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Short Communication

MOLECULAR DOCKING AND ADMET STUDIES OF ETHANONE, 1-(2-HYDROXY-5-METHYL PHENYL) FOR ANTI-MICROBIAL PROPERTIES

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ABSTRACT

Objective: Ethanone 1-(2-hydroxy-5-methyl phenyl) found in the aerial parts of *Rhizophora mucronate*, *Epiphyllum oxypetalum* haw and dried ripened seed extracts of coffee. It has reported anti-microbial properties based on the literature. The objective of the present study is to find the binding efficacy of the compound with proteins in *staphylococcus aureus* and to report the ADMET properties of the compound.

Methods: Rigid docking technique was used for finding the affinities.3D structures of the six proteins of *staphylococcus aureus* are selected from the protein database. Molecule Ethanone 1-(2-hydroxy-5-methyl phenyl) is obtained from PubChem. ADMET studies of the compound are assessed by SWISS-ADME. Molecular docking studies are carried out by using PyRx software.

Results: Ethanone 1-(2-hydroxy-5-methyl phenyl) on molecular docking with S*taphylococcus aureus sortase*-A (PDB ID: 1T2P), Clumping factor A (ClfA) (PDB ID: 1N67), DNA gyrase (PDB ID: 3U2D), Dihydrofolate reductase (DHFR) (PDB ID: 2W9S), Undecaprenyl diphosphate synthase (UPPS) (PDB ID: 4H8E), Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO), their binding affinities were found to be-6.2,-6.3,-5.9,-6.4,-5.3,-6.8 respectively. Out of six proteins, Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO) and Dihydrofolate reductase (DHFR) (PDB ID: 2W9S) has shown better binding affinities.

Conclusion: ADMET studies show that Ethanone 1-(2-hydroxy-5-methyl phenyl) has zero violation to Lipinski's rule and molecular docking with two proteins has shown good binding efficacy with Ethanone 1-(2-hydroxy-5-methylphenyl).

Keywords: Ethanone 1-(2-hydroxy-5-methyl phenyl), SWISS ADME, PyRx, Discovery studios 2021, Swiss-Pdb viewer

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Due to the development of resistance against antimicrobial agents or drugs, the complication arises in treating microbial infections. Over usage of antibiotics leads to antimicrobial resistance and it is becoming difficult to treat bacterial diseases with currently existing drugs [1]. Phytochemicals play an important role in treating microbial diseases and inhibiting the growth of bacteria like *Staphylococcus aureus* [2]. Antimicrobial resistance is a worldwide growing problem and it needs machine learning techniques and artificial intelligence by the use of computational chemistry for designing novel antimicrobial agents. Computational chemistry made drug design easier by reducing the time for screening the molecules for binding affinity and ADMET studies, using *in silico* methods. Ethanone 1-(2-hydroxy-5-methyl phenyl)[fig. 1] found in the *Epiphyllum oxypetalum haw* and coffee(*Coffea Arabica*)[fig. 2]. Ethanone 1-(2-hydroxy-5-methyl phenyl), belongs to the class of alkyl-phenyl ketones, which is substituted by one phenol group and methyl group; it has very strong tasting property. Ethanone 1-(2-hydroxy-5-methyl phenyl) has biological properties like anti-inflammatory, antioxidant and antimicrobial properties [3].

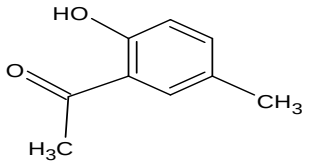

Fig. 1: Structure of Ethanone 1-(2-hydroxy-5-methyl phenyl)

Docking studies were done based on rigid docking using PyRx software, protein preparation was done by using Swiss-pdb viewer and BIOVIA Discovery studio, and visualization and structure generation were done by using Discovery studio 2021. The selected target proteins for *staphylococcus aureus*are S*taphylococcus aureus sortase*-A (PDB ID: 1T2P), Clumping factor A (ClfA) (PDB ID: 1N67), DNA gyrase (PDB ID: 3U2D), Dihydrofolate reductase (DHFR) (PDB ID: 2W9S), Undecaprenyl diphosphate synthase (UPPS) (PDB ID: 4H8E), Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO) [4].

Fig. 2: Picture of *Coffea Arabica*

Molecular docking studies were carried out to calculate the binding efficacy of the compound with proteins. Target proteins in *staphylococcus aureus* were downloaded from the PDB (protein data bank) in PDB format in 3D orientation and ligand was downloaded from PUBCHEM in SDF format. Protein preparation, removal of water molecules and the addition of hydrogen were carried out by using BIOVIA Discovery studio 2021[5], it was saved in PDB format. Docking calculations were carried out by using PyRx software, energy minimization and conversion to PDBQT format were also done in the same software prior to the docking procedure [6]. 3D interactions of the protein and ligand were derived by using Pymol software [7] and 2D structure was generated by using BIOVIA Discovery studios 2021.

