Available online on 15.12.2020 at http://ajprd.com

Asian Journal of Pharmaceutical Research and Development

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Review Article

The Application of Marine Natural Products (MNPS) In Anti-Covid-19 Therapeutics

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A B S T R A C T

The bioprospecting of MNPs for the treatment of COVID-19 virus was attempted. The marine biodiversity is a remarkable source of bioactive chemotherapeuticals. The structural uniqueness of selected MNPs was correlatedwith reported binding energies to ascertain structure activity relationship (SAR) features.

Keywords: Marine, COVID-19, Natural product M^{pro}, Structural uniqueness.

A R T I C L E I N F O: Received 11 August 2020; Review Completed 15 Sept. 2020; Accepted 29 Oct. 2020; Available online 15 Dec. 2020

Cite this article as:

Pawar RS, Dimri M, Maithani A, Kush L, The Application of Marine Natural Products (MNPS) In Anti-Covid-19 Therapeutics, Asian Journal of Pharmaceutical Research and Development. 2020; 8(6):77-80.
DOI: http://dx.doi.org/10.22270/ajprd.v8i6.809

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INTRODUCTION

MNPs are rich source of antivirals for the treatment of viral infections[1-4]. Recently anti-COVID-19 MNPs were searched through chemical data bases. They were isolated and characterized from marine algae and sponges. The structural uniqueness of phlorotannins, oligomers of phloroglucinol, and pseudo peptides are pathologically important for the Covid-19 therapeutics[5-7].

Theoretical methodology

The vast library of MNPs was subjected to virtual screening/ docking for searching Mpro (covenzyme) inhibitors. The outlined molecular modeling procedure was followed to define the pharmacophore for MNPs[8-9].

MNPs Library → Pharmacophore Filter → Virtual Screening → Molecular Dynamics Stimulation (Redocking) → **Pharmacophore**

DISCUSSION AND RESULT

The molecular structure of pharmacophore should have interactional functions between drug and target, including electronic and steric features. The MNPs binding with enzyme(Mpro) active site involves three hydrogen bond

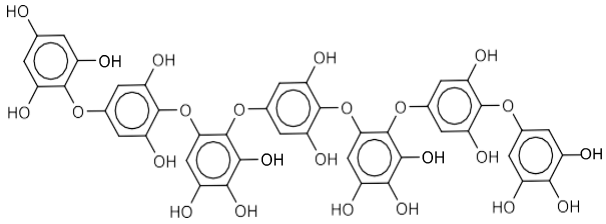
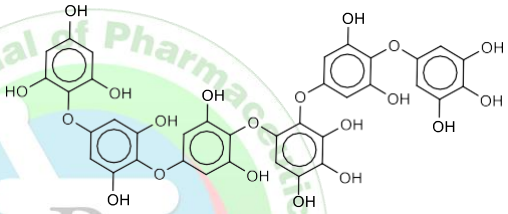
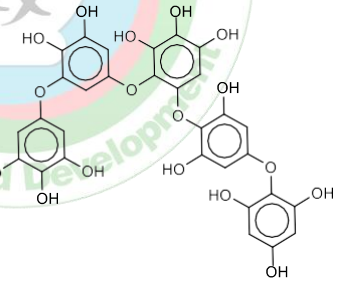
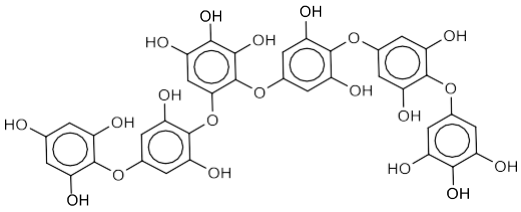
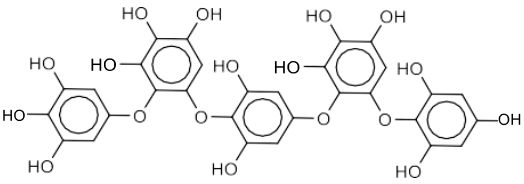
donors (amide nitrogen) and two hydrogen acceptors (negatively charged oxygen-carbonyl group) and

