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Exploring the Virtual Pharmacological Landscape of *Clematis zeylanica* (L.) Poir - An In Silico study

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Clematis zeylanica, Paromomycin, PIM-1 Kinase, RNA polymerase, Anti-cancer, Antibacterial.

Abstract
Clematis zeylanica, (L.) Poir. a climbing shrub is belongs to the family Ranunculaceae and is known for its significant medicinal properties in traditional medicine. It has been used to treat rheumatism, arthritis, inflammation, skin disease (eczema, dermatitis), wounds, ulcers, stock, blood pressure and tumour. GC-MS/MS investigation of the therapeutic potential of bioactive compounds derived from ethanolic extract of C. zeylanica, used for In Silico studies. Molecular docking is a computational method that predicts the interaction between a drug and a target protein, providing insights into the efficacy and mechanism of action of the compounds. In this study, various phytochemicals identified from C. zeylanica, were screened against key protein targets associated with conditions like cancer, and microbial infections. The docking results revealed that the binding energy between Paromomycin and RNA polymerase (RNAP), was 3.22 kcal/mol with a ligand Efficiency of 0.08 kcal/mol. There is 1 Hydrogen bond formed between Paromomycin and RNA polymerase (RNAP) and Paromomycin shows better binding affinity with the Drug Target PIM-1 Kinase. N-(O-Nitrophenylthio)-l-leucine shows better binding affinity with the Drug Target RNA polymerase (RNAP). Thus, it can be a better alternative for treating Cancer and bacterial infections. The findings from this molecular docking study provide a scientific basis for the traditional uses of C. zeylanica and underscore its potential for the development of novel therapeutic agents.

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INTRODUCTION

Cancer is the world's most complicated illness, as well as the largest cause of death (Torre et al., 2015). Higher rates of risk factors such as obesity, lack of exercise, smoking, and changed reproductive patterns caused by modernization and economic expansion are linked to an increase in cancer incidence in emerging and poor nations (Torre *et al*., 2015). Cancer has become a major health burden on society because the main therapies for the disease require expensive and dangerous procedures like surgery, chemotherapy, radiation therapy, and immunotherapy. Moreover, not all cancer patients will benefit from surgery, and cancer patients are still in danger from the side effects of radiation and cancer drugs (Rahman *et al*., 2022). So the global potential of medicinal plants is profoundly rooted in the fact that many people, around 70-90%, rely on herbal medicines as their primary form of healthcare. Medicinal plants have traditionally been significant sources of bioactive compounds such as phytochemicals, essential nutrients, minerals etc. that have been utilized to cure human illnesses (OMS, 2002; Robinson *et al*., 2011; Dorlo *et al*., 2015; Olokokudejo *et al*., 2008; Ladinfeli *et al*., 2022; Ralte *et al*., 2022).

In Silico research is a computer approach (software) for predicting ligand binding affinity to receptor proteins. It has the potential to be a tool for identifying molecular targets and for developing disease-specific novel medicines (Agu *et al*., 2023). Molecular docking is a cost-effective and efficient drug development and testing technique. This approach gives information on drug-receptor interactions, which may be used to anticipate how the medicine model will bind to the protein of interest. As a result, ligands are bound reliably at their binding sites. (Lee and Kim, 2019; Bharathi *et al*., 2014). Moloney murine leukemia virus-1 (PIM-1)'s Proviral integration site is a serine/threonine kinase that regulates a variety of cellular processes such as death, senescence, the cell cycle, drug resistance, and cell survival. Elevated levels of PIM-1 kinases have been linked to various cancer forms, including myeloid leukemia, breast cancer, and prostate cancer. PIM-1 is one of the key targets for anti-tumors due to its interactions with diverse proteins and connections to distinct signaling pathways (Tursynbay *et al*., 2016). Our previous studies identified phytochemicals in GC-MS/MS analysis (Felix *et al*., 2024) are used for docking for antibacterial and anti-cancerous activities.

Clematis zeylanica (L.) Poir. is a species of flowering plant in the family Ranunculaceae. It is commonly known as Sri Lanka clematis and is native to the Indian subcontinent, specifically found in countries such as India, Sri Lanka and Myanmar. *C. zeylanica* is a climbing vine that produces attractive white- or cream-coloured flowers with a pleasant fragrance. *C. zeylanica* has been used in the treatment of pitta, helminthiasis, dermatopathy, leprosy, rheumatalgia, odontalgia, colic inflammation, wounds, and ulcers in the Indian system of medicine Ayurveda and cancer, cardiac disease, inflammatory disease, and neurodegenerative diseases in the traditional Chinese medicine holds it in high respect (Ansari *et al*., 2021, Marclin *et al*., 2024). (Naika *et al*., 2008). In current cancer treatment (chemotherapy), synthetic compounds is used, which have various side effects, so researchers seeking natural based therapies as an alternative in cancer treatment (Rahman *et al*., 2022). So this therapeutic potential of *C. zeylanica*. – *In silico* studies may help to develop natural novel drug for cancer.

MATERIALS AND METHODS

The 2D structures of the substances were obtained in SMILES format from Pubchem (Kim *et al*., 2023). The Smiles format was converted to 3D structure PDB format using the online Smiles Translator tool. The Molsoft Online Software, available at https://molsoft.com/mprop/, was used to determine the Molecular Weight, Hydrogen Bond Donors, Hydrogen Bond Acceptors, and Log P, as well as the Lipinski parameters and Drug Likeness Score. The receptor used in the docking was obtained from the Protein Data Bank. The following technique was used to perform molecular docking of the identified receptor and synthesized ligands with

Autodock Tools (ADT) 1.5.6 (Morris *et al*., 2009).

Preparing files for receptors and ligands

Autodock uses both the receptor and the ligand in PDBQT format to determine their binding affinity. The atomic coordinates, partial charges, and atom kinds are all limited by the PDBQT format. Initially, the PDB receptor file acquired from Protein Databank was accessible in Autodock Workspace. The water molecules from the receptor data were deleted, and implied hydrogen atoms were inserted. Finally, partial charges were applied and the receptor file saved in PDBQT format. Similarly, Autodock obtained PDB ligand files and stored them in PDBQT format.

Preparing Grid and Dock Parameters files

The grid computation was performed using the Autogrid 4.2 program in ADT. The grip maps, measuring 60X60X60 with a spacing of 0.375 A^o, were centered on the ligand binding site. To run the Autogrid application, the grid parameters file was created by saving the ligand and receptor files in PDBQT format, as well as the grid maps. Following the autogrid computation, an autodock parameter file was generated, which included the receptor, ligand, and autodock parameter choices.

Docking

Docking was done using the Lamarckian Genetic Algorithm, with 10 independent runs per ligand and a starting population of 150 randomly inserted ligands on the receptor binding site. A maximum of $2.5X10^5$ energy assessments will be performed across $27X10^3$ generations, with a mutation rate of 0.02 and a cross-over rate of 0.80. For 6% of the population, the local-energy-minimization algorithm could only take 100 steps. To explore the conformational space of ligands, overall translation steps were set to 0.2 Å, while overall rotation and torsion rotation steps were set to 5. The autodock 4.0 software was run in ADT, and the docking scores were calculated using binding free energy energies in kcal/mol.

Molecular Interactions Visualization using PyMOL

PyMOL molecular visualization software was used to view the bound complex with the receptor and ligand (Schrodinger *et al*., 2020). PyMOL is an open-source molecular visualization system developed and maintained by Rosignoli and Paiardini (2022). PyMOL is a cross-platform molecular graphics application that has been widely used to visualize proteins, nucleic acids, tiny molecules, electron densities, surfaces, and trajectories in three dimensions (3D). It can also edit molecules, ray trace, and create videos.

Table 1: Lipinski Rule Parameters and Drug Likeness of the Compounds

SN	Compound	Smiles	Molecular Weight	H bond Donor	H Bond Acceptor	LogP	Lipinski Violation	Drug Likeness
1.	11,13-Dihydroxy-tetradec-5-ynoic acid, methyl ester	CC(CC(CCCCC#CCCCC(=O)OC)O)O	270.18	2	4	1.85	0	-0.88
2.	N-(O-Nitrophenylthio)-l-leucine	CC(C)CC(C(=O)O)NSC1=CC=CC=C1[N+](=O)[O-]	284.08	2	6	1.15	0	0.77
3.	Parthenolide	CC1=CCCC2(C(O2)C3C(CC1)C(=C)C(=O)O3)C	248.14	0	3	2.46	0	1.27

4.	5,7-Dodecadiyn-1,12-diol	C(CCO)CC#CC#CCCCCO	194.13	2	2	1.58	0	-1.05
5.	R-Limonene	CC(=C)C1CCC2(OC(C1)OO2)C	184.11	0	3	2.86	0	1.59
6.	Benzeneacetaldehyde, .alpha.-(hydroxyimino)-oxime	C1=CC=C(C=C1)C(=O)C=NO	149.05	1	3	1.44	0	1.50
7.	Paromomycin	C1C(C(C(C(C1N)OC2C(C(C(C(O2)CO)O)O)N)OC3C(C(C(O3)CO)OC4C(C(C(C(O4)CN)O)O)N)O)O)N	257.11	1	3	2.68	0	0.29
8.	4-(2,5-Dihydro-3-methoxyphenyl)butylamine	COC1=CCC=C(C1)CCCCN	181.15	2	2	1.34	0	0.66
9.	Nitrosothymol	CC1=CC(=C(C=C1N=O)C(C)C)O	179.09	1	3	2.78	0	1.04
10	Benzeneethanol, .alpha.,.alpha.-dimethyl-, acetate	CC(=O)OC(C)(C)CC1=CC=CC=C1	192.12	0	2	2.67	0	1.21
11	3-Acetamido-2-[2-methyl-1-propenyl]phenol	CC(=CC1=C(C=CC=C1O)NC(=O)C)C	205.11	2	2	2.24	0	0.12
12	(-)-Isolongifolol, acetate	CC(=O)OCC1C2CCC3C2C(CCCC31C)(C)C	264.21	0	2	3.96	0	0.64
13	Brefeldin A	CC1CCCC=CC2CC(CC2C(C=CC(=O)O1)O)O	280.17	2	4	2.32	0	0.71

The Lipinski rule was applied to the compounds to filter the Compounds which have Drug Like Properties. A Lipinski violation of 1 and a positive Drug Likeness Score was the criteria for the selection of the Compound for Docking. From the Table it is clear that all the compounds except 11,13-Dihydroxy-tetradec-5-ynoic acid, methyl ester and 5,7-Dodecadiyn-1,12-diol satisfy the criteria and chosen for Docking.

