	IUPAC	1-{6-chloro-3,3-dimethyl-5-methyldiene-1H,3H,4H,5H,6H-pyrano[3,4-c]pyridine-8-yl}-4-(2-methoxyethyl)piperazine	
42	Ppd44.mol		iLOGP:-2.80 XLOGP3:-4.21 WLOGP:-4.74 MLOGP:-2.54 SILICOS-IT:-4.02 Consensus logP O/W:-3.66
	IUPAC	3,3-dimethyl-5-[3-(nitromethyl)phenyl]-8-phenyl-1H,3H,4H-pyrano[3,4-c]pyridine	

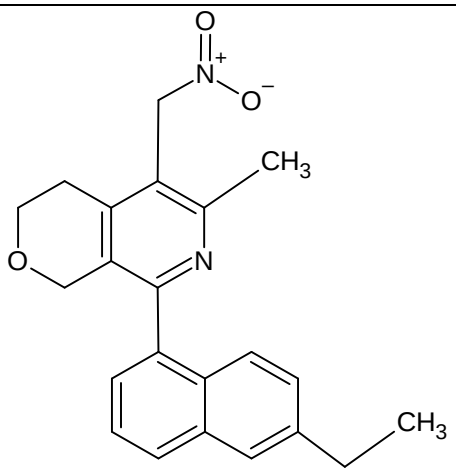
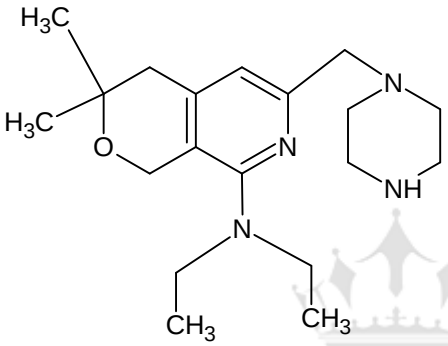
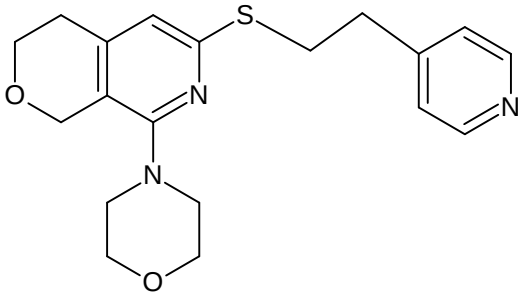
43	Ppd45.mol		iLOGP:-2.64 XLOGP3:--1.94 WLOGP:-0.57 MLOGP:-0.30 SILICOS-IT:-1.79 Consensus logP O/W:-0.67
	IUPAC	2-{8-[2-(dimethylamino)ethoxy]-1H,3H,4H-pyrano[3,4-c]pyridine-5-yl}acetic acid	
44	Ppd46.mol		iLOGP:-2.99 XLOGP3:-2.60 WLOGP:-2.29 MLOGP:-0.92 SILICOS-IT:-3.16 Consensus logP O/W:-2.39
	IUPAC	N-{2-[(3Z)-3-ethylidene-1H,3H,4H-pyrano[3,4-c]pyridine-6-yl]ethyl}-2,3-dihydroxybenzamide	
45	Ppd47.mol		iLOGP:-3.84 XLOGP3:-3.16 WLOGP:-3.51 MLOGP:-1.92 SILICOS-IT:-4.19 Consensus logP O/W:-3.33
	IUPAC	(2-{4-[(3Z)-3-ethylidene-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]phenoxy}ethyl)dimethylamine	

