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Docking Studies between the Protein HMPV SH of the Human Metapneumovirus and compounds of *Ulva fasciata* Delile to prove Antiviral activity

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Abstract

Acute Respiratory infections are the major cause of childhood morbidity and mortality worldwide. Viruses account for the majority of acute respiratory infections in young children. Although Human metapneumovirus (HMPV) infections have been diagnosed in all age groups, this virus has its greatest effects in children. HMPV account for a major proportion of hospitalizations for lower respiratory tract infections in infants and young children. Marine organisms serve as the prolific source of natural products with therapeutic and nutritive properties. Some natural and synthetic compounds can prevent, suppress or reverse the progression of viral infections. Natural products have proven to be the most effective in terms of their ability to act as antiviral agents. Secondary metabolites produced from *Ulva fasciata* Delile exhibit various biological activities such as anti-viral, anti-fungal, anti- inflammatory, anti-cancerous etc. This study gives a supportive element for the development of drug against respiratory infections through docking using bioinformatic tools. The three effective compounds such as Alpha linolenic acid, Stearidonic acid and Sphingosine present in *Ulva fasciata* Delile were docked against HMPV SH protein, that is responsible for respiratory diseases. Energy values of the 3 docked compounds were noted and the best compound was selected by comparing the values with each compound.

Keywords: *Antiviral, Ulva fasciata Delile, Human Metapneumovirus, Hex, Docking, Energy Value*

Introduction

Algae are simple plants and diverse group of aquatic organisms that have the ability to conduct photosynthesis. Marine macro algae are considered as a source of bioactive compounds as they are able to produce great variety of secondary metabolites characterized by broad spectrum of biological activities such as antibacterial, anti-fungal, anti-inflammatory, antiviral etc. which acts as potential bioactive compounds of pharmaceutical applications. *Ulva fasciata* Delile, a marine macroalga produces some secondary metabolites that exhibit various biological activities such as anti-bacterial, anti-inflammatory, anti-proliferative, antiviral etc (Shalaby, 2011). Antimicrobial activity was reported in *Ulva fasciata* due to the presence of Guainane sesquiterpene derivatives (guai-2-en-10a-ol and guai-2-en-10a-methanol), polyunsa-turated fatty acids (stearidonic acid and α-linolenic acid), ulvanobiuronic acid 3-sulphate, bromophenolic and sphingosine (Chakraborty *et al*., 2010; Selvin *et al.,* 2004). It is reported that *Ulva fasciata* extract possesses anti-bacterial and anti-viral activities. Sulphated polysaccharide extract collected by maceration and decoction from *Ulva fasciata* possesses 100% inhibitory activity against Human metapneumovirus (Paulert *et al*., 2009 ; Mendes *et al*., 2010). Human metapneumovirus is a paramyxovirus that was discovered in 2001 in the Netherlands. Epidemiologic studies have shown it to be a major cause of acute respiratory tract disease in normal infants and children worldwide. Human metapneumovirus is also a significant cause of acute respiratory disease in adults, particularly the elderly and those with conditions such as chronic obstructive pulmonary disease, asthma, and cancer. As there is no rapid diagnostic assay, reverse transcriptase polymerase chain reaction is most widely used (Williams *et al*., 2005). HMPV SH is one of the proteins present in HMPV, and can inhibit membrane fusion function. By using bioinformatic techniques, the binding affinity of the components present in *Ulva faciata,* that have the antiviral property with the HMPV SH protein can be detected. It will further lead to a stepping stone for drug designing against HMPV. The selected major components are Alpha linolenic acid, Stearidonic acid and Sphingosine. The study of the docking between the components present in the alga and protein in virus gives a satisfying energy value after binding. Docking

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of the components with the protein gives supportive evidence to the antiviral activity of *Ulva fasciata* against HMPV.

Materials and Methods

In the present study, online and offline tools were used for the structural identification at molecular level and for carrying out the docking between the components in the alga and the protein of the virus. The selected HMPV SH protein is retrieved from Protein Data Bank (PDB). From HMPV SH, 5U68 is selected for the current study which shows host as human in PDB. PubChem is used to retrieve the physical and chemical properties such as molecular weight, hydrogen bond donor and acceptor count and Log P value of selected compounds namely Alpha linolenic acid, Stearidonic acid and Sphingosine. It was to check whether they obey Lipinski's rule of five. PubChem is also used to retrieve the canonical SMILES of the selected compounds. Rasmol is used for graphic visualization of ribbon model of protein (Fig.1) and stick model of compounds (Fig.2). Hex used for docking of compounds with 5U68 HMPV SH protein. Swiss-pdb is used to view the active site of the protein and 3D structure of the docked complex.

Results and Discussion

Molecular docking of the protein and compounds from the alga was done by using Bioinformatics tool Hex. Docking of the compounds (ligand) present in *Ulva fasciata* Delile and 5U68 HMPV SH protein present in Human metapneumovirus using n Hex is done for the identification of binding affinity by calculating the energy values. The 3D structure of docked complex and the active site of the protein were analyzed in Swiss-pdb (Fig.3). The energy values obtained from docking of each compound with protein were noted (Table 1). The docking value of Alpha linolenic acid with 5U68 HMPV SH protein was -301.95, Stearidonic acid was -317.48 and that of Sphingosine was -294.39. In the binding of the three active compounds with 5U68 HMPV SH protein, the energy value was found to be maximum in Sphingosine with -294.39.