RESULTS AND DISCUSSIONS

Bacterial RNA polymerase (RNAP), the enzyme responsible for bacterial RNA synthesis, acts as a binding site for chemicals that block bacterial RNA production and kill bacteria (Srivastava *et al*., 2011). Thus the Phyto-compounds were docked against RNA polymerase (RNAP) whose structure in PDB format was retrieved from Protein Data Bank (4kbj).

The binding energy between N-(O-Nitrophenylthio)-l-leucine and RNA polymerase (RNAP), was -6.98 kcal/mol with a ligand Efficiency of -0.37 kcal/mol. 7.67 mM of N-(O-Nitrophenylthio)-l-leucine is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 4 Hydrogen bonds formed between N-(O-Nitrophenylthio)-l-leucine and RNA polymerase (RNAP). The binding energy between Parthenolide and RNA polymerase (RNAP), was -5.85 kcal/mol with a ligand Efficiency of -0.32 kcal/mol. 51.75 mM of Parthenolide is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 3 Hydrogen bonds

formed between Parthenolide and RNA polymerase (RNAP). The binding energy between R-Limonene and RNA polymerase (RNAP), was -4.89 kcal/mol with a ligand Efficiency of -0.38 kcal/mol. 259.29 mM of R-Limonene is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 2 Hydrogen bonds formed between R-Limonene and RNA polymerase (RNAP).

Table 2: Antibacterial Activity

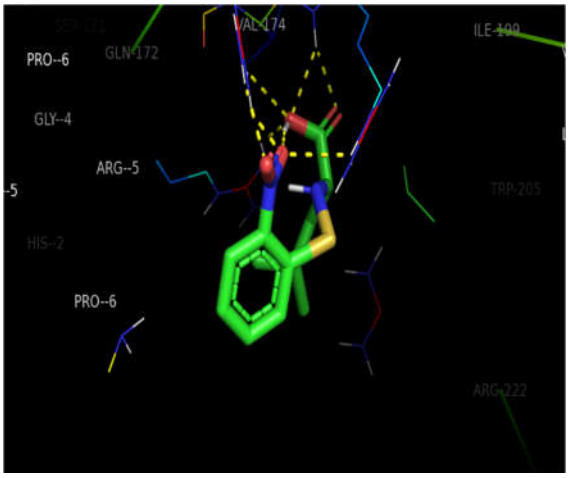
S. N.	Compound	Binding energy (KJ/mol)	Ligand efficiency (KJ/mol)	Inhibitory constant	No. of hydrogen bonds	Hydrogen bond
1.	N-(O-Nitrophenylthio)-l-leucine	-6.98	-0.37	7.67 mM	4	Arg 5:H12::Lig:O Arg 370:H22:Lig:O Arg 370:H12:Lig:O Arg 175:N::Lig:O
2.	Parthenolide	-5.85	-0.32	51.75 mM	3	His 2:N::Lig:O Met1:N::Lig:O Lig:O::Met1:O
3.	R-Limonene	-4.89	-0.38	259.29 mM	2	Lig:O::Leu173:O Arg370:H::Lig:O
4.	Benzeneacetaldehyde, .alpha.- (hydroxyimino)- oxime	-3.94	-0.36	1.3 mM	2	Lig:H::Leu173:O Arg370:H::Lig:N
5.	Paromomycin	3.22	0.08	-	1	Lig:H::Met1:O
6.	4-(2,5-Dihydro-3-methoxyphenyl)butylamine	-2.95	-0.23	6.91mM	1	Pro6:N::Lig:O
7.	Nitrosothymol	-4.84	-0.37	281.42µM	3	Arg175:H::Lig:O Arg370:H::Lig:O Lig:H::Asp365:O
8.	Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate	-4.11	-0.29	972.35 µM	1	Arg370:H::Lig:O
9.	3-Acetamido-2-[2-methyl-1-propenyl]phenol	-4.59	-0.31	434.88 µM	2	Lig:H::Asn369:O Arg175:H::Lig:O
10.	(-)-Isolongifolol, acetate	-5.58	-0.29	81.33 µM	1	Arg175:N::Lig:O
11.	Brefeldin A	-5.98	-0.3	41.7 µM	3	Lig:H::Leu173:O Arg175:H::Lig:O Lig:H::Pro6:O

The binding energy between Benzeneacetaldehyde,. alpha.- (hydroxyimino)-oxime and RNA polymerase (RNAP), was -3.94 kcal/mol with a ligand Efficiency of -0.36 kcal/mol. 1.3 mM of Benzeneacetaldehyde, .alpha.- (hydroxyimino)- oxime is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 2 Hydrogen bonds formed between Benzeneacetaldehyde,. alpha.- (hydroxyimino)-oxime and RNA polymerase (RNAP).

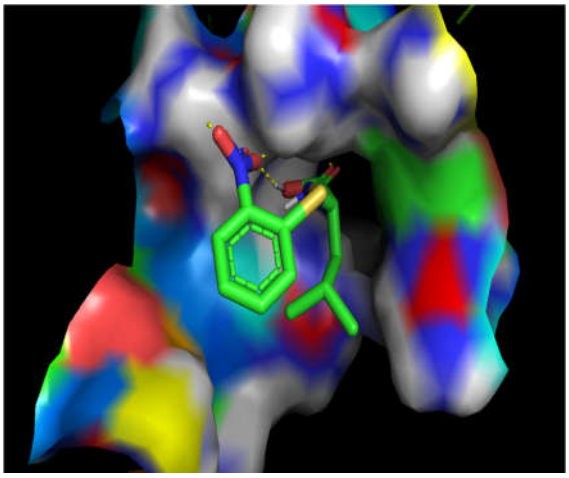
The binding energy between Paromomycin and RNA polymerase (RNAP), was 3.22 kcal/mol with a ligand Efficiency of 0.08 kcal/mol. There is 1 Hydrogen bond formed between Paromomycin and RNA polymerase (RNAP). The binding energy between 4-(2,5-Dihydro-3-

methoxyphenyl) butylamine and RNA polymerase (RNAP), was -2.95 kcal/mol with a ligand Efficiency of -0.23 kcal/mol. 6.91 mM of 4-(2,5-Dihydro-3-methoxyphenyl) butylamine is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There is 1 Hydrogen bond formed between 4-(2,5-Dihydro-3-methoxyphenyl) butylamine and RNA polymerase (RNAP). The binding energy between Nitrosothymol and RNA polymerase (RNAP), was -4.84 kcal/mol with a ligand Efficiency of -0.37 kcal/mol. 281.42µM of Nitrosothymol is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 3 Hydrogen bonds formed between Nitrosothymol and RNA polymerase (RNAP).

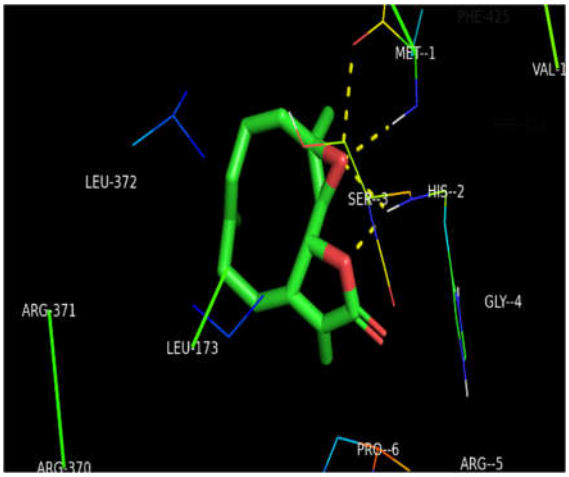
The binding energy between Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate and RNA polymerase (RNAP), was -4.11 kcal/mol with a ligand Efficiency of -0.29 kcal/mol. 972.35 µM of Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There is 1 Hydrogen bond formed between Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate and RNA polymerase (RNAP). The binding energy between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and RNA polymerase (RNAP), was -4.59 kcal/mol with a ligand Efficiency of -0.31 kcal/mol. 434.88 µM of 3-Acetamido-2-[2-methyl-1- propenyl]phenol is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 3 Hydrogen bonds formed between 3-Acetamido-2-[2-methyl-1- propenyl] phenol and RNA polymerase (RNAP). The binding energy between (-)-Isolongifolol, acetate and RNA polymerase (RNAP), was -5.58 kcal/mol with a ligand Efficiency of -0.29 kcal/mol. 81.33 µM of (-)-Isolongifolol, acetate is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There is 1 Hydrogen bond formed between (-)-Isolongifolol, acetate and RNA polymerase (RNAP). The binding energy between Brefeldin A and RNA polymerase (RNAP), was -5.98 kcal/mol with a ligand Efficiency of -0.3 kcal/mol. 41.7 µM of Brefeldin A is required to acquire half maximum Inhibition in RNA polymerase (RNAP) protein. There are 3 Hydrogen bonds formed between Brefeldin A and RNA polymerase (RNAP).