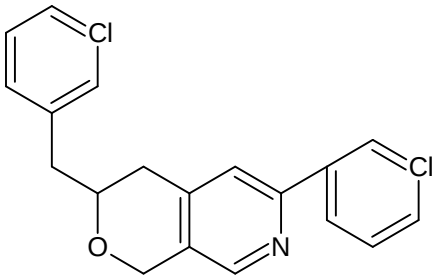
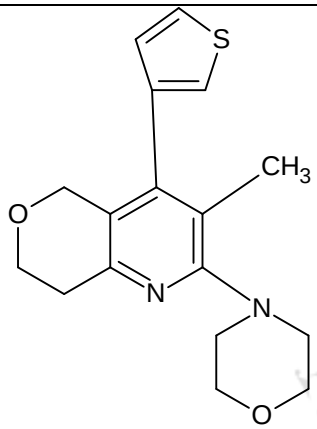
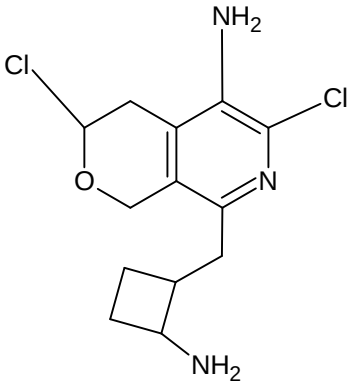
46	Ppd48.mol		iLOGP:-2.84 XLOGP3:-3.29 WLOGP:-3.12 MLOGP:-2.14 SILICOS-IT:-4.68 Consensus logP O/W:-3.21
	IUPAC	8-(2-phenyl-2,3-dihydro-1H-indol-6-yl)-1H,3H,4H-pyrano[3,4-c]pyridine-4-one	
47	Ppd49.mol		iLOGP:-2.70 XLOGP3:-2.28 WLOGP:-3.33 MLOGP:-2.05 SILICOS-IT:-4.57 Consensus logP O/W:-2.98
	IUPAC	1-[6-(4-methylphenyl)-1H,3H,4H-pyrano[3,4-c]pyridine-3-yl]propan-2-one	

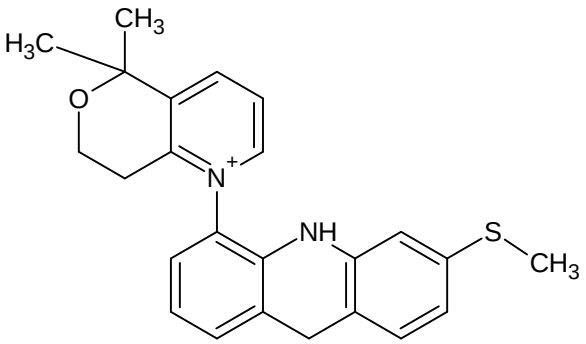
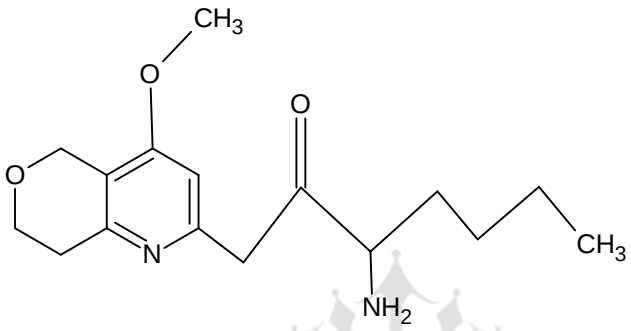
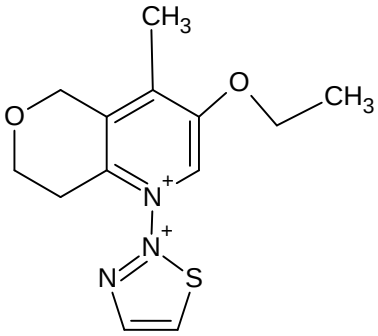
48	Ppd50.mol		iLOGP:-3.61 XLOGP3:-4.42 WLOGP:-4.66 MLOGP:-3.00 SILICOS-IT:-5.47 Consensus logP O/W:-4.23
	IUPAC	4-[3,3-dimethyl-6-(3-methylbut-2-en-1-yl)-1H,3H,4H-pyrano[3,4-c]pyridine-8-yl]phenol	
49	Ppd51.mol		iLOGP:-3.51 XLOGP3:-4.30 WLOGP:-5.02 MLOGP:-3.08 SILICOS-IT:-5.85 Consensus logP O/W:-4.35
	IUPAC	(2E)-1-(3-{4-methyl-1H,3H,4H-pyrano[3,4-c]pyridin-6-yl}phenyl)-3-phenylprop-2-en-1-one	
50	Ppd52.mol		iLOGP:-2.29 XLOGP3:--1.20 WLOGP:-1.32 MLOGP:-1.19 SILICOS-IT:-3.09 Consensus logP O/W:-1.33
	IUPAC	2-{5-methyl-8-[(piperidin-4-yl)methyl]-1H,3H,4H-pyrano[3,4-c]pyridin-3-yl}acetic acid	

