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INSILICO MOLECULAR DOCKING STUDY ON POLYPHENOLS OF ELEUSINE CORACANA AGAINST COVID -19

[1]K.SADHANA, [2]S.ARUNA, [3]R.GIRIJA

[1]Assistant Professor, Adhi college of Engineering & Techonology, Sankarapuram, Kanchipuram Dist-631605.
[2]Assistant professor PG & Research Department of Chemistry, Queen Mary's College, Chennai-600 004. India
[3]Assistant Professor Bio informatics infrastructure facility centre, Queen Mary's college. Chennai-600 004.India

ABSTRACT

The new strain of Covid-19 identified in the year end of 2019. It is caused us sever acute respiratory syndrome. Currently no specific treatment for Covid-19. The worldwide Scientist have involved to discover newer, affordable, effective with minimum side effects drugs to treat Covid-19. Many of them analysing medicinal plants. *Eleusinecoracana* is a medicinal plant as well as food plant from native of Ethiopia, but spread out to Asia few thousand years ago. This is belongs to poaceae family. It contains different types of secondary metabolites with wide range of therapeutic effects. Especially phenolic compounds of this plants promise in the management of several disease conditions. In this present study investigate bioactive compounds of Eleusinecoracana plant with Covid-19 inhibitors using molecular docking studies.

KEYWORDS: Eleusinecoracana, Covid-19, Schrodinger Maestro 11.9, Molecular docking, Glide score

1.INTRODUCTION

The new pandemic disease was reported in wuhan, China in the year end of 2019 and its named as Covid -19 by WHO. Its spread worldwide and causing sever Public issues. The common symptoms are fever, cough, muscle and body aches and sore throat. The first identification of human coronavirus discovered in mid-1960 s[1,2].Coronaviruses members of family coranaviridae and sub family Coronaviriniae are enveloped positive stranded RNA viruses which have spike of glycoproteins projecting from their viral envelops thus exhibiting a corona appearance [3]. Covid-19 belongs to beta coronavirus family [3] out of Four genera alpha coronavirus, beta coronavirus, gamma cororavirus and delta coronavirus of subfamily Coronavirinae. These coronaviruses are transmitted in mammals and cause severe respiratory syndrome such as SARS and middle East Syndrom[MERS-

Cov][4]. Covid-19 has largest genomes range from 26 to 32 kb in length with comparing all well-known RNA viruses [5]. The structural protein are mainly responsible to entry in host cell followed by replication, assembly and propagation at lungs other cells carrying into ACE2 receptors[6].There is no specific drug and vaccine for Covid-19 and additionally 75% Ethanol containing disinfectants can inactive Covid-19[7]. It is one of the challenge for researchers to finding an inhibitor for Covid-19 by protease activity.

The protease tease's activity is triggered by the binding of molecules to specific points on the protease called active sites. However, the protease's activity can also be blocked by molecules called inhibitors. The malaria drug hydroxychloroquine approved by FDA is inhibiting coronavirus[8,9].Others potential inhibitors such as remdesivir, nelfifinavir, lopinavir, and ritonavir used to treatment for SARS,MERS[10] and Ebola[11].It was observed that nelfifinavir has best potential against Covid-19[12].A great heed has been focus on secondary metabolism on plants that may be synthesis to medicine[13].Novel drugs have been prepared from medicinal plants with high potential and minimum side effects[14].Apart from this plants contains secondary metabolism such as flavonids, phenols, alkaloids, tannins, steroids and other phytochemicals [15].Some the plants are observed by their excellent management of disease controls Ficus congensis for curing arthritis,Allium sativum for treating colds, Ipomea batatas for diabetes[16,17].Millets are major group of ceral grains are small grained, annual, warm wether crops consisting 8000 species[18]. Eleusine coracana is an important miller cultivated in India and African countries[19]. Poaceae family well known for management for different diseases. Among them Cymbopogon citratus[lemon grass] used in the treatment of malaria[21,22], and Verivera nigitana[black vertiver grass] used for HIV/AIDS[21].Eleusine coracane has been observed by several researchers for their antioxidant properties[23] and also reported antimicrobial activity by phenolic compounds of this plants[24].Inhibition of aldose reductase from cataracted eye lenses by Eleusine coracane was also reported[25].In this present work ,we focus on identified potential drug for to treat Covid-19 by using antimicrobial activity of Eleusine coracane .However the molecular docking studies was performed by using Nine phenolic compounds on Covid-19 main protein 5R7Y.This work will help to future researchers to find out high efficacy drug with minimal side-effect for Covid-19

2.MATERIALS AND METHODS

All nine Chemical structures namely Protocatechuic acid , P-hydroxylbenzoic acid, P-coumaric acid, Vanillic acid, Syringic acid, Ferulic acid, Trans-cinnamic acid, Quercetin and Gallic acid (X1-X9) were retrieved from PubChem website in SDF format. The docking studies were performed with standard precision (SP) Glide, and extra precision (XP) Glide and MGBSA Prime in Schrodinger software.