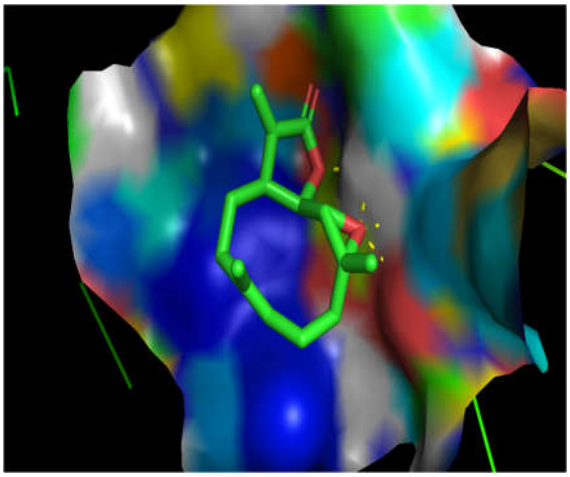
Docked conformation between N-(O-Nitrophenylthio)-l-leucine and RNA polymerase (RNAP)



Surface representation of Docked conformation between N-(O-Nitrophenylthio)-l-leucine and RNA polymerase (RNAP)



Docked conformation between Parthenolide and RNA polymerase (RNAP)



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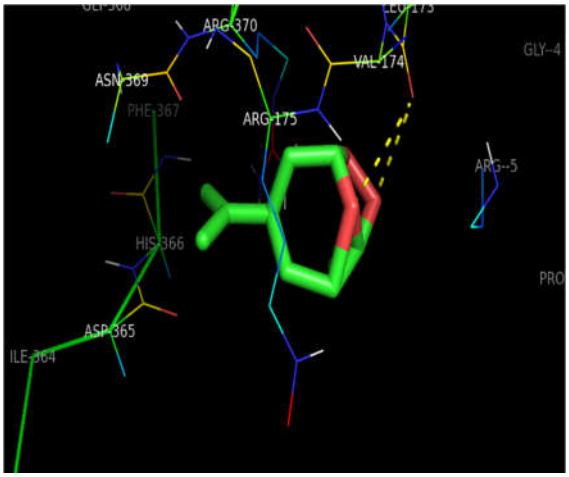
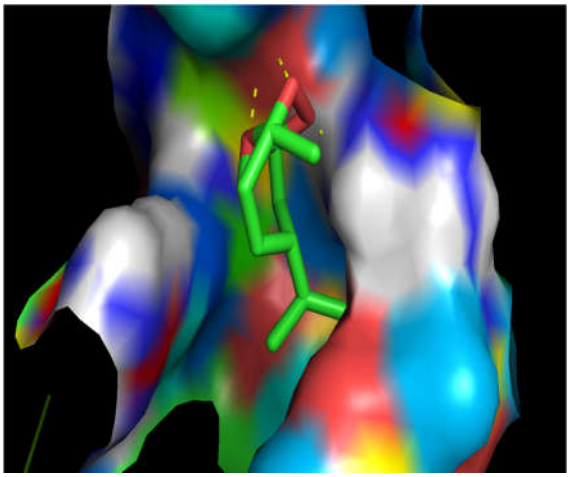
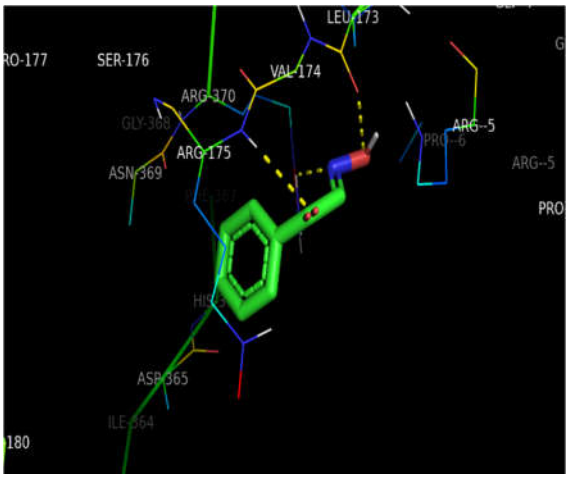


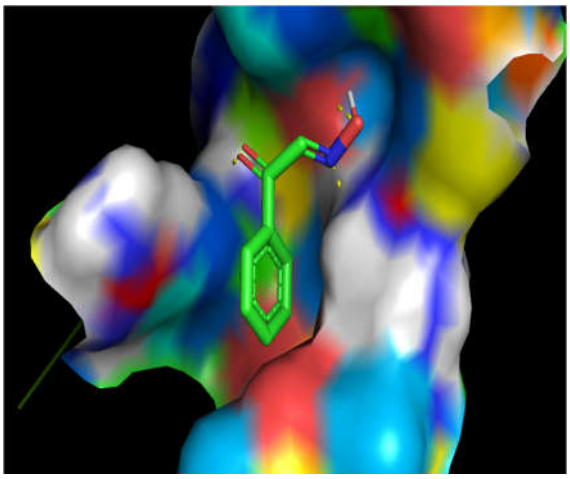
Docked conformation between R-Limonene and RNA polymerase (RNAP)



Surface representation of Docked conformation between R-Limonene and RNA polymerase (RNAP)



Docked conformation between Benzeneacetaldehyde, .alpha.- (hydroxyimino)- oxime and RNA polymerase (RNAP)



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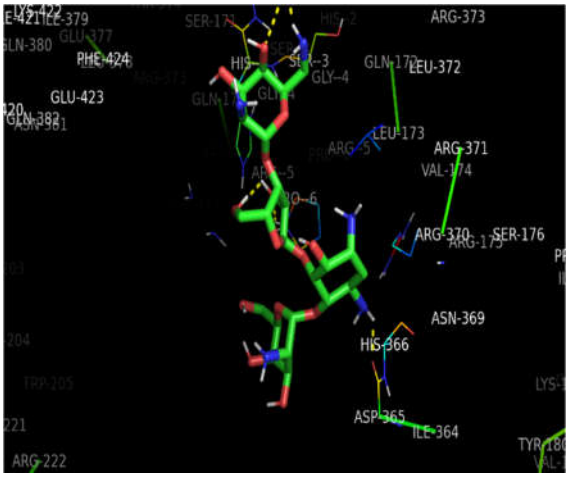
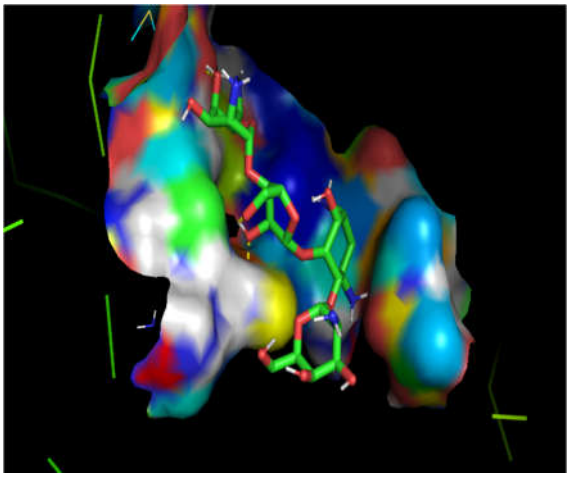
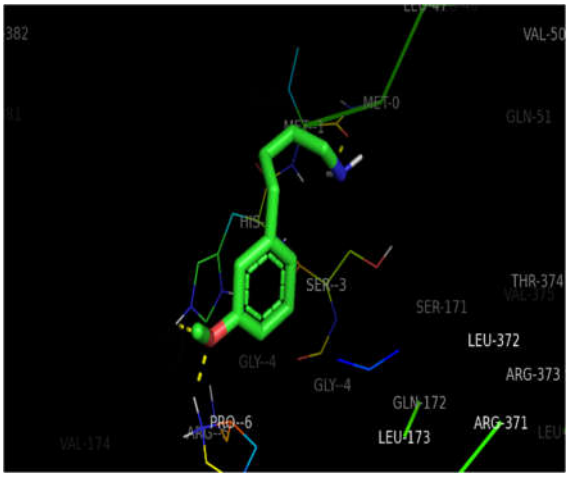