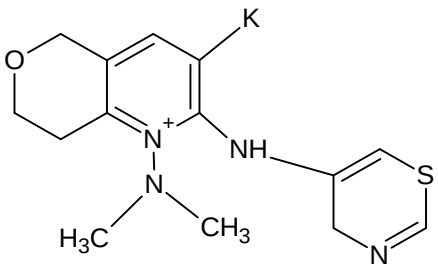
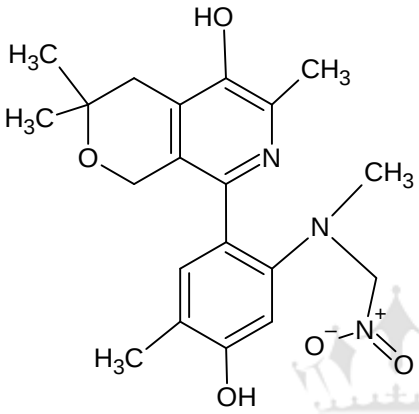
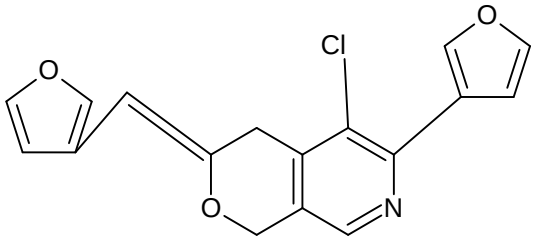
51	Ppd53.mol		iLOGP:-3.16 XLOGP3:-2.83 WLOGP:-1.91 MLOGP:-1.97 SILICOS-IT:-3.46 Consensus logP O/W:-2.66
	IUPAC	8-[(1,3-diazinan-1-yl)methyl]-3-[2-(2-methylprop-2-en-1-yl)cyclobutyl]-1H,3H,4H-pyrano[3,4-c]pyridin-5-ol	
52	Ppd54.mol		iLOGP:-3.21 XLOGP3:-2.36 WLOGP:-1.96 MLOGP:-1.75 SILICOS-IT:-340 Consensus logP O/W:-2.53
	IUPAC	4-[6-(propylsulfanyl)-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl]morpholine	
53	Ppd55.mol		iLOGP:-1.73 XLOGP3:-1.37 WLOGP:-1.67 MLOGP:-1.36 SILICOS-IT:-2.09 Consensus logP O/W:-1.65
	IUPAC	N-{8-amino-1H,3H,4H-pyrano[3,4-c]pyridin-6-yl}-4-hydroxy-3-methylbenzamide	

