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Review Article

Anti-Covid-19 Phytochemicals

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A B S T R A C T

The Phytochemicals are the future phytomedicine for Covid-19 virus, therefore their antiviral affinity was differently viewed.

Keywords: Phytochemical, Covid-19, IC_{50}, Binding affinity, Structural resemblance.

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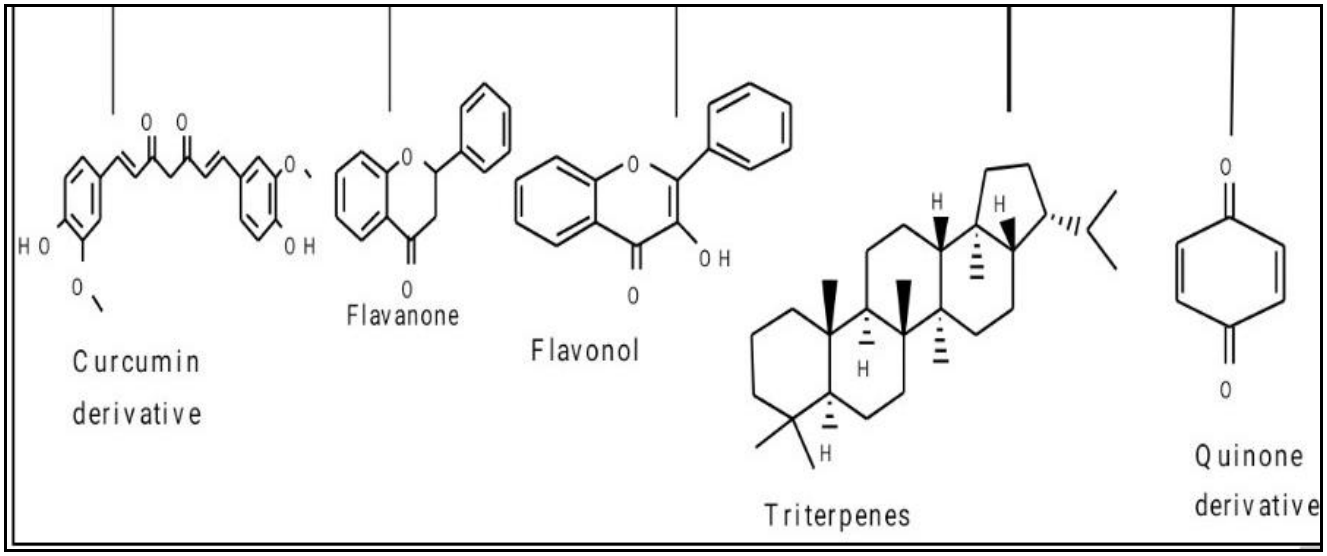
INTRODUCTION

Corona virus[1-5] pandemic posed a great medical challenge for the prevention of public health in 21st century. The natural products and their metabolites are used in traditional medicine for viral infections[6-8]. The vast library of phytochemicals was screened by molecular modeling, docking, virtual screening and molecular dynamics stimulation for the identification of potential anti-covid-19 phytochemicals.The basic structures of natural metabolites inhibitors (anti covid-19 bio products)[9,12] are.



Natural products highlighted their inhibitory actions against covid-19 proteins- $3CL^{pro}$, PL^{pro}, S, and ACE.Anti-covid-19 Phytochemicals can be classified in various chemical classes.

1. Alkaloids- Emetine, Tylophorine
2. Flavonoids and Chalcones- Quercetin, Apigenin
3. Steroids- Beta sitosterol
4. Glycosides- Rutin, Juglanin
5. Phenolic compounds- Aloeemodincurcumin
6. Tannins- Tannic acid, Eckol
7. Ligand- Savinin
8. Terpenoids- Ginkgolide A
9. Miscellaneous- Silvestrol

Natural products targeted spike-glycoprotein, an envelope glycoprotein, a nucleocapsid phosphoprotein and replicase complex for inhibitory action. The various inhibitory approaches[13] classify them as-

- Viral spike protein inhibitors
- Human ACE-2 receptor inhibitors
- $3CL^{pro}$ inhibitors
- PL^{pro} inhibitors
- Viral growth inhibitors
- Helicase inhibitors
- Cellular entry inhibitors

Theoretical methodology

The development of bioactive natural products against covid-19 involved the screening of phytochemicals[14-16] by molecular docking and virtual screening. Recently the virtual docking calculations for binding affinity of anti-Covid-19 phytochemicals were reported. The top ranked phytochemical structures against Covid-19 $3CL^{Pro}$ receptor and IC_{50}(vitro) are given in tables 1 and 2 respectively.

Table:1 . The top ranked phytochemicals against SARS-CoV-2 $3CL^{pro}$ receptor[17-18].

S.no	Phytochemicals	Docking score	Binding affinity (kcal\mole)
1	5,7,3′,4′- tetrahydroxy-2′-(3,3-dimethylallyl) isoflavone	-16.35	-29.57
2	Myricitrin	-15.64	-22.13
3	Methyl rosmarinate	-15.44	-20.62
4	3,5,7,3′,4′,5′-hexahydroxyflavanone 3-O-beta-D- glucopyranoside	-14.42	-19.10
5	(2S)-Eriodictyol 7-O-(6″-O-galloyl)-6beta-D-glucopyranoside	-14.41	-19.47
6	Calceotarioside B	-14.36	-19.87
7	Myricetin-3-O-beta-D- glucopyranoside	-13.70	-18.42
8	Licoleafol	-13.63	-19.64
9	Amaranthin	-12.67	-18.14
10	Nelfinavir	-12.20	-17.31
11	Prulifloxacin	-11.32	-15.40