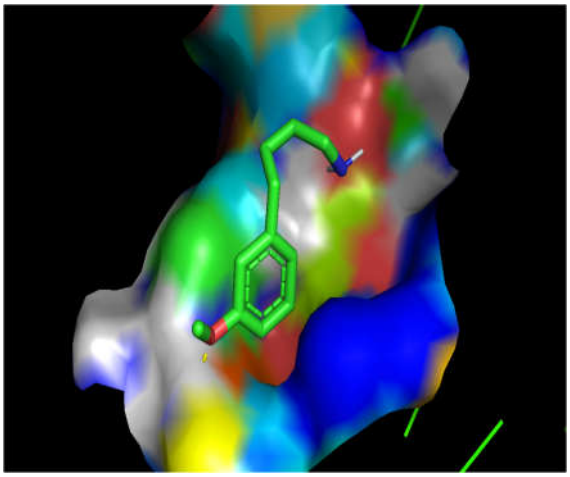
Docked conformation between Paromomycin and RNA polymerase (RNAP)



Surface representation of Docked conformation between Paromomycin and RNA polymerase (RNAP)



Docked conformation between 4-(2,5-Dihydro-3-methoxyphenyl)butylamine and RNA polymerase (RNAP)



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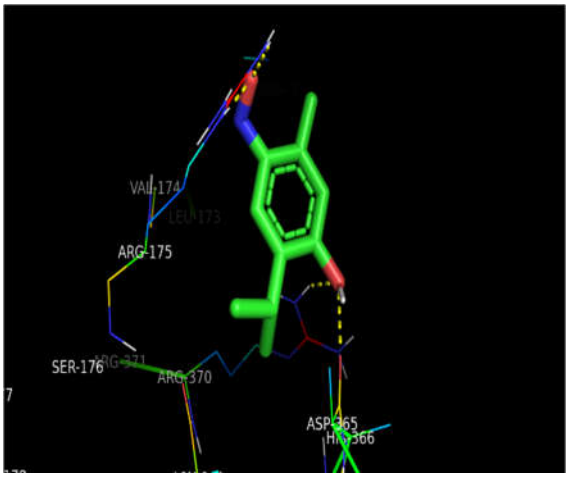
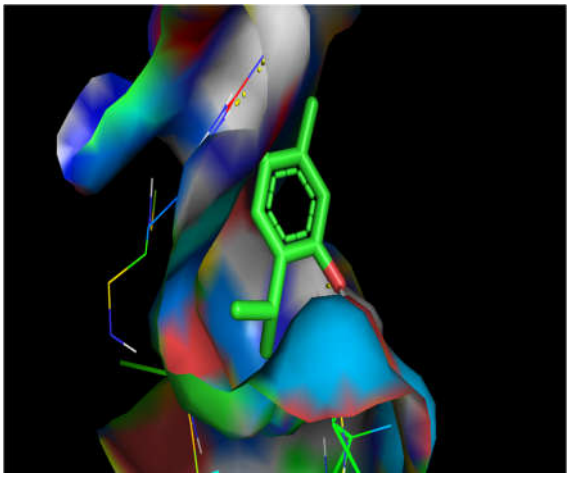


Docked conformation between Nitrosothymol and RNA polymerase (RNAP)



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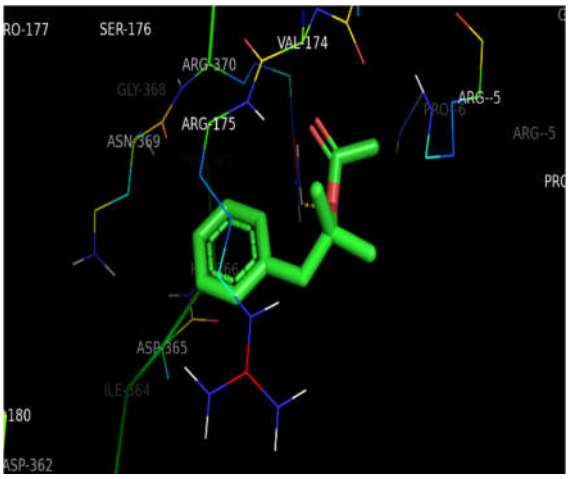
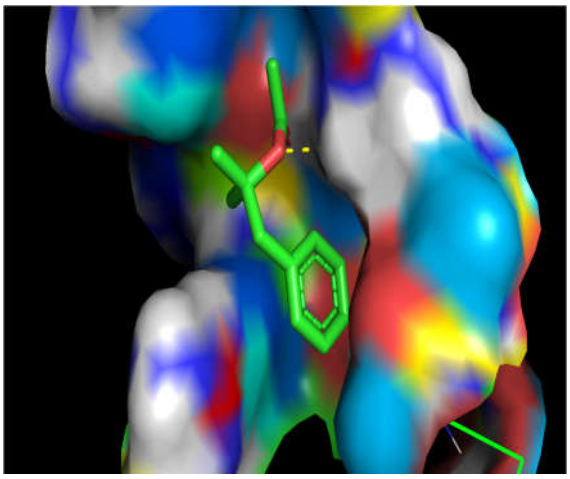


Docked conformation between Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate and RNA polymerase (RNAP)



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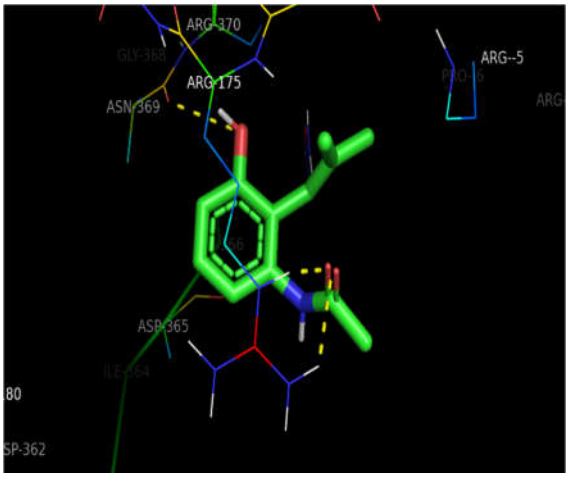
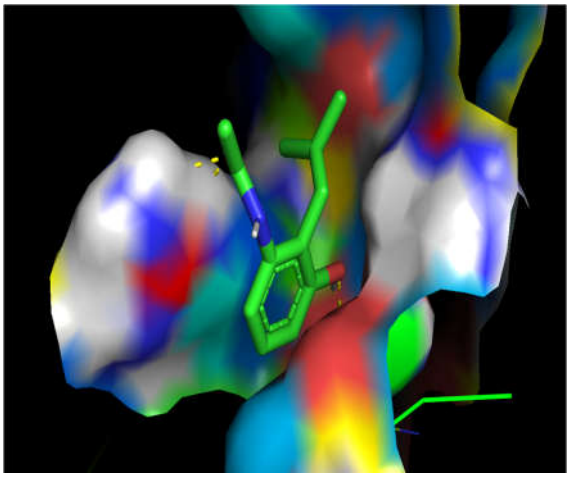
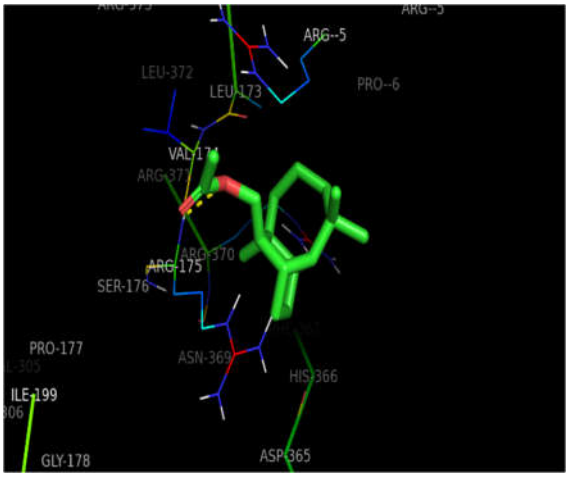


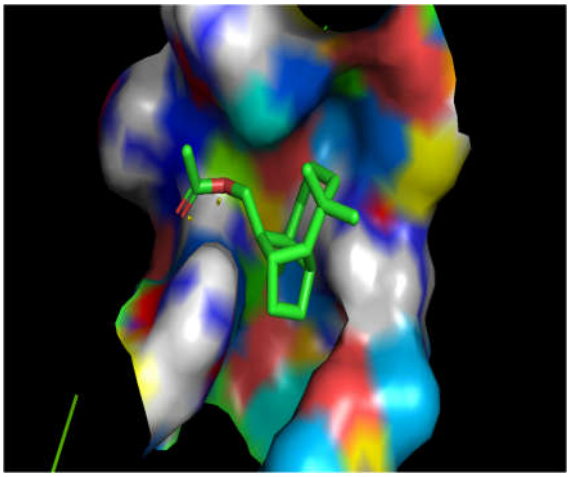
Docked conformation between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and RNA polymerase (RNAP)



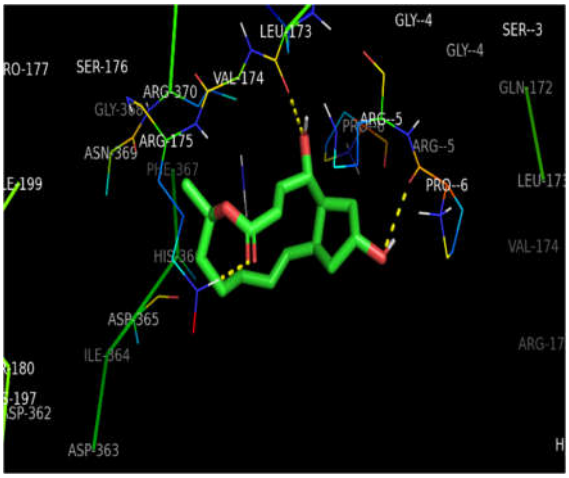
Surface representation of Docked conformation between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and RNA polymerase (RNAP)