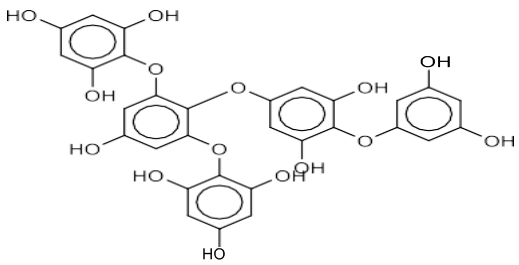
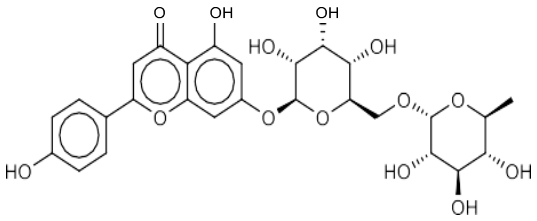
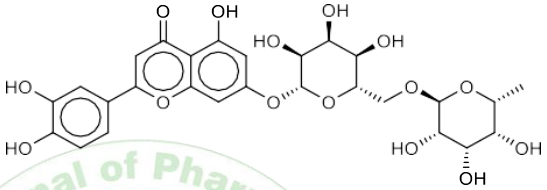
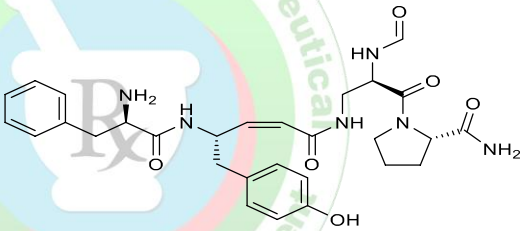
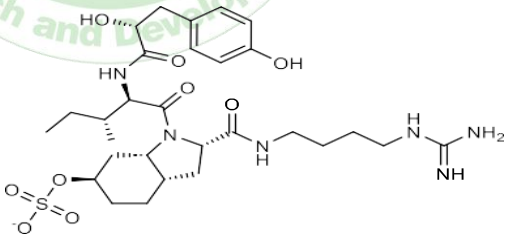
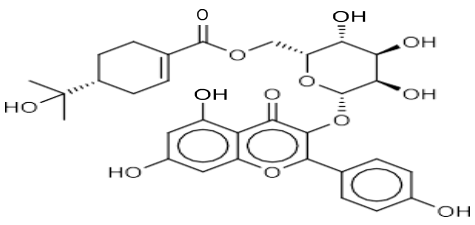
hydrophobic pocket (alkyl group-isopropyl). The pharmacophore of MNPs is composed of H-bond donor and acceptor and hydrophobic pocket. The range of (Compound-1) 7 aryls to (Compound-14) Zero revealed decline in binding energy due to loss of hydrophobicity. The high ΔG binding energy is supported by possible π-bond stacking with aromatic amino acids at enzymatic active site. The phenolic groups offered a network of hydrogen bonding. It is speculated that H-donors plays role in improving binding energy. The hetero atom nitrogen Lopinavir markedly lowers hydrogen donor capacity.

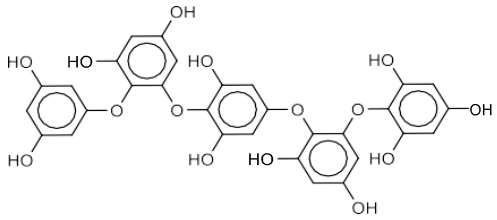
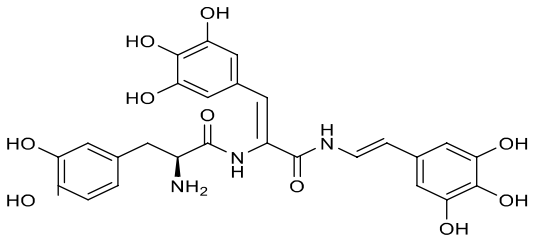
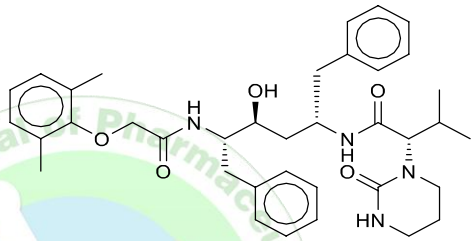
Phlorotannins have strong acidic nature due to presence of phenolic groups (range is between 5-7). They contribute oxygen atoms for the binding affinity. The lower pka are more favourable than higher ones for efficacy. They possess the pharmacophoric moieties for potent inhibitory action. The introduction of nitrogen atoms reduces acidic character, enhance H-bond acceptability and pka with reducing the inhibitory potency. All this can be considered as putative SAR comments for the poly phenolic structures of MNPs.

The structural anomalies are an exceptional feature of MNPs for Lipsinki's rule compliance which is widely violated in tabulated marine compounds due to molecular size, ionic property and hydroxyl prominence as H-donor bonds.

Table: 1 Selected MNPs-structures[7,9] and their binding free energies (ΔG_B, in Kcal/mol) are given in Table-one

Compound/Name	Structure	ΔG_B
1 Heptafuhalol A		-15.4
2 Phlorethopentafuhalol B		-14.6
3 Pseudopentafuhalol C		-14.5
4 Phlorethopentafuhalol A		-14.0
5 Hydroxypentafuhalol A		-14.6

6 Pentaphlorethol B		-13.9
7 Apigenin-7-O-neohesperidoside		-12.4
8 Luteolin-7-rutinoside		-12.1
9 Pseudotheonamide D		-12.2
10 Aeruginosin 98B		-12.1
11 Resinoside B		-12.2

12 Pentaphlorethol A		-12.8
13 Tunichrome An2		-11.5
14 Lopinavir		-10.3

CONCLUSION

An extensive study of MNPs is done by modern computational techniques since 2019. The advanced experimental research for the real medicinal application is still in progress. The marine pharmacology of MNPs can ensure the efficacy and safety of anti-covid-19 marine natural products. Moreover they have nutritional (sea weeds) and pharmacological properties therefore offer dual therapeutic options.

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