2.1 Preparation of Protein

X-ray crystalline Structure of protein 5R7Y was imported from Protein Data Bank (PDB) to workspace. Protein was prepared with the Protein Preparation Wizard in Maestro 11.9 using default options, bond orders were assigned, hydrogens were added, metals were treated, and water molecules 5A˚ beyond hetero groups were deleted, which further set to pre-process followed by review and modify to remove unwanted chains and residues, further refined under force field of OPLS3e. The results were monitored in job monitor.

2.2 Preparation of Ligands

Structures of ligands sketched and saved in SDF format were imported via selecting file. The imported ligands(X1-X9) were set to minimize under force field OPLS3e. Minimization calculations can be performed on all structures of Eleusine coracane phenolic derivatives.

2.3 Molecular Docking

As for Glide docking, crystal structures of 5R7Y should be prepared by the protein preparation wizard in Schrodinger suite. Afterwards, receptor grids were generated before docking with the active site determined by the position of co crystal ligand. Crystal structures of 5R7Y were imported into Glide, defined as the receptor structure and the location of active site with a box. The OPLS3e force field was used for grid generation. The standard precision (SP) and the extra precision (XP) protocols were set for docking studies with crucial residues, in constrained binding to get accurate results. Binding affinity was retrieved running Prime MM-GBSA. All other parameters were maintained as default. Docking programs have proven relatively successful in accurately

reproducing known poses of drug-like molecules from co-crystal structures, with Glide consistently performing among the top of the programs.

3.RESULT AND DISCUSSION

3.1 Molecular Docking

To date, nine structures of ligands have been determined. Meanwhile, these ligands were used for docking to measure the docking conformations. Three different docking programs—SP Glide, and XP Glide, Prime MM-GBSA—were used for improving the accuracy of prediction. Then, X-score followed by molecular docking was reliable and accurate for forecasting protein-ligand binding free energies(Table 1).The docking results were evaluated by comparing values of score energy, SP Glide, XP Glide, and Binding energy. Through analysis of these results of docking simulations, most binding energy scores could accurately forecast the ligand activities. The lowest binding energy and the highest docking score demonstrated that these compounds (ligands) presented well favorable interactions. The docked ligands X1-X9 showed the best range of Docking score, XP Gscore and Binding energy(Table 1).

Table-1

Table 1. Glide Docking and binding energy scores

Title	Docking score	Glide gscore	Glide emodel	XP GScore	MM GBSA dG Bind
X8	-7.14	-7.14	-43.741	-7.14	-39.778
X5	-5.377	-5.377	-25.165	-5.377	-26.69
X9	-5.229	-5.229	-36.477	-5.229	-30.129
X6	-5.229	-5.229	-33.067	-5.229	-27.079
X4	-4.848	-4.848	-30.075	-4.848	-26.452
X1	-4.841	-4.841	-26.333	-4.841	-23.485
X2	-4.515	-4.515	-28.774	-4.515	-24.641
X3	-4.216	-4.216	-35.624	-4.216	-33.31
X7	-3.075	-3.075	-21.032	-3.075	-21.032

3.2 Inhibitor Binding Analysis:

The least binding energy and the most rational binding pattern between the inhibitors and 5R7Y were selected by the three docking protocols. As expected, phenolic derivatives of Eleusine coracane bound in the active site validating the prediction by molecular docking with 5R7Y. Among the set, top three compounds were selected, which represented good interactions with the target protein. From the docking results, 2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-Benzopyran-4-one(Quercetin) (X8) shown interaction with THR-25, GLN-189,HIS-41(Fig-8) which had three Hydrogen bond interactions. *Viz* 3,5 dimethoxy -4-hudroxybenzoic acid (Syringic acid) (X5) showed Two Hydrogen bonds such as GLN-189, HIS-41(Fig-5).Similarly3,4,5-Trihydroxylbenzoic acid(Gallic acid) (X9) showed two Hydrogen bond GLN-189, HIS-41.(Fig-9)