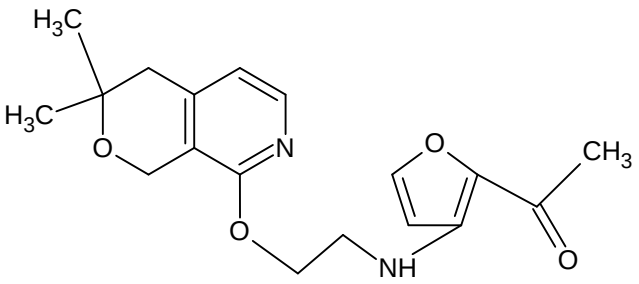
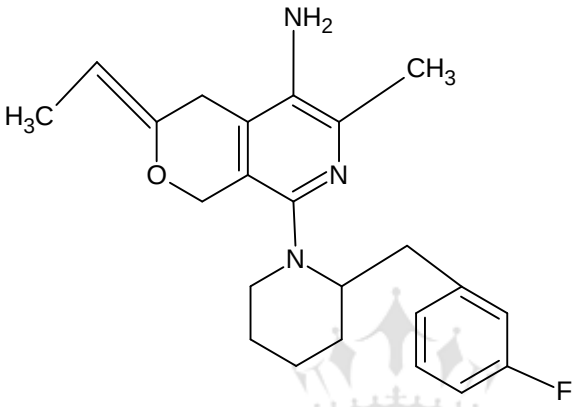
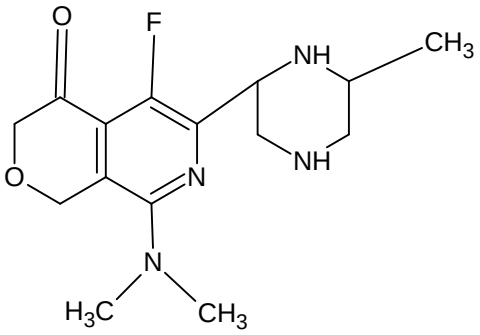
54	Ppd56.mol		iLOGP:-1.11 XLOGP3:-4.55 WLOGP:-4.18 MLOGP:-0.31 SILICOS-IT:-4.36 Consensus logP O/W:-2.90
	IUPAC	4-{3,3-dimethyl-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl}-1,1-diphenyl-1?^5-piperazin-1-ylium	
55	Ppd57.mol		iLOGP:--0.20 XLOGP3:--3.15 WLOGP:-1.23 MLOGP:--0.18 SILICOS-IT:--0.77 Consensus logP O/W:--0.31
	IUPAC	2-[1-(2-aminoethyl)-1H,3H,4H-pyrano[3,4-c]pyridin-5-yl]ethane-1-sulfonic acid	
56	Ppd58.mol		iLOGP:-2.41 XLOGP3:-2.03 WLOGP:-2.69 MLOGP:-1.83 SILICOS-IT:-4.21 Consensus logP O/W:-2.63
	IUPAC	2-{4-[3-(2-chloroethyl)-1H,3H,4H-pyrano[3,4-c]pyridin-6-yl]phenyl}acetamide	

57	Ppd59.mol		iLOGP:-3.11 XLOGP3:-4.41 WLOGP:-4.32 MLOGP:-2.36 SILICOS-IT:-4.30 Consensus logP O/W:-3.70
	IUPAC	8-(6-ethylnaphthalen-1-yl)-6-methyl-5-(nitromethyl)-1H,3H,4H-pyrano[3,4-c]pyridine	
58	Ppd60.mol		iLOGP:-3.60 XLOGP3:-1.56 WLOGP:-1.12 MLOGP:-1.61 SILICOS-IT:-3.08 Consensus logP O/W:-2.19
	IUPAC	N,N-diethyl-3,3-dimethyl-6-[(piperazin-1-yl)methyl]-1H,3H,4H-pyrano[3,4-c]pyridin-8-amine	
59	Ppd61.mol		iLOGP:-3.14 XLOGP3:-2.35 WLOGP:-2.19 MLOGP:-1.62 SILICOS-IT:-3.88 Consensus logP O/W:-2.63
	IUPAC	4-(6-{[2-(pyridin-4-yl)ethyl]sulfanyl}-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl)morpholine	

60	Ppd62.mol		iLOGP:-0.00 XLOGP3:-4.40 WLOGP:-4.28 MLOGP:-3.46 SILICOS-IT:-4.69 Consensus logP O/W:-3.37
	IUPAC	3-{3-[(1?^3-chlorinin-3-yl)methyl]-1H,3H,4H-pyrano[3,4-c]pyridin-6-yl}-1?^3-chlorinine	
61	Ppd63.mol		iLOGP:-3.16 XLOGP3:-2.33 WLOGP:-2.50 MLOGP:-1.75 SILICOS-IT:-4.77 Consensus logP O/W:-2.90
	IUPAC	4-[3-methyl-4-(thiophen-3-yl)-5H,7H,8H-pyrano[4,3-b]pyridin-2-yl]morpholine	
62	Ppd64.mol		iLOGP:-2.21 XLOGP3:-1.74 WLOGP:-2.09 MLOGP:-1.34 SILICOS-IT:-2.68 Consensus logP O/W:-2.01
	IUPAC	8-[(2-aminocyclobutyl)methyl]-3,6-dichloro-1H,3H,4H-pyrano[3,4-c]pyridin-5-amine	