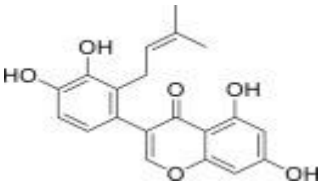
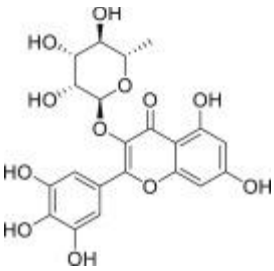
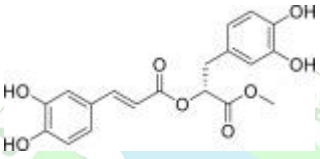
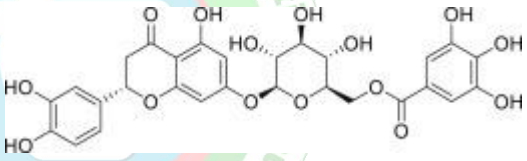
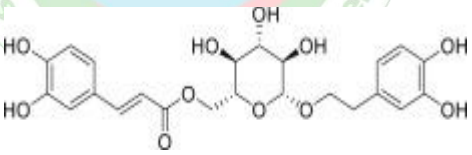
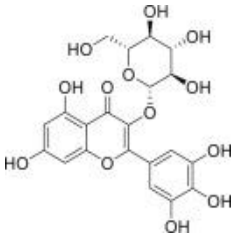
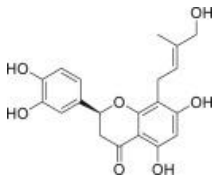
The amino acids Cysteine, Serine, Glutamine, Histidine, Methonine, Proline, Thronine, Glycine, Lucine, Arginine, Asparagine, Alanine are involved in hydrogen bonding and hydrophobic interaction at receptor site for compounds tabulated in table-1.

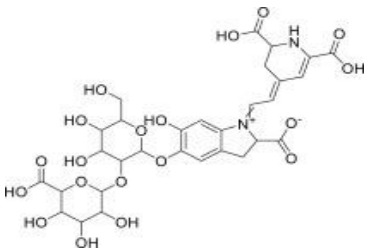
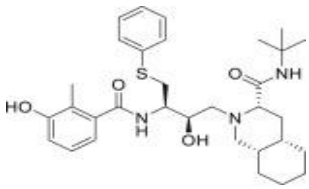
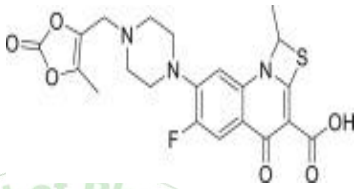
Table:2. IC_{50} values of selected Anti- SARS-Cov-1 natural metabolites[15].

S.no	Compound	IC_{50}
1	Isotheaflavin-3-gallate	7µm
2	Tannic acid	3 µm
3	Scutellarein	10 µm
4	Mycalamide A	0.2µg kg^{-1c}
5	Tetrandrine	295.6nM
6	Fangchinoline	919.2nM
7	Cepharanthine	729.7nM
8	Isolinoleic acid	50µM
9	Pristimerin	5.5mM
10	Tingenone	9.9mM
11	Iguesterin	2.6mM
12	Lycorine	15.7mM

The inhibitory concentrations of *Mycalamide A, Iguesterin, Tannic acid, Pristimerin* revealed that they have important structural features of lead or compounds for the drug development.

Table: 3. Top ranked phytochemical structure against covid-19 $3CL^{pro}$ receptor with their binding affinities[14].

S.no	Phytochemical name	Phytochemical structue	Binding affinity (kcal/mole)
1	5,7,3′,4′-Tetrahydroxy-2'-(3,3-dimethylallyl) isoflavone		−29.57
2	Myricitrin		−22.13
3	Methyl rosmarinate		−20.62
4	(2S)-Eriodictyol 7-O-(6″-O-galloyl)-beta-D-glucopyranoside		−19.47
5	Calceolarioside B		−19.87
6	Myricetin 3-O-beta-D-glucopyranoside		−18.42
7	Licoleafol		−19.64

8	Amaranthin		−18.14
9	Nelfinavir		−17.31
10	Prulifloxacin		−15.40

RESULT AND DISCUSSION

The interpretation of Table-3 Compounds- The mutual structural resemblance of compounds one to eight is noteworthy. The catecholic hydroxyls, hydroxylatedpyran | pyranone, and aliphatic chain of three or four carbons with pi-bond, hydroxyl and carbonyl impart range of binding affinity between -29.57 to -19.64 kcal/mole with an exception of compound seven, being glycoside. The sugar moiety may deviate the degree of structural resemblance due to unfavorable hydrophilicity.

The compounds nine to eleven have heteroatoms (N, O, S) of heterocyclics with lack of catecholic moiety contribution lowers the binding affinity. The compounds eleven is a structural analog of 6F- quinolone type of antibiotic. The binding affinity involves H-bondings and hydrophobic interactions at receptor site of $3CL^{pro}$.

The receptor aminoacids set the trending pattern for the affinity. The aminoacids- Cysteine, Serine, Glutamine, Histidine, Methonine, Proline, Threonine, Glycine, Leucine, Arginine, Asparagine and Alanine participate in binding affinity of tabulated compounds (Table.3).

CONCLUSION

The phytochemicals of angiospermic plants provide optimized |assertive treatment of Covid-19. The study of their drugability, solubility, stability and herbal standardization has progressed in recent times. The smart drug delivery technologies have overcomed the limitations in bioavailability and clinical efficacy by nanoparticle drone technique.

Finally the blocking of Covid-19 virulence by phytochemicals offer therapeutic alternative for drug-design and development.

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