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# A COMPUTATIONAL APPROACH FOR PREDICTING THE INTERACTION OF COMPOUNDS FROM ULVA LACTUCA L. WITH LOW DENSITY LIPOPROTEIN

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***Abstract***

Hyperlipidemia is the condition in which the blood contains high levels of fats. Hypercholesteromia is a type of hyperlipidemia in which blood contains high levels of LDL cholesterol or bad cholesterol. This condition is characterized by increased fatty deposits in the arteries and thereby increases the risks of atherosclerosis. So increased levels of Low Density Lipoprotein increases the risks of cardiovascular diseases. Algae can be used as an effective source against hyperlipidemia. *Ulva lactuca* Linneaus is a green marine macroalgae which have many therapeutic effects. Sulfated polysaccharides of *Ulva lactuca* commonly called Ulvan is mainly composed of Rhamnose-3-sulfate, Glucuronic acid and Xylose. These compounds exhibit anti-hyperlipidemic property. These compounds have been taken for the present study. Molecular docking is done to perform the binding affinity of these compounds with Low Density Lipoprotein by using HEX software. This study reveals that the highest energy value observed for the three compounds with the target are- Rhamnose-3-sulfate with energy value -198.11, Glucuronic acid with energy value -175.05 and Xylose with energy value -161.56. From the results it can be concluded that Rhamnose-3-sulfate have less energy and hence strong interaction with the Low Density Lipoprotein when compared to other two. Further research is required to find out the interaction of the compounds in *invitro* conditions.

**Key words:** Hyperlipidemia, Hypercholesteromia, *Ulva lactuca*, Molecular Docking

## Introduction

The algae are chlorophyll containing primitive plants. Often fast growing and able to live in freshwater, sea water, or damp soils. The marine environment is a rich source of chemical structures with numerous beneficial health effects. Among marine organisms, marine algae have been identified as an underexploited plant resource and they are recognised as valuable sources of structurally diverse bioactive compounds. Many bioactive and pharmacologically active substances have been isolated from algae. Of the total 221 worldly known seaweeds species, about two-third are reported for food application (Zemke White & Ohno.,1999). These seaweeds, since prehistoric time, had been remained a staple food and vital part in Chinese, Japanese and Korean diet. 20% of Asian diet is comprised of seaweeds that are relished not for their nutritional viewpoint but of unique and enchanting flavor. But in Western diet, seaweeds are just used as food additives or extracts (Carvalho *et al*.,2009). Moreover, biologically active compounds isolated from marine macroalgae exhibit various biological activities such as antioxidant, antiviral, anti-allergic, anti-inflammatory, anti-cancer etc. The green algae *Ulva lactuca* Linnaeus have been found to have antimicrobial, antibacterial, preservative, anticoagulant, antiperoxidative (Hanaa *et al*.,2009), antihyperlipidemic, hepatoprotective, anti-inflammatory, antiprotozoal, antiviral activities and also employed as dietary fibres in areas of Scotland. The methanolic extract of *Ulva lactuca* was found to have anti-inflammatory activity (Margret *et al*.,2009). One of the major bioproducts of interest from *Ulva* is the sulfated polysaccharide known as ulvan. Ulvan has demonstrated significant biological activities in both animal and

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plant systems in *in vitro* and *in vivo* studies. It has reported that this green algae has sufficient antioxidants, antimicrobial, antiviral, antihyperlipidemic, antitumour, anti-inflammatory properties which suggest it a potent source against various ailments. Hyperlipidemia is a major risk factor for heart disease that represents a major problem and affects public health. Polysaccharides isolated from *Ulva lactuca* showed anti-hyperlipidemic activity (Pengzhan *et al*.,2003). Sulfated polysaccharides are complex and heterogenous, and they are appropriate to reduce hyperlipidemia so they are promising substances in reducing coronary heart disease.

The bioactive properties of green algae *Ulva lactuca* were assessed through computational approach. Computational studies were carried out using the selected compounds with the proteins responsible for the diseases using molecular docking software. From the docking results it is able to predict and find the compound with least binding energy. The suitable interaction of ligands with active site of protein indicate that it has the potential to use as a drug against hyperlipidemia. The compounds from algae taken as ligands and protein associated with hyperlipidemia taken as the target.