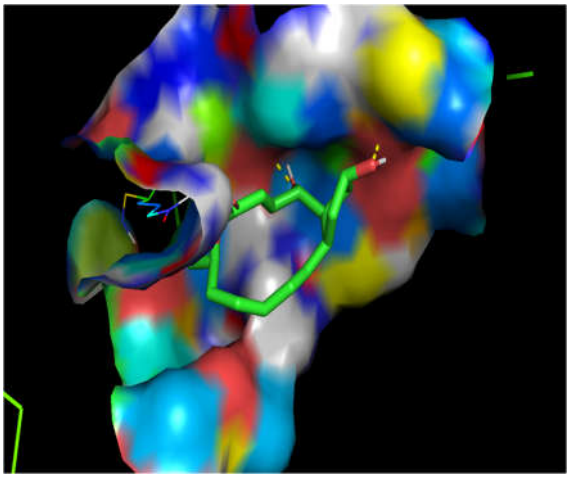
Docked conformation between (-)-Isolongifolol, acetate and RNA polymerase (RNAP)



Surface representation of Docked conformation between (-)-Isolongifolol, acetate and RNA polymerase (RNAP)



Docked conformation between Brefeldin A and RNA polymerase (RNAP)



Surface representation of Docked conformation between Brefeldin A and RNA polymerase (RNAP)

Figure 1: Docked conformation & Surface representation of docked conformation of antibacterial activities of phytochemicals found in the *C. zeylanica* leaves ethanolic extract in GC-MS/MS analysis.

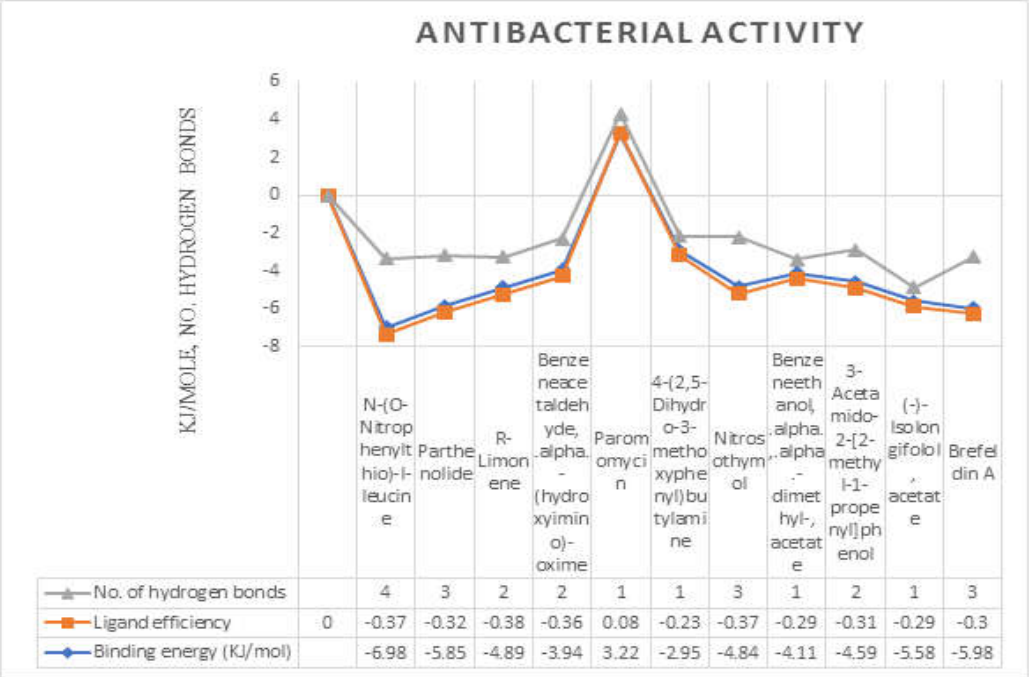


Figure 2: Binding energy, ligand efficiency and number of hydrogen bonds in *In silico* Study of bioactive compounds of *C. zeylanica* and RNA polymerase (RNAP).

Among the compounds that were docked, N-(O-Nitrophenylthio)-l-leucine shows better binding affinity with the Drug Target RNA polymerase (RNAP) as the binding energy is less. Thus, it can be a better alternative for treating Bacterial infection.

Table 3: Anticancer Activity

S. No	Compound	Binding energy (KJ/mol)	Ligand efficiency (KJ/mol)	Inhibitory constant	No. of hydrogen bonds	Hydrogen bond
1.	N-(O-Nitrophenylthio)-l-leucine	-3.52	-0.19	2.64 mM	1	Asp 186:N::Lig:O
2.	Parthenolide	-6.36	-0.35	21.85 µM	-	-
3.	R-Limonene	-6.76	-0.52	11 µM	-	-
4.	Benzeneacetaldehyde, .alpha.- (hydroxyimino)-oxime	-7.9	-0.72	1.62 µM	4	His159:H::Lig:O Ile168:N::Lig:O Arg166:N::Lig:N His165:N::Lig:O
5.	Paromomycin	-8.23	-0.2	933 nM	7	Lig:H::Asp167:O Lig:H::Asp186:O Lig:H::Asp186:O Lig:H::Asp128:O Lig:H::Asp128:O Lig:H::Glu171:O

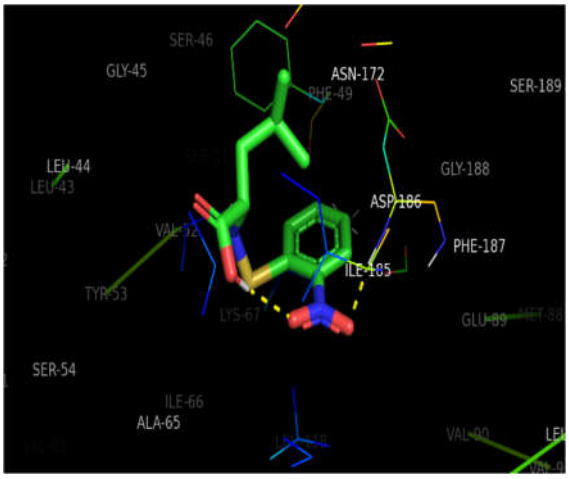
						Asn172:H::Lig:O
6.	4-(2,5-Dihydro-3-methoxyphenyl)butylamine	-7.11	-0.55	6.16 µM	3	Lig:H::Asp186:OD2 Lig:H::Asn172:OD1 Asp186:N::Lig:O
7.	Nitrosothymol	-7.96	-0.61	1.47 µM	3	Ile168:N::Lig:O Ser227:H::Lig:N Lig:H::Gly220:O
8.	Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate	-5.88	-0.42	49.31 µM	-	-
9.	3-Acetamido-2-[2-methyl-1-propenyl]phenol	-7.14	-0.48	5.83 µM	2	Lig:H::Glu89:O Phe187:N::Lig:O
10.	(-)-Isolongifolol, acetate	-7.47	-0.39	3.36 µM	-	-
11.	Brefeldin A	-7.61	-0.38	2.65 µM	3	Lig:H::Glu89:O Lig:H::Phe49:O Phe187:N::Lig:O

PIM-1 Kinase is a drug target for Cancer (Tursynbay et al, 2016) which is a Serine/Threonine Kinase that regulates cellular functions such as Cell Cycle and Cell Survival. Thus the Phyto-compounds were docked against PIM-1 Kinase whose structure in PDB format was retrieved from Protein Data Bank (1xws).

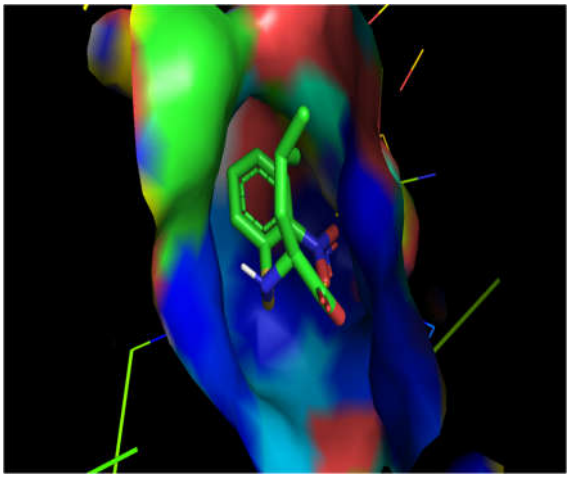
The binding energy between N-(O-Nitrophenylthio)-l-leucine and PIM-1 Kinase, was -3.52 kcal/mol with a ligand Efficiency of -0.19 kcal/mol. 2.64 mM of N-(O-Nitrophenylthio)-l-leucine is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There is 1 Hydrogen bond formed between N-(O-Nitrophenylthio)-l-leucine and PIM-1 Kinase. The binding energy between Parthenolide and PIM-1 Kinase, was -6.36 kcal/mol with a ligand Efficiency of -0.35 kcal/mol. 21.85 µM of Parthenolide is required to acquire half maximum Inhibition in PIM-1 Kinase protein. The binding energy between R-Limonene and PIM-1 Kinase, was -6.76 kcal/mol with a ligand Efficiency of -0.52 kcal/mol. 11 µM of R-Limonene is required to acquire half maximum Inhibition in PIM-1 Kinase protein. The binding energy between Benzeneacetaldehyde,. alpha.- (hydroxyimino)-oxime and PIM-1 Kinase, was -7.9 kcal/mol with a ligand Efficiency of -0.72 kcal/mol. 1.62 µM of Benzeneacetaldehyde, .alpha.- (hydroxyimino)-oxime is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There are 4 Hydrogen bonds formed between Benzeneacetaldehyde, .alpha.- (hydroxyimino)-oxime and PIM-1 Kinase. The binding energy between Paromomycin and PIM-1 Kinase, was -8.23 kcal/mol with a ligand Efficiency of -0.2 kcal/mol. There are 7 Hydrogen bonds formed between Paromomycin and PIM-1 Kinase.

