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Research Article

Molecular docking analysis of SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) with compounds from *Plectranthus amboinicus*

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Abstract:
It is of interest to document the moelcular docking analysis of SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) with compounds from Plectranthus amboinicus. Hence, we report the binding features of rutin, Luteolin, Salvianolic acid A, Rosmarinic acid and p-Coumaric acid with the target protein SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) for further consideration.

Key words: SARS-CoV-2, RdRp, *Plectranthus amboinicus*, molecular docking

Background:
The new strain of coronavirus SARS-CoV-2 (Severe Acute Respiratory Syndrome) is the infectious disease COVID-19 **[1]**. The structures of different SARS-CoV-2 protein / enzymes were solved. The structure data of RNA-dependent RNA polymerase (RdRp) and papa protease and key protease is relevant in drug discovery **[2,3]**. RdRp is the main enzyme that replicates the viral RNA genome and is it is a promising drug target **[3-4]**. RdRp of the SARS-CoV-2 shares 96 per cent of the sequence identity with SARS-CoV19 and hence the compounds or medications that are efficient towards RdRp of SARS-CoV are considered to be effective against the novel CoV. Molecular docking analysis of known RdRp-inhibiting antivirals, other FDA-approved medications, and phytochemicals to repurpose SARS-CoV-2 is documented **[5]**. The use of conventional medicines as an adjuvant for the treatment of COVID-19 is known **[6,7,8]**. Therefore, it is of interest to document the moelcular docking analysis of SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) with compounds from Plectranthus amboinicus.

Table 1: List of Selected compounds from *Plectranthus amboinicus*

S.No	Compound Name
1	1,2-Benzenediol 4-(1,1 dimethylethyl)_CID_12290195
2	1-Epi-cubenol_CID_519857
3	2-Phenyl ethyl tiglateStructure_SID_316964912
4	3,7,11,15–Tetramethyl-2-hexadecen-1-ol_CID_5366244
5	4 1 ,5,7-Trihydroxyflavone (apigenin)_CID_5280443
6	5,4' -Dihydroxy-3,7-dimethoxy flavone_CID_5318869
7	Aromadendrene_CID_91354
8	Carvacrol_CID_10364
9	Chavicol_CID_68148
10	Chrysoeriol_CID_5280666
11	Cirsimaritin_CID_188323
12	Durohydroquinone_CID_136346
13	Eriodictyol_CID_440735
14	Eugenol_CID_3314
15	Geraniol_CID_637566
16	Germacrene D_CID_521569
17	Luteolin_CID_5280445
18	p-Coumaric acid_CID_637542
19	Rosmarinic acid_CID_5281792
20	Rutin_CID_5280805
21	Salvianolic acid A_CID_5281793
22	Salvigenin_CID_161271
23	Spathulenol_CID_92231
24	Thymoquinone_CID_10281
25	Trans-sabinene hydrate_CID_12315151
26	Trans-α-Bergamotene_CID_521569
27	α-AmorpheneCID_12306052
28	β-Cedrene epoxideCID_91749511
29	β-Sesquiphellandrene_CID_519764
30	δ-3-Carene_CID_442461

Table 2: Molecular docking results obtained from PyRx

S.No	Compound Name	Binding Energy Kcal/mol	Hydrogen bond interaction	Length
1	Rutin_CID_5280805	-8.1	THR-556	2.3
			TYR-619	2.2
			CYS-622	2.2
			ASN-691	2.4
			ASP-760	2.5
2	Luteolin_CID_5280445	-7.5	THR-394	2.6
			ARG-457	1.9
			ASN-459	1.9
			ASN-628	2.2
3	Salvianolic acid A_CID_5281793	-7.2	ARG-555	2.1
			TYR-619	2.1
			LYS-621	1.9
			ASN-691	2.1
4	Rosmarinic acid_CID_5281792	-6.8	LYS-621	2.2
			CYS-622	2
			ASP-623	2
5	P-Coumaric acid_CID_637542	-6.7	TYR-456	
			ARG-553	
			ARG-555	
			SER-682	

Materials and Methods:

Protein Preparation:
The three-dimensional structure of the protein RdRp of SARS-CoV-2 (PDB ID: 6M71) was downloaded from the Protein Data Bank (www.rcsb.org/pdb). This structure is solved **[10]** with 2.90 Å resolution using electron microscopy. Three non-structured proteins (NSPs) such as one NSP7 and two NSP8 are involved in the structure as cofactors. NSP12, which is RdRp, is chain A and consists 851 amino acids. All water molecules, ions, and ligands were separated from the protein molecule using the PyMOL software. The hydrogen atoms were applied to the receptor molecule using the AutoDock Vina software's MG Tools **[11]** and saved in the Pdbqt format.
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Compound preparation:
Thirty compounds from the *Plectranthus amboinicus* plant were gleaned from literature. The compound structures were downloaded in .sdf format from the database of PubChem compounds (www.pubchem.ncbi.nlm.nih.gov/). All the compounds were translated to .Pdb format by using the online smiles converter. The energy of all ligands was minimized and translated to the PDBQT file format.

Molecular docking and interaction analysis:
The grid box around the binding pocket is positioned using a standard protocol **[12]**. PyRx has been used to screen the ligand files against the protein **[13]**. The interactions between the targeted protein and the ligands were analysed using the Pymol Molecular Visualization Tools **[14]**.