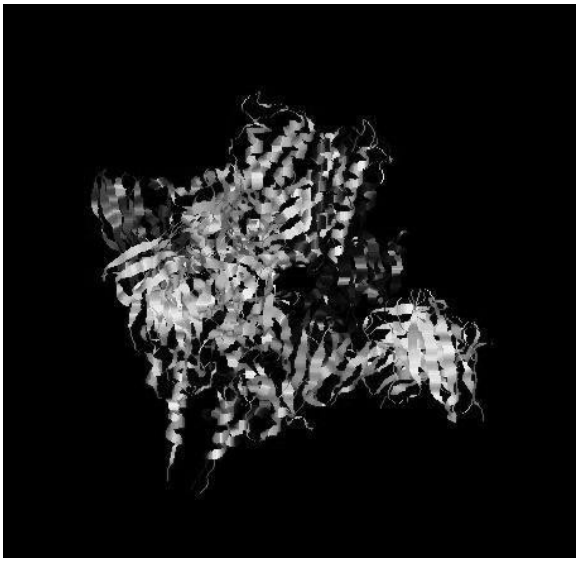

Fig.1: Ribbon model of 5U68 HMPV SH Protein

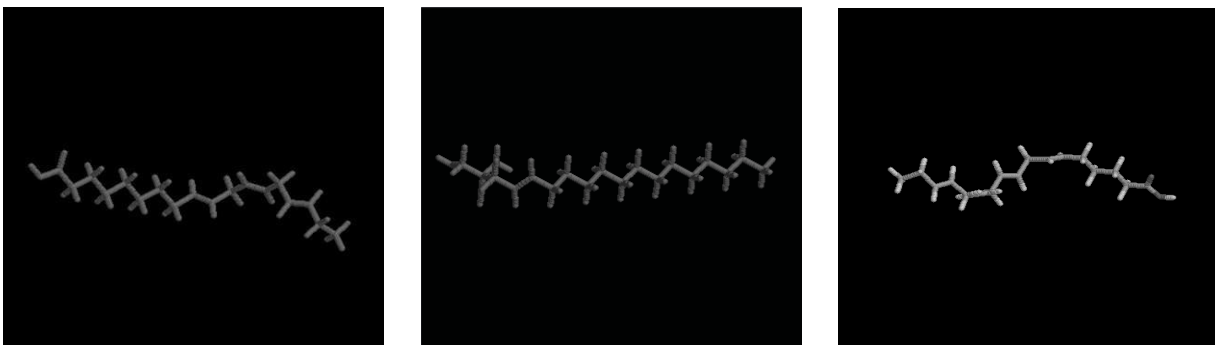

Fig.2: Stick model of Alpha-linolenic acid, Sphingosine and Stearidonic acid

Fig 3: Docked complexes of Alpha-linolenic acid, Sphingosine and Stearidonic acid bound with the active site of 5U68 HMPV SH Protein

Lipinski's rule of five is a rule of thumb to evaluate drug likeness to determine if a chemical compound with a certain pharmacological or biological activity has properties that would make it a likely orally active drug in humans. The rule describes molecular properties important for a drug's pharmacokinetics in the human body including their absorption, distribution, metabolism and excretion. Lipinski's rule states that, in general, an orally active drug has no more than one violation of some criteria i.e, Molecular weight<500, Log P value<5, H-bond donor<5, H-bond acceptor<10. Lipinski's rule of five for the selected compounds taken in the study is shown in (Table 2). In the present study all the three compounds did not obey the Lipinski's rule of five as in the case of Log P value. The violation of one rule may not necessarily result in poor absorption. However poor absorption increases with the number of rules broken and the extents which they exceed.

Table 1: Energy Values Obtained After Docking

Sl.No	Compounds	EnergyValue
1	Alpha-linolenicacid	-301.95
2	Stearidonicacid	-317.48
3	Sphingosine	-294.39

Table 2: Physical Property Value of the Compounds

Sl.No	Properties	Alpha-linolenicacid	Stearidonicacid	Sphingosine
1	Molecularweight	278.4	276.4	299.5
2	H-bonddonorcount	1	1	3
3	H-bondacceptorcount	2	2	3
4	LogPValue	5.9	5.2	5.3

Conclusions

In the present study, molecular docking of protein and compounds from the alga *Ulva fasciata* Delile was done using the bioinformatics tool Hex. The docking of the 3 compounds in *Ulva fasciata* was carried out to find the binding affinity of those compounds with the protein 5U68 HMPV SH present in the virus Human metapneumovirus causing respiratory diseases. From the energy values obtained, Sphingosine showed the highest value of 294.39. Hence of the three compounds, Sphingosine shows the highest binding affinity with the protein HMPV SH. Hence on the basis of docking study, it can be concluded that the compound Sphingosine from the green alga *Ulva fasciata* Delile can be used as a drug to treat against the Human metapneumovirus causing respiratory diseases.

Acknowledgements

We thank the Principal and Staff of Sree Narayana College, Cherthala for the support offered to complete this work.

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