The binding energy between 4-(2,5-Dihydro-3-methoxyphenyl) butylamine and PIM-1 Kinase, was -7.11 kcal/mol with a ligand Efficiency of -0.55 kcal/mol. 6.16 µM of 4-(2,5-Dihydro-3-methoxyphenyl)butylamine is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There are 3 Hydrogen bonds formed between 4-(2,5-dihydro-3-methoxyphenyl) butylamine and PIM-1 Kinase. The binding energy between Nitrosothymol and PIM-1 Kinase was -7.96 kcal/mol with a ligand Efficiency of -0.61 kcal/mol. 1.47 µM of Nitrosothymol is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There are 3 Hydrogen bonds formed between Nitrosothymol and PIM-1 Kinase. The binding energy between Benzeneethanol, .alpha.,.alpha.-dimethyl-, acetate and PIM-1 Kinase, was -5.88 kcal/mol with a ligand Efficiency of -0.42 kcal/mol. 49.31 µM of Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate is required to acquire half maximum Inhibition in PIM-1 Kinase protein. The binding energy between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and PIM-1 Kinase, was -7.14 kcal/mol with a ligand Efficiency of -0.48 kcal/mol. 5.83 µM of 3-

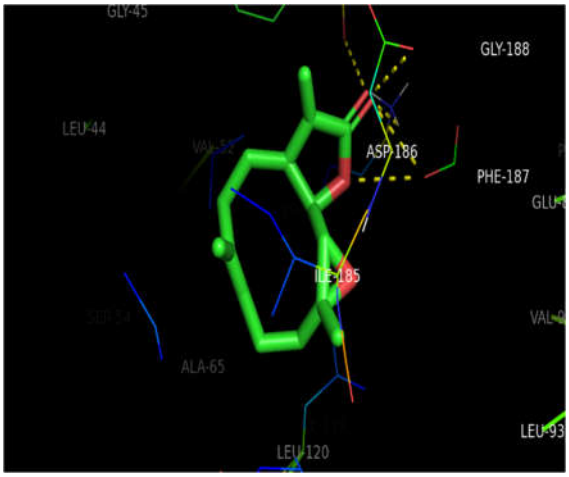
Acetamido-2-[2-methyl-1- propenyl]phenol is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There are 2 Hydrogen bonds formed between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and PIM-1 Kinase. The binding energy between (-)-Isolongifolol, acetate and PIM-1 Kinase, was -7.47 kcal/mol with a ligand Efficiency of -0.39 kcal/mol. 3.36 µM of (-)-Isolongifolol, acetate is required to acquire half maximum Inhibition in PIM-1 Kinase protein. The binding energy between Brefeldin A and PIM-1 Kinase, was -7.61 kcal/mol with a ligand Efficiency of -0.38 kcal/mol. 2.65 µM of Brefeldin A is required to acquire half maximum Inhibition in PIM-1 Kinase protein. There are 3 Hydrogen bonds formed between Brefeldin A and PIM-1 Kinase.



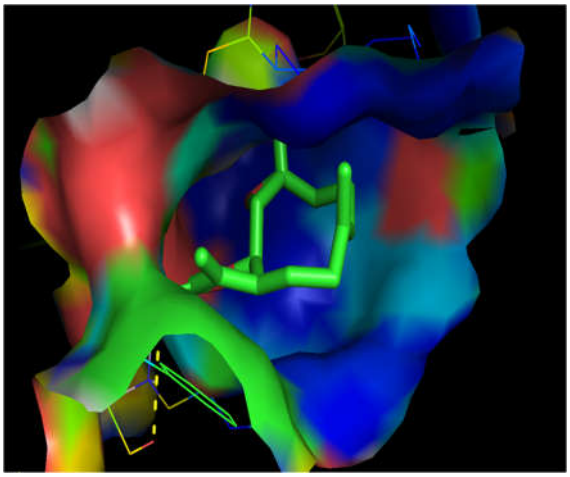
Docked conformation between N-(O-Nitrophenylthio)-l-leucine and PIM Kinase 1



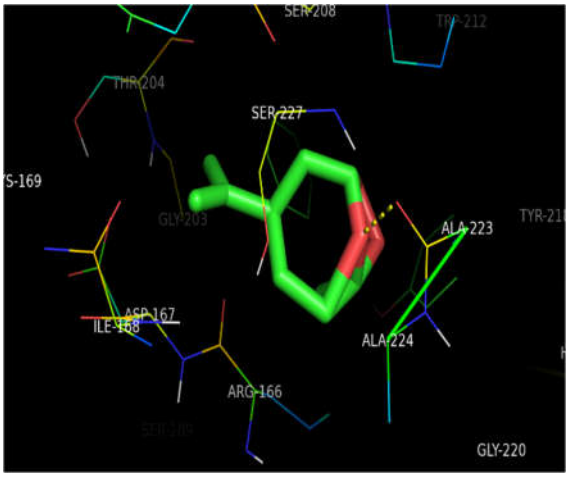
Surface representation of Docked conformation between N-(O-Nitrophenylthio)-l-leucine and PIM Kinase 1



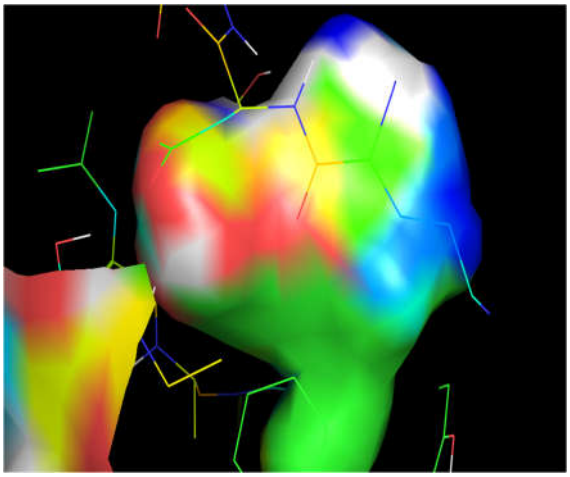
Docked conformation between Parthenolide and PIM Kinase 1



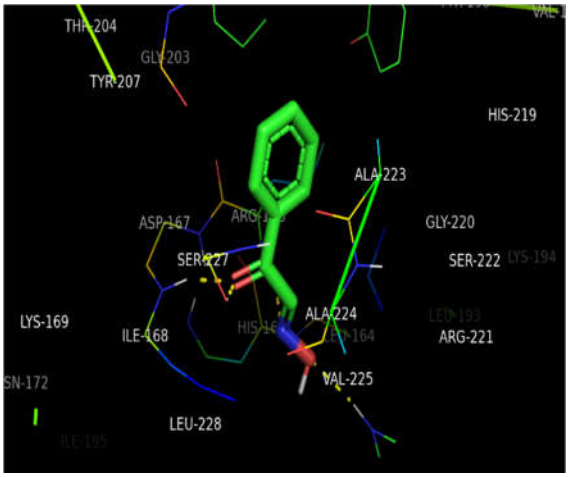
Surface representation of Docked conformation between Parthenolide and PIM Kinase 1



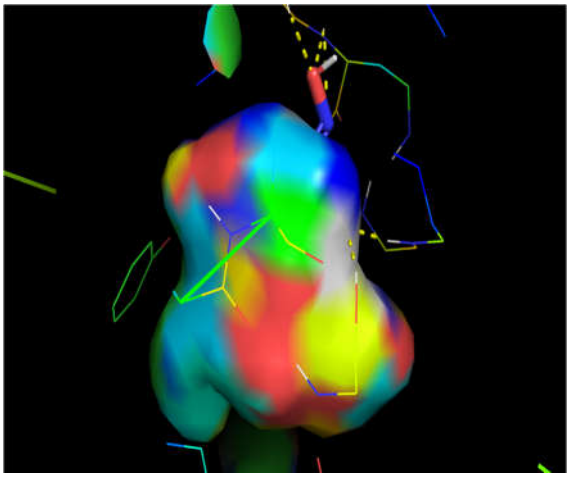
Docked conformation between R-Limonene and PIM Kinase 1