ADMET studies were carried out by using the SWISS ADME website by converting the structure into the smiles format [8].

Result showed that molecular docking for Ethanone 1-(2-hydroxy-5-methyl phenyl) with different target proteins of *staphylococcus aureus* were done, binding scores of ligand with proteins like Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO) and Dihydrofolate reductase (DHFR) (PDB ID: 2W9S) were shown good results. Binding energies of the ligand with six proteins are given in the following table 1.

Table 1: Molecular docking scores of Ethanone 1-(2-hydroxy-5-methyl phenyl) with different target proteins of *staphylococcus aureus*

Protein	Binding affinity	
	Ethanone 1-(2-hydroxy-5-methyl phenyl)	Penicillin G
Staphylococcus aureus sortase-A (PDB ID: 1T2P)	-6.2	-7.0
Clumping factor A (ClfA) (PDB ID: 1N67)	-6.3	-8.2
DNA gyrase (PDB ID: 3U2D)	-5.9	-7.5
Dihydrofolate reductase (DHFR) (PDB ID: 2W9S)	-6.4	-8.7
Undecaprenyl diphosphate synthase (UPPS) (PDB ID: 4H8E)	-5.3	-6.4
Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO)	**-6.8**	-8.2

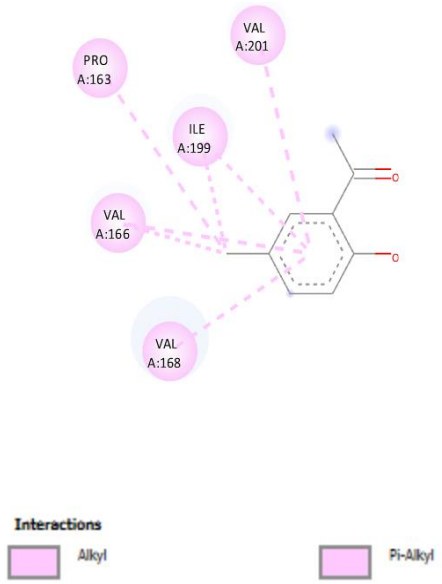

Fig. 3: 2D representation of the interaction between Ethanone 1-(2-hydroxy-5-methyl phenyl) and staphylococcus aureus sortase-A (PDB ID: 1T2P)

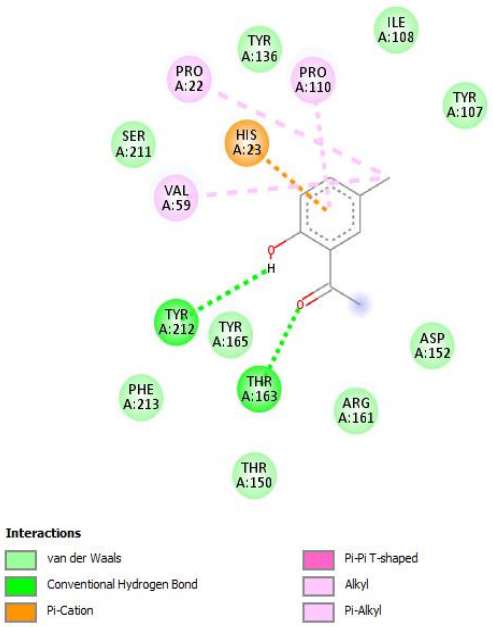

Fig. 4: 2D representation of the interaction between Ethanone 1-(2-hydroxy-5-methyl phenyl) and Clumping factor A (ClfA) (PDB ID: 1N67)

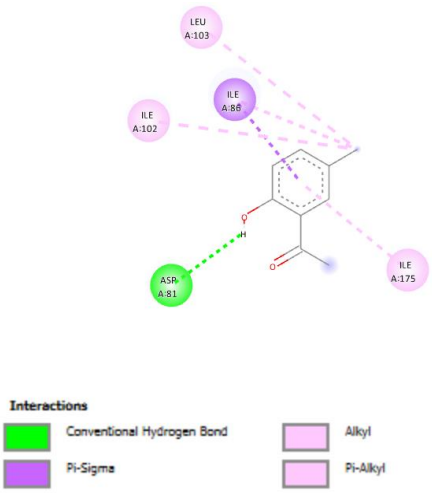

Fig. 5: 2D representation of interaction between ethanone 1-(2-hydroxy-5-methyl phenyl) and DNA gyrase (PDB ID: 3U2D)

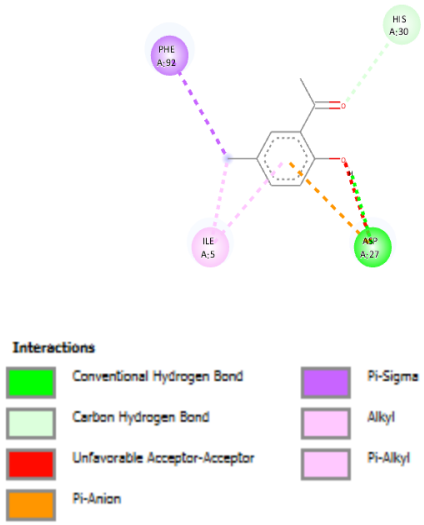

Fig. 6: 2D representation of interaction between Ethanone 1-(2-hydroxy-5-methyl phenyl) and Dihydrofolate reductase (DHFR) (PDB ID: 2W9S)