2D Representation of Molecular docking analysis

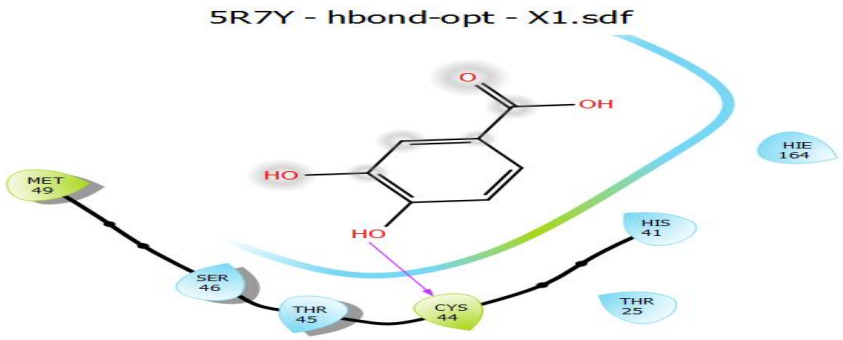

Fig-1. Schematic 2D representation of X1(3,4-dihydroxybenzoic acid) in the binding pocket inhibition of Covid-19 5R7Y

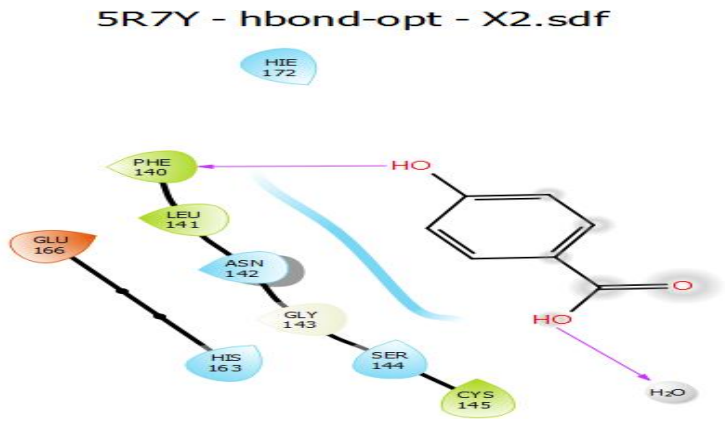

Fig-2. Schematic 2D representation of X2(4-hydroxylbenzoic acid) in the binding pocket inhibition of Covid-19 5R7Y

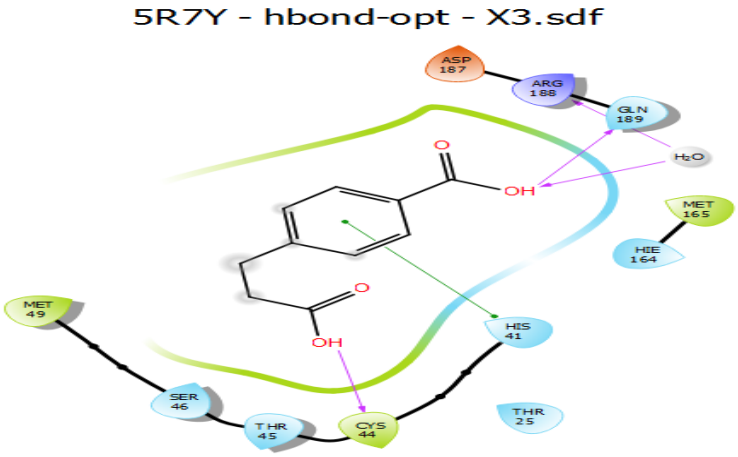

Fig-3. Schematic 2D representation of X3(Trans-4-hydroxycinnamic acid) in the binding pocket inhibition of Covid-19 5R7Y