In the present study, three compounds from *Ulva lactuca* namely Rhamnose-3-sulfate, Glucuronic acid and Xylose were studied to find the binding affinity with Low Density Lipoprotein (LDL) using Hex software.

**Materials and Methods:**

In the study, Online Tools, Online Servers and Offline Tools of Bioinformatics are used. The receptor protein responsible for the hyperlipidemia and the compounds in *Ulva lactuca* showed antihyperlipidemic property. The 3D structure of receptor LDL were retrieved from PDB. The ligands such as Rhamnose-3-sulfate, Glucuronic acid and Xylose are retrieved from Online Tool and Online Server. Collection of Canonical SMILES of the compounds are from structure database PubChem. PubChem consists of three inter-linked databases, Substance, Compound and BioAssay. PubChem is used to retrieve the properties of compounds such as Lipinski's rule of Five. Canonical SMILES are converted to 3D structure using Online SMILES Translator. Then the receptor molecule LDL and compounds as ligands are loaded in the Hex software for molecular docking. Hex can calculate protein ligand docking, assuming the ligand is rigid, and it can superpose pairs of molecules using only knowledge of their 3D shapes. The parameters used in HEX for the docking process are correlation type - shape only, FFT mode - 3D fast lite, grid dimension – 0.75, receptor range – 180, ligand range 180, twist range– 360, distance range– 40. After the docking of each compounds with LDL, the docked complexes of three different energy values are obtained based on their binding affinity. RasMol and Swiss pdb viewer are the efficient tools for viewing and modelling of proteins as well as small molecules. Swiss- PDB Viewer is used for structural alignments, homology modelling, mutating molecular models, energy minimization, and many other modeling tasks. In this study, the visualization of docked complexes of protein and compounds is by RasMol and Swiss-PDB Viewer. The visualization of active site of protein is by Swiss-PDB Viewer

**Results and Discussion:**

In this study, a docking tool named Hex is used to find the affinity between the compound and the target (Mathew and Raj.,2009). Figure 1 shows the secondary structure of Low Density Lipoprotein. Figure 2 represents the stick model of Rhamnose-3-sulfate as in green colour, Glucuronic acid in pink colour and blue coloured Xylose. The energy values of three compounds after docking is tabulated in Table 1. The Lipinski's rule of five of the three compounds are tabulated in Table 2. Figure 3 depicts the docked complexes of Rhamnose-3-sulfate (green), Glucuronic acid (blue) and Xylose (white) with LDL (pink). The protein and compounds are in spacefill model. All the three compounds obeys the Lipinski's rule (Lipinski *et al*.,2001). Violation of one rule may not -

necessarily result in poor absorption. However, poor absorption increases with the number of rules broken and the extent to which they are exceeded. Lipinski's properties are useful in screening good drug.

## Conclusion

The present study is carried out to establish the binding affinity of the compounds isolated from the green algae *Ulva lactuca* L. with Low Density Lipoprotein receptor through docking studies. Compounds isolated from this algae such as Rhamnose-3-sulfate, Glucuronic acid and Xylose which exhibit antihyperlipidemic activity. Docking is applied to perform the binding affinity of these compounds with LDL by using Hex. This study reveals that the highest energy value observed for the three compounds with the target are: Rhamnose-3-sulfate with -244.214 energy value, Glucuronic acid with energy value -103.32 and Xylose with energy value -120.05. From this results it can be concluded that the compound Rhamnose-3-sulfate have less energy value when compared with the other compounds Glucuronic acid and Xylose. Hence strong interaction with the LDL and found to have good anti-hyperlipidemic property.

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**Table 1.** Energy values obtained after docking

| Compounds | Energy Value |
|---|---|
| Rhamnose-3-sulfate | -198.11 |
| Glucuronic acid | -175.05 |
| Xylose | -161.56 |

**Table 2.** Properties of Compounds

| Properties | Glucuronic acid | Rhamnose-3-sulfate | Xylose |
|---|---|---|---|
| Molecular Weight | 194.139 g/mol | 244.214 g/mol | 150.13 g/mol |
| H- Bond Donor Count | 5 | 4 | 4 |
| H- Bond Acceptor Count | 7 | 8 | 5 |
| LogP | -2.3 | -2.8 | 2.5 |