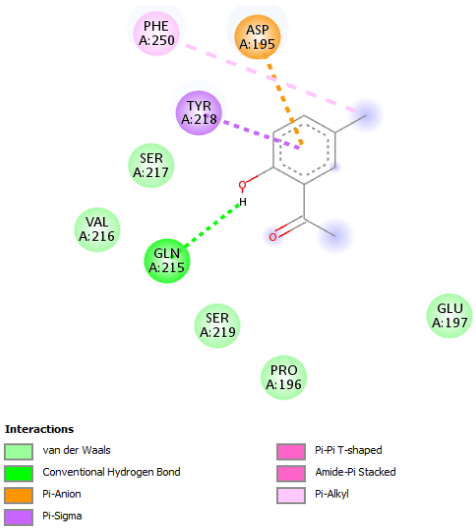

Fig. 7: 2D representation of the interaction between Ethanone 1-(2-hydroxy-5-methyl phenyl) and Undecaprenyl diphosphate synthase (UPPS) (PDB ID: 4H8E)

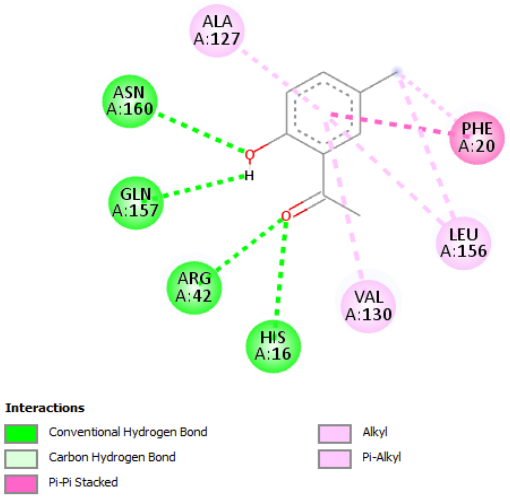

Fig. 8: 2D representation of the interaction between Ethanone 1-(2-hydroxy-5-methyl phenyl) and Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO*)*

Table 2: ADMET results of Ethanone 1-(2-hydroxy-5-methyl phenyl)

Parameters	Ethanone 1-(2-hydroxy-5-methyl phenyl)	Condition for druglike property
Mass	150.17 g/mol	<500
Hydrogen bond donor	1	<5
Hydrogen bond acceptor	2	<10
Log *p*	1.96	<5
Molar refractivity	43.63	40-130

Mainly ADMET studies were carried out using a Swiss ADME website. According to Lipinski's rule of five, an orally active drug should have less than two violations; Ethanone 1-(2-hydroxy-5-methyl phenyl) has shown zero violation for the Lipinski's rule and the parameters are shown in the following table 2.

In conclusion, molecular docking and ADMET properties of Ethanone 1-(2-hydroxy-5-methyl phenyl) were studied and the binding affinities of Ethanone 1-(2-hydroxy-5-methyl phenyl) to Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO) and Ethanone 1-(2-hydroxy-5-methyl phenyl) and Dihydrofolate reductase (DHFR) (PDB ID: 2W9S) are-6.8 and-6.4 respectively. Even ADMET properties of the compound showed a zero violation to Lipinski's rule. Hence Ethanone 1-(2-hydroxy-5-methyl phenyl) is a potential anti-microbial agent and it acts by inhibiting the proteins Dehydrosqualene synthase (CrtM) (PDB ID: 2ZCO) and Dihydrofolate reductase (DHFR) (PDB ID: 2W9S) in *staphylococcus aureus*. By comparing the docking scores of Ethanone 1-(2-hydroxy-5-methyl phenyl) to Penicillin G, binding affinities of Ethanone 1-(2-hydroxy-5-methyl phenyl) found to be less, but according to the results obtained and interactions observed between the proteins and ligand, Ethanone 1-(2-hydroxy-5-methyl phenyl) can be a potent anti-microbial agent. The interactions were compared with other studies and it has shown the involvement of certain important amino acids like lysine, glycine, Glutamine, Leucine, Histidine, Alanine, Tyrosine and Phenylalanine [9]. Further research has to be done for *in vitro* studies.

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M. Sri Satya and Aiswariya have carried out the docking studies and prepared the manuscript; Suma B V has helped in reviewing and correcting the manuscript

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AUTHORS CONTRIBUTIONS

All the authors have contributed equally.

CONFLICT OF INTERESTS

We hereby declare there is no conflict of interest.

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