63	Ppd65.mol		iLOGP:-0.52 XLOGP3:-5.01 WLOGP:-4.65 MLOGP:-4.29 SILICOS-IT:-5.30 Consensus logP O/W:-3.96
	IUPAC	5,5-dimethyl-1-[6-(methylsulfanyl)-9,10-dihydroacridin-4-yl]-5H,7H,8H-1?^5-pyrano[4,3-b]pyridin-1-ylium	
64	Ppd66.mol		iLOGP:-3.16 XLOGP3:-1.12 WLOGP:-1.64 MLOGP:-0.40 SILICOS-IT:-3.37 Consensus logP O/W:-1.94
	IUPAC	3-amino-1-{4-methoxy-5H,7H,8H-pyrano[4,3-b]pyridin-2-yl}heptan-2-one	
65	Ppd67.mol		iLOGP:--11.28 XLOGP3:-3.28 WLOGP:-0.66 MLOGP:-1.67 SILICOS-IT:-3.37 Consensus logP O/W:--0.63
	IUPAC	2-{3-ethoxy-4-methyl-5H,7H,8H-1?^5-pyrano[4,3-b]pyridin-1-ylium-1-yl}-1,2?^5,3-thiadiazol-2-ylium	

66	Ppd68.mol		iLOGP:-0.00 XLOGP3:-1.53 WLOGP:-0.35 MLOGP:-1.30 SILICOS-IT:-0.45 Consensus logP O/W:-0.72
	IUPAC	1-(dimethylamino)-3-potassio-2-[(4H-1,3-thiazin-5-yl)amino]-5H,7H,8H-pyrano[4,3-b]pyridin-1-ium	
67	Ppd69.mol		iLOGP:-2.32 XLOGP3:-2.89 WLOGP:-3.15 MLOGP:-1.33 SILICOS-IT:-1.69 ConsensuslogP O/W:-2.27
	IUPAC	8-{4-hydroxy-5-methyl-2-[methyl(nitromethyl)amino]phenyl}-3,3,6-trimethyl-1H,3H,4H-pyrano[3,4-c]pyridin-5-ol	
68	Ppd70.mol		iLOGP:-3.12 XLOGP3:-3.17 WLOGP:-4.44 MLOGP:-1.31 SILICOS-IT:-4.73 Consensus logP O/W:-3.35
	IUPAC	(3Z)-5-chloro-6-(furan-3-yl)-3-[(furan-3-yl)methylidene]-1H,3H,4H-pyrano[3,4-c]pyridine	

69	Ppd71.mol		iLOGP:-3.24 XLOGP3:-2.77 WLOGP:-2.88 MLOGP:-0.54 SILICOS-IT:-4.73 Consensus logP O/W:-2.60
	IUPAC	1-(3-{[2-({3,3-dimethyl-1H,3H,4H-pyrano[3,4-c]pyridin-8-yl}oxy)ethyl]amino}furan-2-yl)ethan-1-one	
70	Ppd72.mol		iLOGP:-3.48 XLOGP3:-4.63 WLOGP:-4.58 MLOGP:-3.63 SILICOS-IT:-4.97 Consensus logP O/W:-4.26
	IUPAC	(3Z)-3-ethylidene-8-{2-[(3-fluorophenyl)methyl]piperidin-1-yl}-6-methyl-1H,3H,4H-pyrano[3,4-c]pyridin-5-amine	
71	Ppd73.mol		iLOGP:-2.48 XLOGP3:--0.14 WLOGP:--0.20 MLOGP:-0.14 SILICOS-IT:-1.73 Consensus logP O/W:-0.80
	IUPAC	8-(dimethylamino)-5-fluoro-6-(6-methylpiperazin-2-yl)-1H,3H,4H-pyrano[3,4-c]pyridin-4-one	

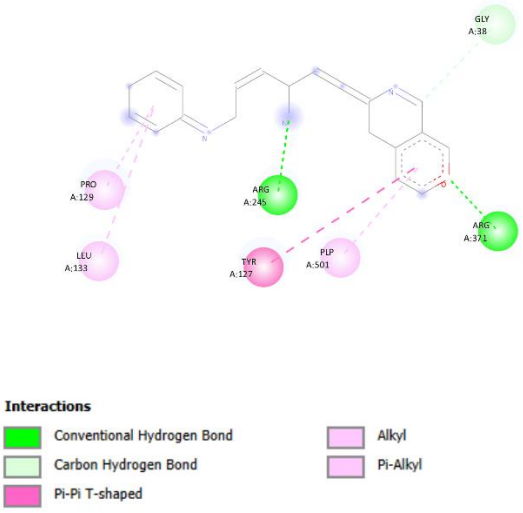


FIGURE 9: - Amino Acid interactions of pyranopyridine derivates with the protein 1Xi9