Drug-likeness prediction:
The Lipinski filters (http:/www.scfbio-iitd.res.in / software / drugdesign / lipinski.jsp) were used to measure the drug likeness of the compounds from the docking calculation. Four of the five parameters defined for drug likeness are molecular mass, cLogP, hydrogen donor and acceptor and molar refractive index **[14]**.

Results and Discussion:
It is of interest to document the moelcular docking analysis of SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) with compounds **(Table 1)** from Plectranthus amboinicus. Hence, we report the binding features of rutin, Luteolin, Salvianolic acid A, Rosmarinic acid and p-Coumaric acid with the target protein SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) for further consideration **(Table 2)**. The interactions between the targeted protein and the ligands were analysed using the Pymol Molecular Visualization Tools as shown in **Figure 1**.

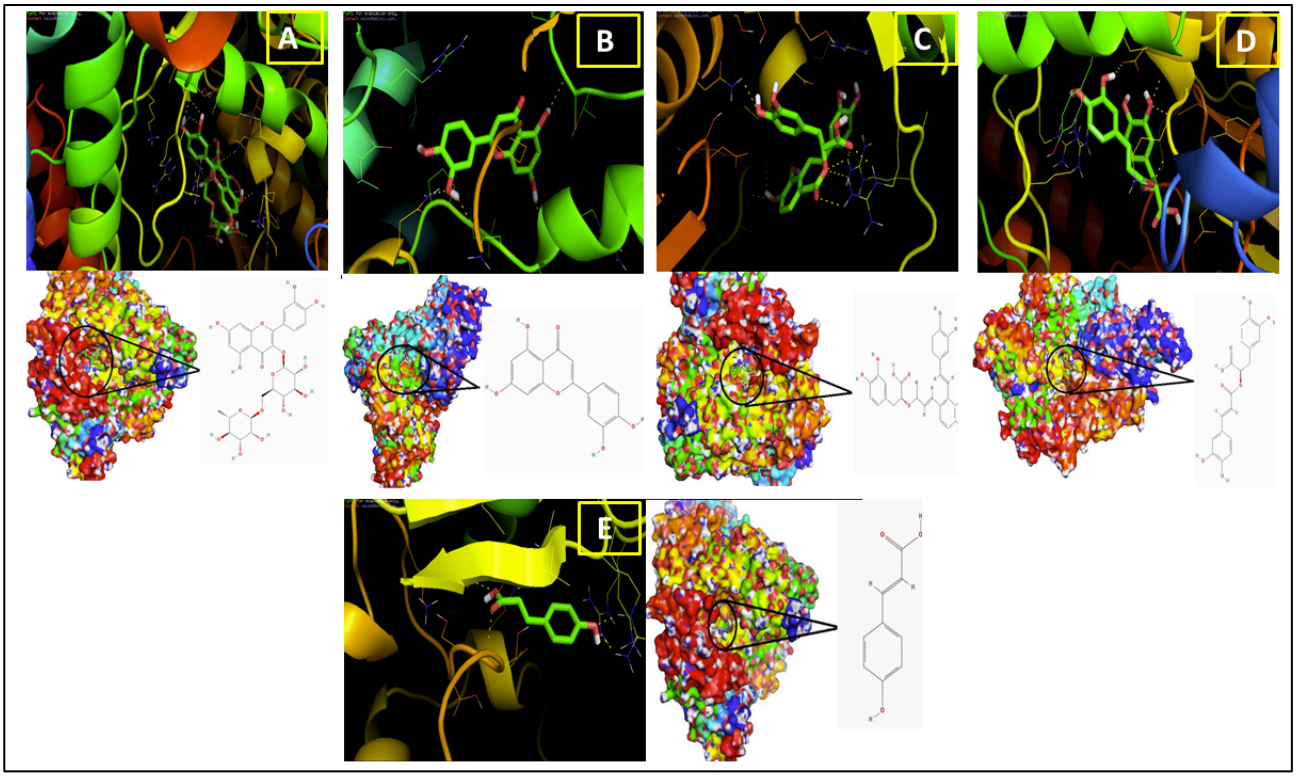

Figure 1: Molecular docking data of SARS-CoV-2 RdRp with (**a)** Rutin; (**b)** Luteolin; **(c)** Salvianolic acid A; **(d)** Rosmarinic acid and (**e)** p-Coumaric acid. Proteins are shown in ribbon and compounds are shown with stick representations

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Table 3: **The drug likeness properties of selected compounds**

Compound name	Molecular Mass [a]	Hydrogen bond donor[b]	Hydrogen bond donor [c]	LOGP[d]	Molar Refractivity[e]
Rutin	610	10	16	-1.8788	137.495483
Luteolin	280	4	6	-1.66883	61.014198
Salvianolic acid	494	7	10	3.3429	128.496552
Rosmarinic acid	360	5	8	1.7613	89.796974
P-Coumaric acid	164	2	4	1.49	44.776596

- [a]Molecular mass less than 500 Dalton; - [b]Less than 5 hydrogen bond donors; - [c]Less than 10 hydrogen bond acceptors; - [d]High lipophilicity (expressed as LogP less than 5)
- [e]Molar refractivity should be between 40-130

Conclusion:

We report the binding features of rutin, Luteolin, Salvianolic acid A, Rosmarinic acid and p-Coumaric acid with the target protein SARS-CoV-2 linked RNA dependent RNA polymerase (RdRp) for further consideration.

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