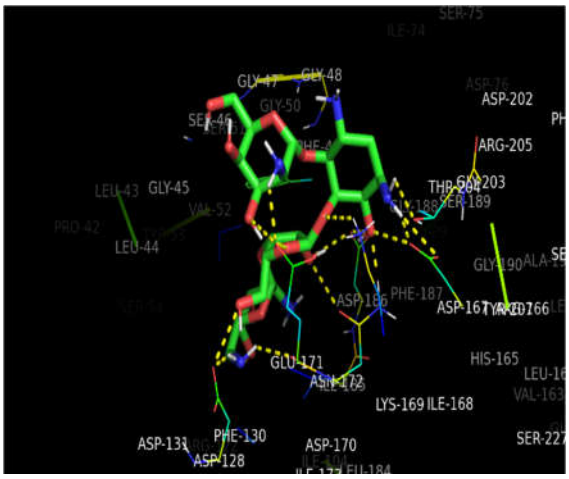
Surface representation of Docked conformation between R-Limonene and PIM Kinase 1



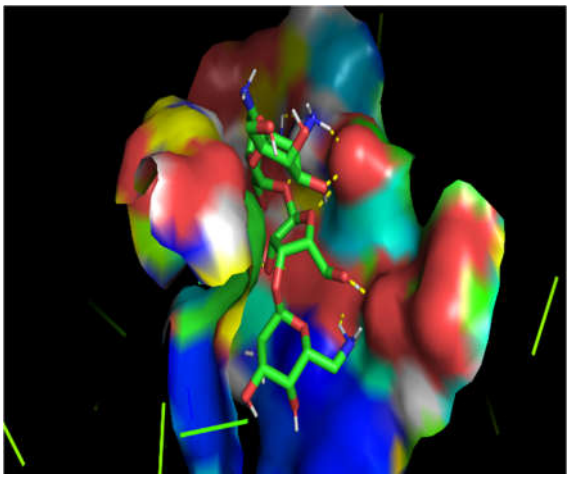
Docked conformation between Benzeneacetaldehyde, .alpha.- (hydroxyimino)- oxime and PIM Kinase 1



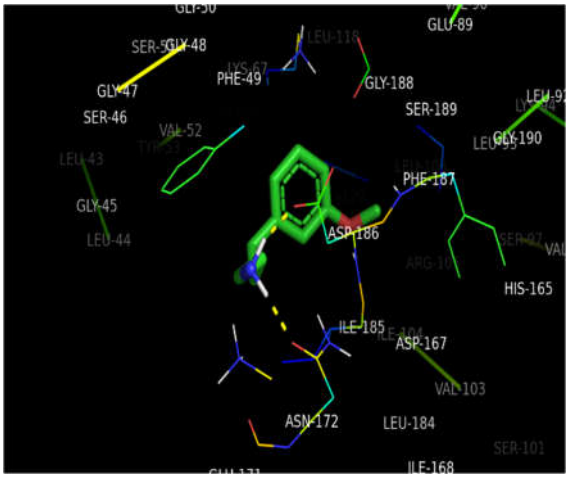
Surface representation of Docked conformation between Benzeneacetaldehyde, .alpha.- (hydroxyimino)- oxime and PIM Kinase 1



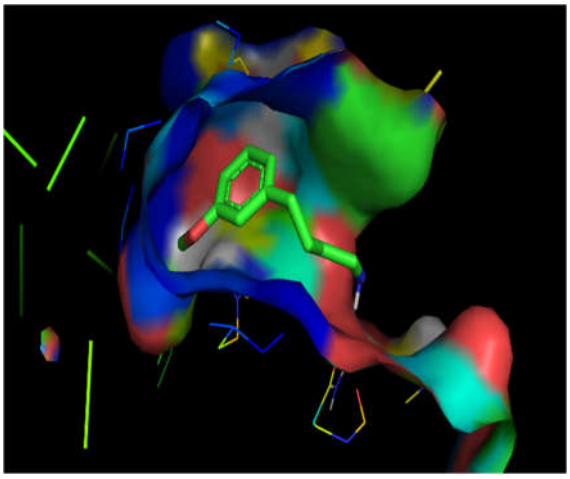
Docked conformation between Paromomycin and PIM Kinase 1



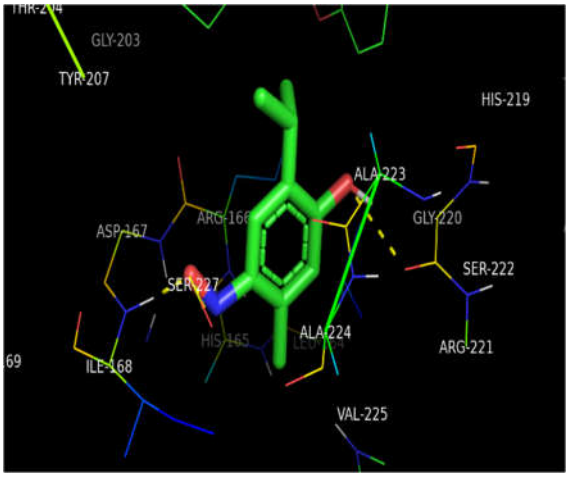
Surface representation of Docked conformation between Paromomycin and PIM Kinase 1



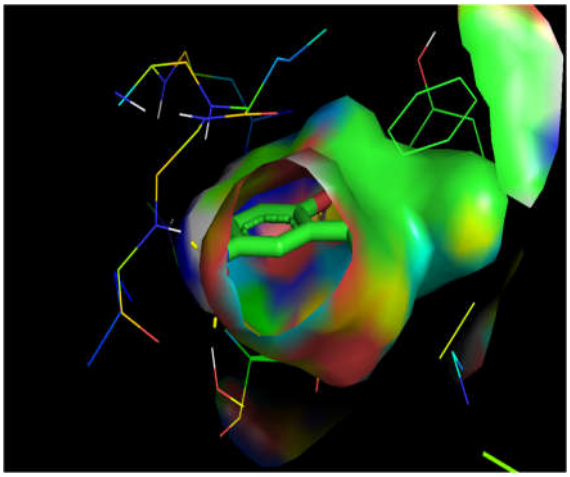
Docked conformation between 4-(2,5-Dihydro-3-methoxyphenyl)butylamine and PIM Kinase 1



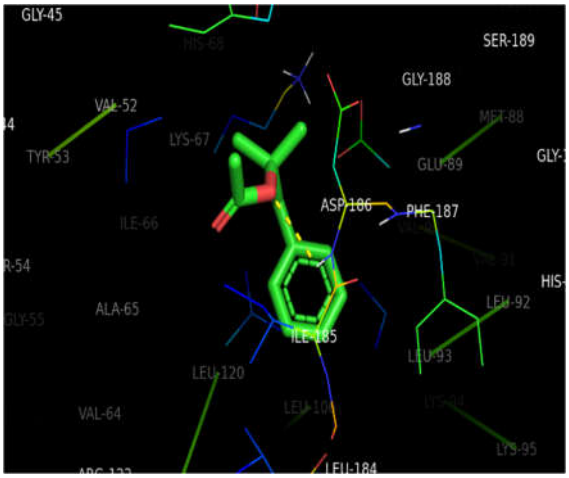
Surface representation of Docked conformation between 4-(2,5-Dihydro-3-methoxyphenyl)butylamine and PIM Kinase 1



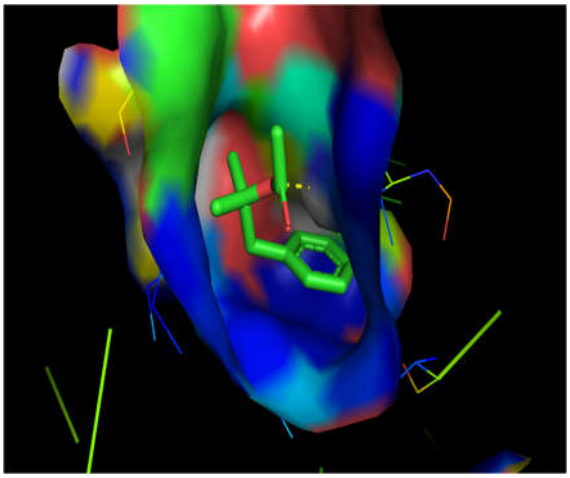
Docked conformation between Nitrosothymol and PIM Kinase 1



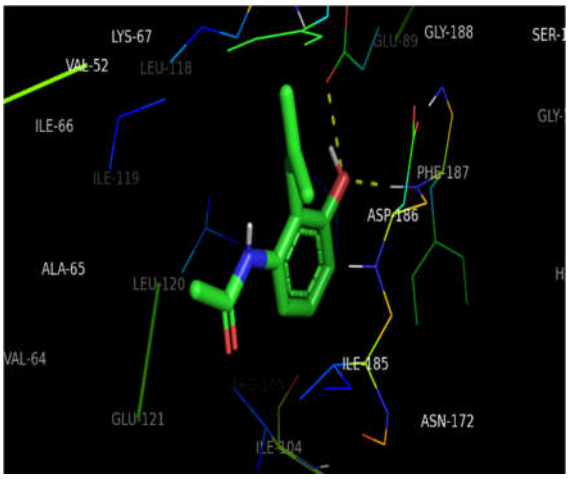
Surface representation of Docked conformation between Nitrosothymol and PIM Kinase 1