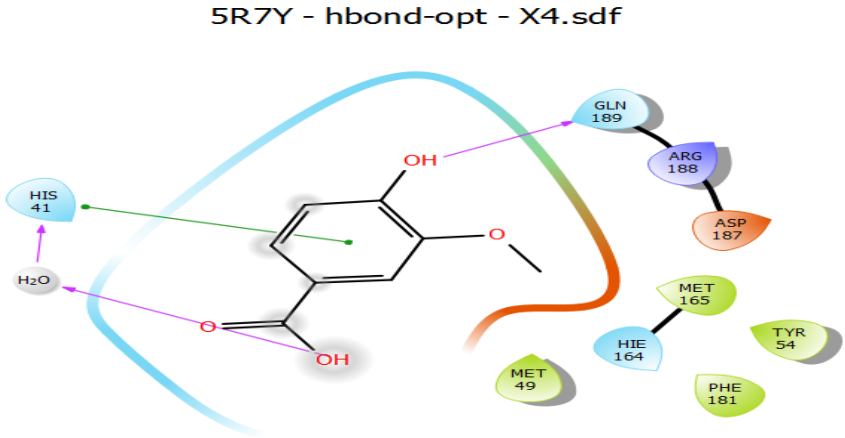

Fig-4. Schematic 2D representation of X4(4-Hydroxy-3-methoxy benzoic acid) in the binding pocket inhibition of Covid-19 5R7Y

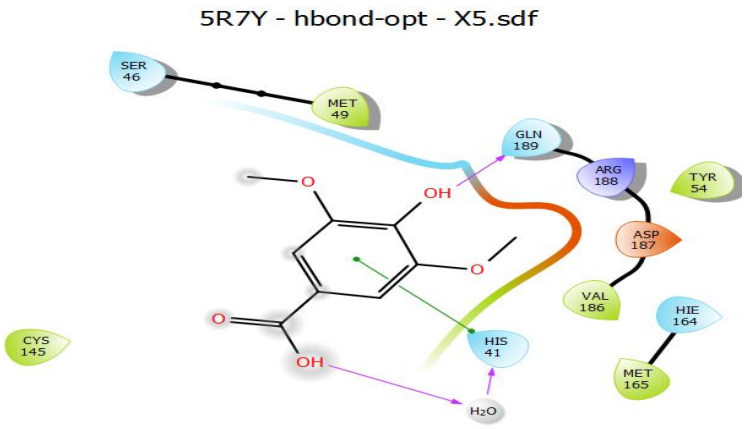

Fig-5. Schematic 2D representation of X5(3,5-dimetoxy-4-hydroxybenzoic acid) in the binding pocket inhibition of Covid-19 5R7Y

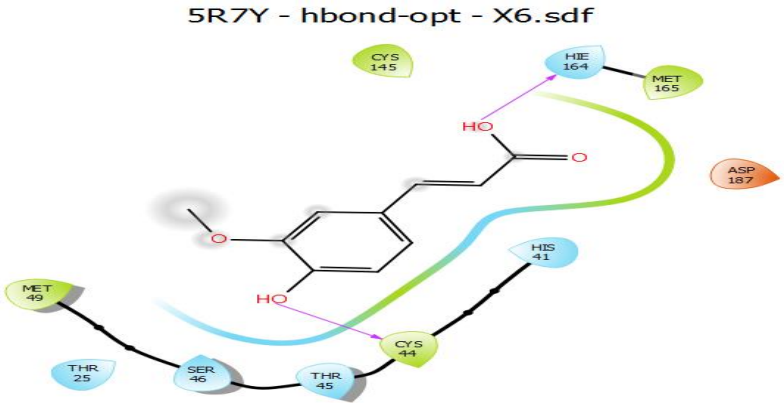

Fig-6. Schematic 2D representation of X6(4-hydroxy-3-metoxycinnamic acid) in the binding pocket inhibition of Covid-19 5R7Y

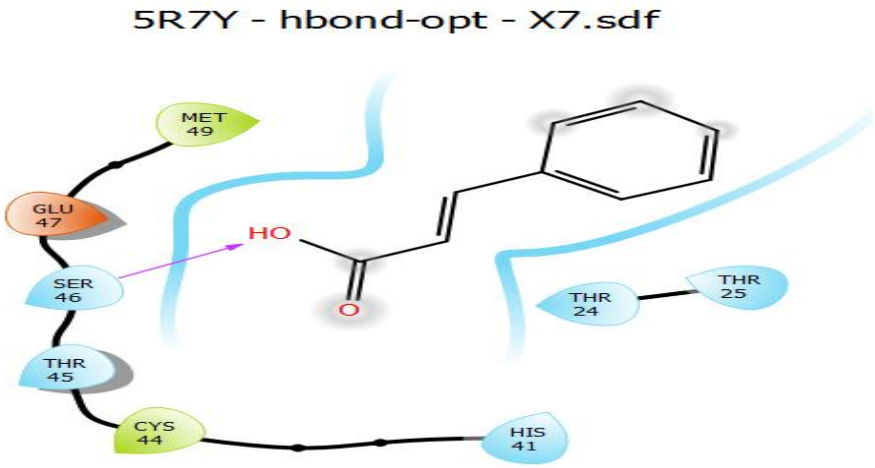

Fig-7. Schematic 2D representation of X7(3-phenylacrylic acid) in the binding pocket inhibition of Covid-19 5R7Y