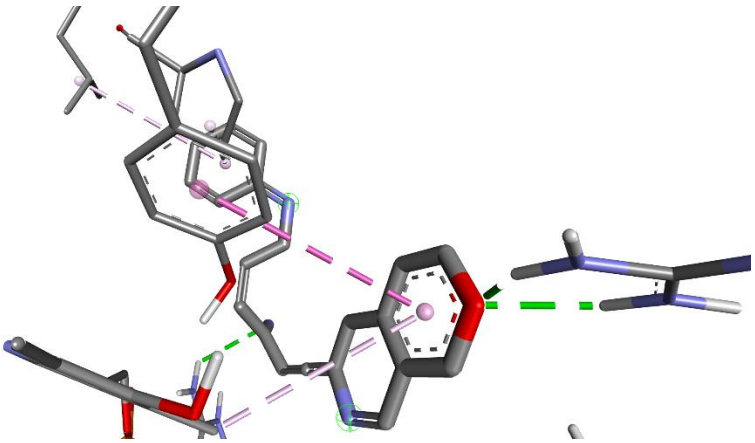


FIGURE 10: - Amino Acid interactions of pyranopyridine derivates with the protein 1Xi9

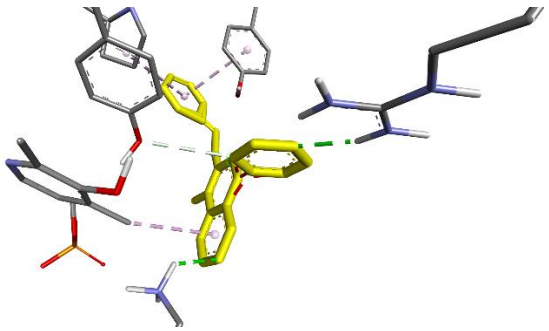


FIGURE 11: - Amino Acid interactions of pyranopyridine derivates with the protein 1Xi9

5.2 Amino acids interacted, and several H-bonds formed with different classes of pyranopyridine derivates: -

FILE NAME	PROTEIN NAME	NO. OF HYDROGEN BONDS	AMINO ACID INTERACTED
P2	1xi9	3H	ARG245, TYR13, THR103, PRO129, LEU133
P3	1xi9	1H	ASP39, ILE37, TYR328
P4	1xi9	4H	ARG245, ARG371, ARG371, GLY38, TYR127, PRO129, LEU133, PLP501
P5	1xi9	3H	LYS237, ARG371, TYR127, PRO129,TYR13, PLP501
P6	1xi9	4H	ASN177, LYS237, ARG371, PLP501, ARG371, ILE37
P7	1xi9	4H	LYS237, LYS237, ARG371, TYR127
P8	1xi9	8H	ARG245, THR103, LYS237, LYS237, PLP501, GLY38, PLP501, TYR13, PLP501
P9	1xi9	2H	TYR13, TYR127, TYR127, PLP501, PRO129
P10	1xi9	6H	GLY38, ASN177, ARG245, TYR328, ARG371, THR103, LYS237, PRO128, VAL357, TYR13, PHE362, PLP501, PLP501
P11	1xi9	5H	GLY38, TYR328, ARG371, ARG371, GLY38, ILE37, ILE37
P12	1xi9	4H	ASN177, TYR328, ARG371, ARG371, TYR127, PRO128, VAL357, PLP501, TYR13, PHE362
P13	1xi9	6H	ASN177, ARG245, ARG371, THR103, PLP501, TYR13, TYR127, PRO129, LEU133, PLP501
P14	1xi9	3H	TYR13, LYS237, LYS237, TYR13, TYR13, TYR13, PRO129, PLP501
P15	1xi9	8H	ASN177, ARG245, ARG245, TYR328,