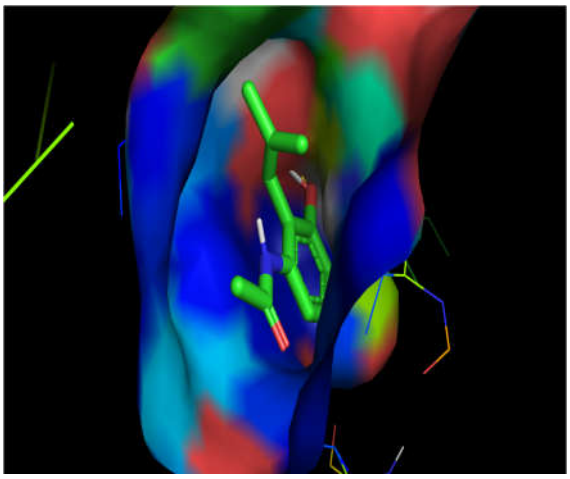
Docked conformation between Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate and PIM Kinase 1



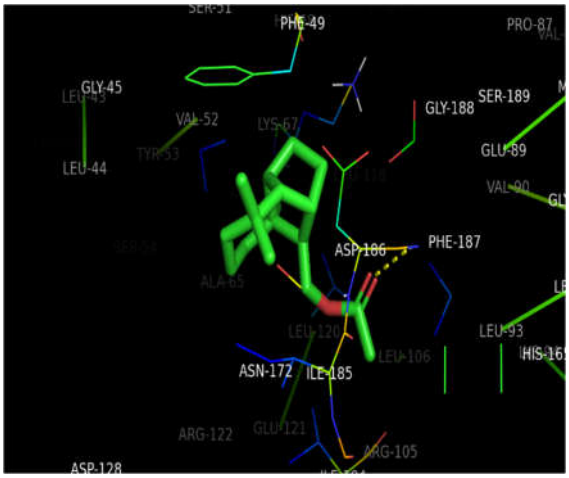
Surface representation of Docked conformation between Benzeneethanol, .alpha.,.alpha.- dimethyl-, acetate and PIM Kinase 1



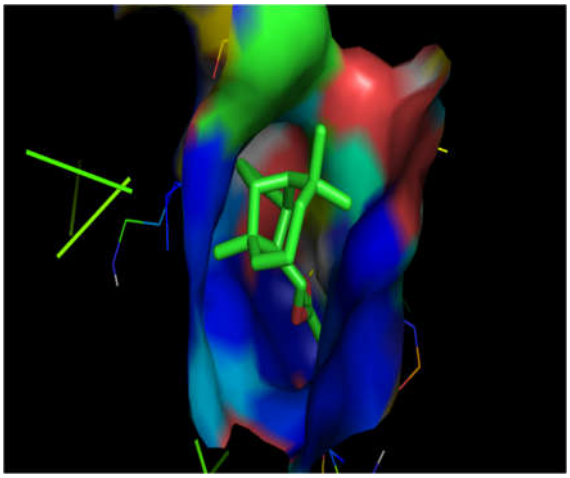
Docked conformation between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and PIM Kinase 1



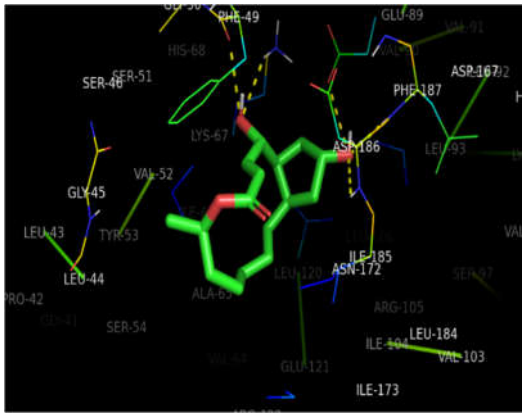
Surface representation of Docked conformation between 3-Acetamido-2-[2-methyl-1- propenyl]phenol and PIM Kinase 1



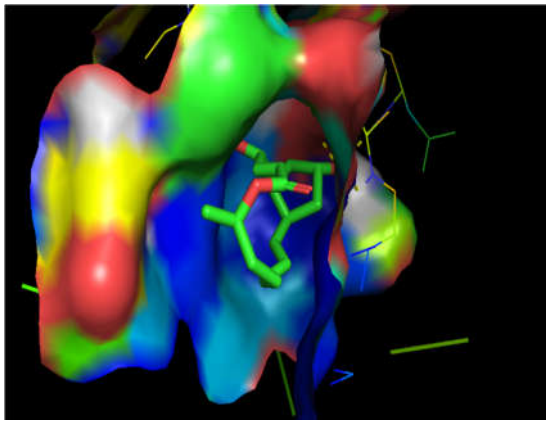
Docked conformation between (-)-Isolongifolol, acetate and PIM Kinase 1



Surface representation of Docked conformation between (-)-Isolongifolol, acetate and PIM Kinase 1

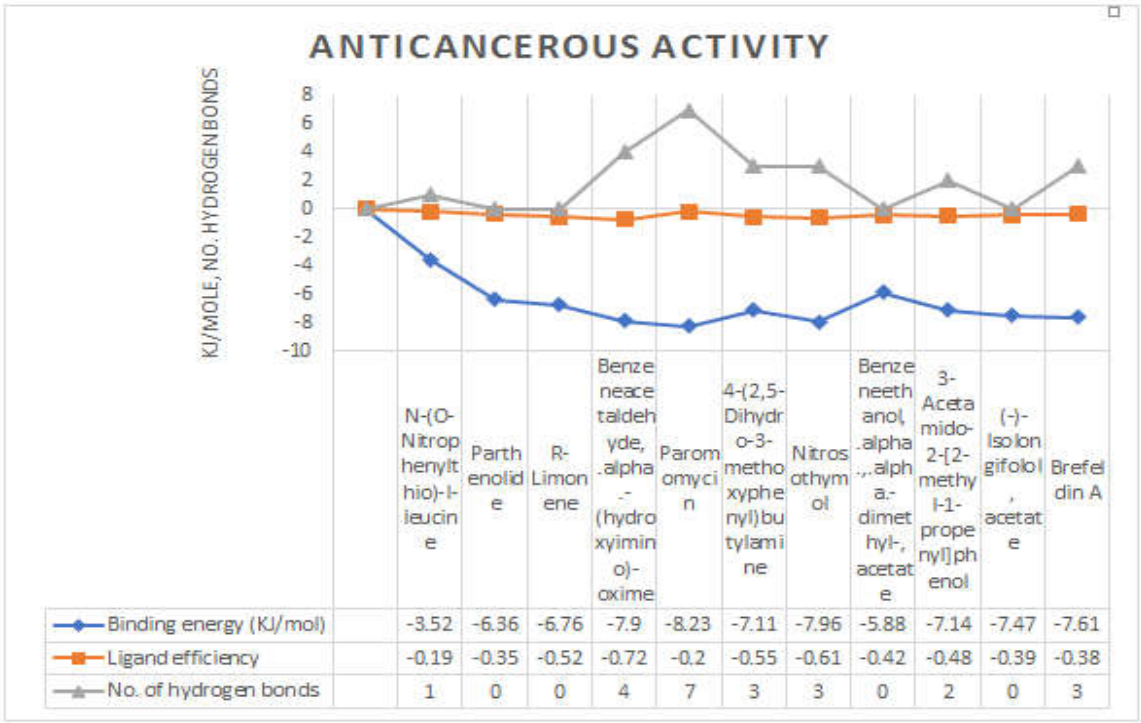


Docked conformation between Brefeldin A and PIM Kinase 1



Surface representation of Docked conformation between Brefeldin A and PIM Kinase 1

Figure 3: Docked conformation & Surface representation of docked conformation of anticancerous activities of phytochemicals found in the C. zeylanica leaves ethanolic extract in GC-MS/MS analysis.



	N-(O-Nitrophenylthio)-l-leucine	Parthenolide	R-Limonene	Benzeneacetaldehyde, .alpha.-(hydroxyimino)-oxime	Paromomycin	4-(2,5-Dihydro-3-methoxyphenyl)butylamine	Nitrosothymol	Benzeneethanol, .alpha.,.alpha.-dimethyl-, acetate	3-Acetamido-2-[2-methyl-1-propenyl]phenol	(-)-Isolongifolol, acetate	Brefeldin A
Binding energy (KJ/mol)	-3.52	-6.36	-6.76	-7.9	-8.23	-7.11	-7.96	-5.88	-7.14	-7.47	-7.61
Ligand efficiency	-0.19	-0.35	-0.52	-0.72	-0.2	-0.55	-0.61	-0.42	-0.48	-0.39	-0.38
No. of hydrogen bonds	1	0	0	4	7	3	3	0	2	0	3

Figure 4: Binding energy, ligand efficiency and number of hydrogen bonds in *In silico* Study of bioactive compounds of *C. zeylanica* and PIM-1 Kinase.

Among the compounds that were docked, Paromomycin shows better binding affinity with the Drug Target PIM-1 Kinase as the binding energy is less. Thus, it can be a better alternative for treating Cancer.

CONCLUSION

In silico studies of phytochemicals in the phytotherapeutic plant *Clematis zeylanic* (L.) Poir suggest that parmomycine may be a better choice for treating cancer and N-(O-Nitrophenylthio)-l-leucine may be a better alternative for treating bacterial infections. The results of this study provide credence to the necessity for additional validation and investigation into the potential therapeutic uses of this herb.

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