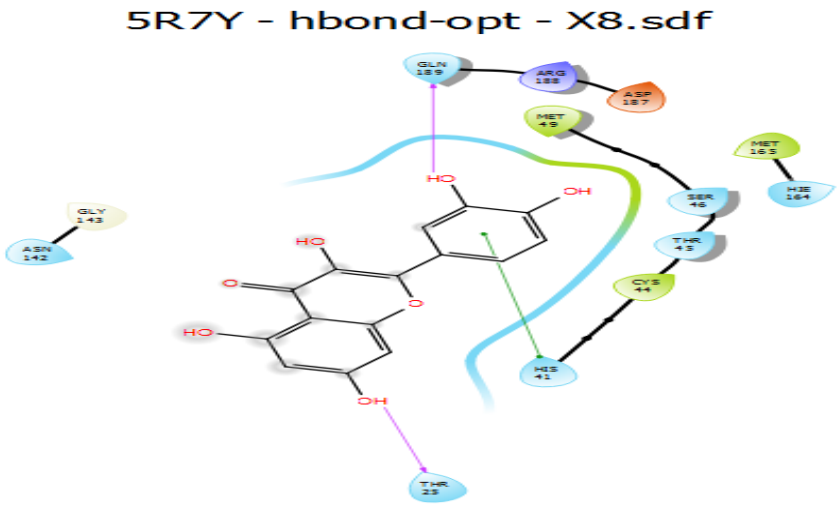

Fig-8. Schematic 2D representation of X8(2-(3,4-Dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-Benzopyran-4-one) in the binding pocket inhibition of Covid-19 5R7Y

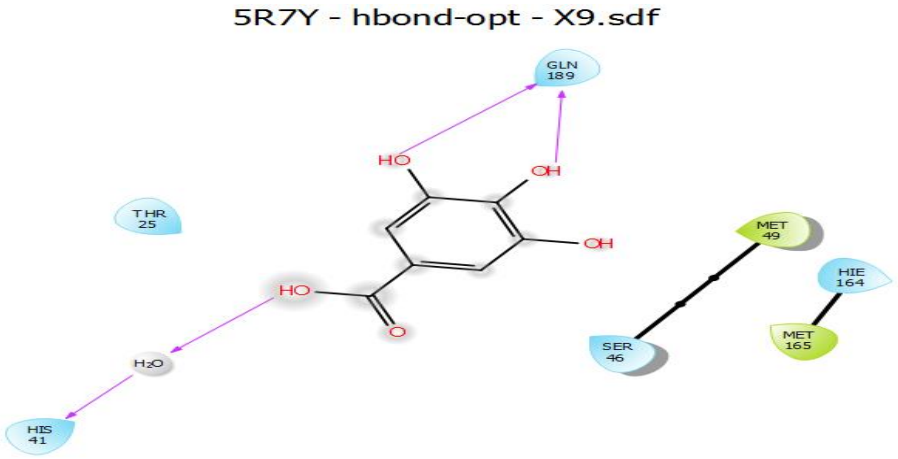

Fig-9. Schematic 2D representation of X9(3,4,5-Trihydroxylbenzoic acid) in the binding pocket inhibition of Covid-19 5R7Y

4. CONCLUSION

Currently Covid-19 has emerged in the human population due to no perfect drug. This aim of this study was to identify perfect inhibitor for Covid-19 by molecular dockings. As a result of this computational experimental study of Nine competitive ligands of Eleusine coracane and 5R7Y. To identify the docking accuracy about this target, docking simulation were evaluated. Interestingly, these docking results showed good interactions for all X1-X9 inhibitors. Especially among the set three compounds X8, X5,X9 reveled good binding interactions with 5R7Y.Further results proves, these compounds has high binding affinity and low binding energy. Therefore we concluded that phenolic derivatives of Eleusine coracane may represent for potential treatment option for covid-19. Based on these findings further research is necessary to find potential inhibitory activity of these phenolic compounds.

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6. AUTHORS CONTRIBUTION STATEMENT

Mrs.K.Sadhana performed computational Molecular docking and wrote the paper.Dr.S.Aruna and Dr.R.Girija are designed the project supervised and wrote the paper. The manuscript was written through contributions of all authors.

7. CONFLICT OF INTEREST

Conflict of interest declared none.

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