			ARG371, THR103, GLY38, PLP501
P16	1xi9	8H	ASP39, GLY38, ARG245, ARG371, TYR127, THR103, ILE37, ASP39, ASN36, PLP501
P17	1xi9	3H	PLP501, THR103, ARG245, PLP501,TYR13, PLP501
P18	1xi9	9H	PLP501, TYR13, ASN177, LYS237, LYS237, TYR328, TYR328, ARG371, ARG371, GLY38, TYR127, TYR13, TYR13, PLP501
P19	1xi9	4H	ARG371, ARG371, TYR127, TYR127, LYS237, PLP501
P20	1xi9	2H	PLP501, TYR13, TYR127, TYR13, TYR127PRO128, VAL357, TYR13, PHE362, PRO129
P21	1xi9	6H	ASN177, ARG245, TYR328, TYR127, THR242, GLY38, ARG245
P22	1xi9	3H	THR103, PRO129, PLP501, ARG245, PRO129, LEU133
P23	1xi9	3H	THR103, TYR127, PLP501, ARG245, ARG371, ILE37
P24	1xi9	3H	GLY38, TYR127, TYR13, LYS237, PRO129, TYR13, PLP501, PLP501, PRO129
P26	1xi9	3H	THR103, TYR13, TYR13, PRO129, LEU133, TYR13
P27	1xi9	3H	TYR127,GLY38, TYR13, LEU133, PLP501, PLP501, VAL11
P28	1xi9	6H	ASP39, THR103, ARG371, TYR127, PLP501, ASP39, TYR127, PRO129, TYR13
P29	1xi9	4H	LYS237, LYS237, TYR13, GLY38, TYR13, TYR13, PRO129, LEU133, PLP501
P30	1xi9	5H	GLY38, TYR328, ARG371, ARG371, THR103, PLP501, TYR13, TYR127, VAL11, TYR13, TYR13
P31	1xi9	4H	LYS237, ARG371, ARG371, GLY38, PLP501,

			TYR127, PRO129, PLP501
P32	1xi9	11H	GLY38, GLY38, THR103, ASN177, ARG245, TYR328, ARG371, ARG371,LYS237, PLP501, PLP501
P33	1xi9	2H	TYR13, TYR127, TYR127, TYR13, PHE362, TYR13, PLP501, PRO128, VAL357, PRO129
P34	1xi9	5H	ASN177, TYR328, ARG371, THR242, TYR127, LYS237, ARG245, ARG245, PRO129, TYR13, PLP501
P35	1xi9	5H	GLY38, ASN177, TYR328, ARG371, ARG371
P36	1xi9	5H	ASP39, GLY38, TYR328, ARG371, ARG371THR242, ARG371, TYR13, PLP501, PRO128
P37	1xi9	6H	LYS237, LYS237, TYR13, TYR127, PLP501,,TYR13, TYR13, PRO129, PRO129
P38	1xi9	2H	THR103, THR242, ASP39, TYR13, TYR13, PLP501, PRO129, PRO129
P39	1xi9	13H	GLY38, THR103,ASN177, LYS237, TYR328, ARG371, ARG371, PLP501, TYR13, PLP501:C4A, PLP501:C4A
P40	1xi9	3H	LYS237, ARG371, ARG371, TYR127, PLP501, PLP501
P41	1xi9	3H	LYS237, LYS237, GLY38, TYR13, ILE37, PLP501, PRO129, PRO129, LEU133
P42	1xi9	5H	LYS237, ARG371, ARG371, GLY38, TYR13, PHE362, ILE37, PLP501, PLP501
P43	1xi9	4H	LYS237, GLY38, TYR13, TYR127, TYR13, TYR13, TYR13, PRO129
P44	1xi9	4H	PLP501, TYR13, ARG371, ARG371THR103, PLP501
P45	1xi9	5H	GLY38, ASN177, TYR328, ARG371, ARG371, LYS237, LYS237, PLP501, PLP501