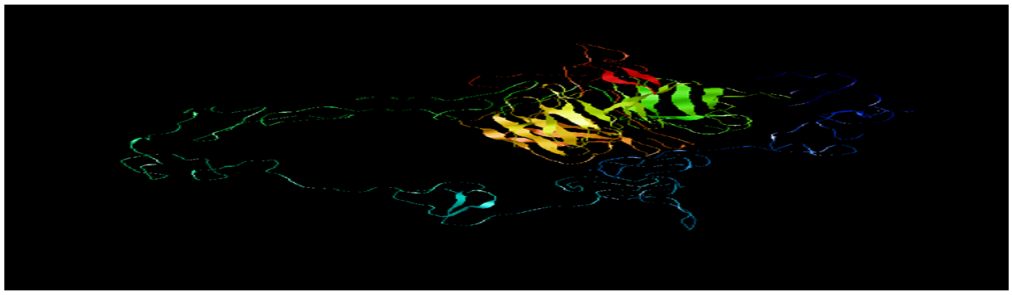

**Figure 1.** Secondary structure of LDL

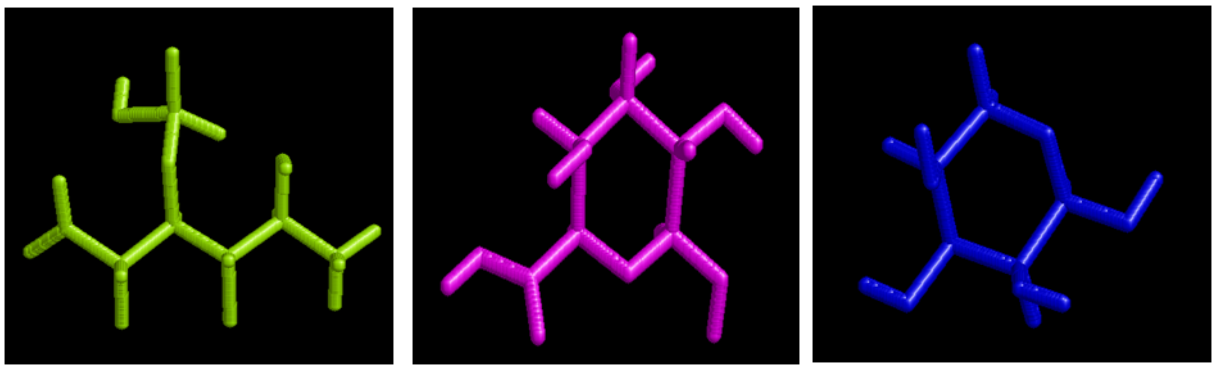

**Figure 2.** Stick Models of Rhamnose-3-sulfate, Glucuronic acid and Xylose

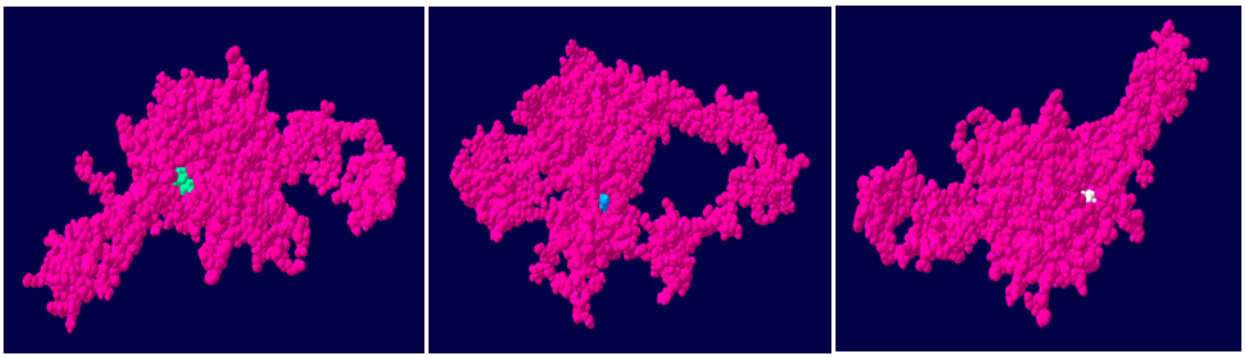

**Figure 3.** Docked Complexes of Rhamnose-3-sulfate, Glucuronic acid and Xylose bound with the active site of Low Density Lipoprotein

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