P46	1xi9	7H	GLY38, ASN177, TYR328, ARG371, ARG371, ARG371, ASN36, TYR13, TYR13 ,VAL11, LEU133
P47	1xi9	5H	LYS237, ARG371, ARG371, PLP501, TYR13, PHE362, GLY38, GLY38, PLP501, PLP501
P48	1xi9	4H	LYS237, ASP39, THR242, ARG371, TYR13, TYR13, PHE362 ,PLP501, PRO128, PRO128, VAL357
P49	1xi9	5H	LYS237, ARG245, ARG371, ARG371, GLY38, PLP501, PRO128, VAL357, PHE362, PRO128, VAL357
P50	1xi9	4H	GLY38, TYR328, ARG371, ARG371, TYR127, PRO129, TYR13, PLP501, PLP501
P51	1xi9	5H	LYS237, LYS237, PRO129, PLP501, PLP501, PLP501, TYR13, PRO129
P52	1xi9	6H	TYR13, GLY38, LYS237, TYR328, GLY38, PLP501, PLP501, PRO129, LEU133
P53	1xi9	5H	LYS237, TYR328, GLY38, ASP39, ASP39, PRO128, VAL357, PRO128, TYR13, TYR13, TYR13, PHE362 ,PLP501
P54	1xi9	3H	LYS237, LYS237, ARG371, PLP501, PRO129, PLP501, PLP501
P55	1xi9	8H	GLY38, THR103, ASN177, TYR328, ARG371, ARG371, TYR127, TYR13, PRO129, PRO129, PLP501
P56	1xi9	2H	PLP501, THR103, TYR13, TYR13, PLP501, PRO129
P57	1xi9	10H	LYS237, ARG371, ASN177, LYS237, TYR328, TYR328, ARG371, ARG371, PLP501, GLY243, GLY38, ASP39, ASP39, TYR127
P58	1xi9	4H	LYS237, ARG371, GLY243, ARG245, TYR127,

			VAL357, PHE362, PLP501
P59	1xi9	4H	GLY38, ASN177, ARG371, ARG371, PLP501, PLP501, PRO129
P60	1xi9	2H	TYR127, THR242, TYR13
P61	1xi9	5H	ASN177, LYS237, LYS237, GLY38, PLP501, ARG371, TYR13, TYR127, PLP501, PLP501, PRO128, VAL357
P62	1xi9	2H	TYR328, GLY38, TYR13, TYR127, PLP501, PRO128
P63	1xi9	4H	ASN177, TYR127, THR103, PLP501 PLP501
P64	1xi9	3H	LYS237, ARG245, THR103, PLP501, PRO129, PLP501
P65	1xi9	2H	ARG371, ARG371, TYR127, PHE362, TYR13, TYR127, PRO128, TYR13, TYR13, TYR127, PHE362, PRO129, PLP501, PLP501,PLP501
P66	1xi9	5H	GLY38, TYR328, ARG371, ARG371, TYR127, LYS237, TYR13, PLP501
P67	1xi9	3H	ARG371, ARG371, TYR13, PRO128, TYR127, PHE362, PLP501
P68	1xi9	3H	THR103, TYR13, GLY38, TYR127, PRO129
P69	1xi9	6H	ASN177, TYR328, ARG371, ARG371, ARG371, TYR13
P70	1xi9	3H	LYS237, LYS237, PLP501, ARG245, THR103, PRO129, LEU133, PLP501
P71	1xi9	4H	ASP39, LYS237, LYS237, GLY38, PLP501, THR242, PLP501
P72	1xi9	3H	GLY38, ARG371, ARG371, PRO129, PLP501
P73	1xi9	5H	LYS237, GLY38, ARG371, GLY38, LYS237 PLP501

6. ANALYSIS OF THE DOCKED RESULTS: -

The docking results that were predicted by AutoDock Vina revealed that hydrogen bonds were formed between the proteins and the inhibitors used. The finest compound which showed development towards a new drug was chosen concerning binding energy. On basis of the analysis made by Autodock Vina, the binding energies of the compound were approximately the same. Docking studies with AutoDock Vina showed that the novel synthetic pyranopyridine derivates showed the approvable readings. Based on these findings, these compounds can be further synthesized and studied further.

7. CONCLUSION: -

In this research paper, the novel classes of pyranopyridine derivates were docked to show via structure-based drug design. These compounds have been found to show marked binding activity which can lead to synthesis and pharmacological activity of pyranopyridine derivates as a drug. Nevertheless, Autodock Vina was comparatively more effective in blind docking pose prediction and steadily exceeded in comparison to other programs. Furthermore, the study of the docked ligands with the protein gathered the attention of a few main interactions running at the molecular level. To conclude, we have come across the finest powerful compound that will be conveniently useful for the outline of a novel nonpoisonous and extremely effective drug for the treatment.

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