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IN SILICO STUDY ON ALPHA-AMYLASE AND ALPHA-GLUCOSIDASE INHIBITORY ACTIVITY OF COMPOUNDS FROM SARGASSUM WIGHTII GRIVELLI EX J. AGARDH

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Abstract

Type II Diabetes mellitus is the most common diabetes which is characterized by the insulin resistance of the body. Treatment of this disease without any side effects is still a challenge to the medical system. In the present study, the compounds from Sargassum wightii namely Hexadecanoic acid, Fucosterol and Hentriacontate were used to perform molecular docking with the enzymes Alpha-amylase and Alpha-glucosidase. The docking is conducted using the software Hex. Docking energy values obtained for Alpha-amylase with Fucosterol, Hexadecanoic acid and Hentriacontate were -268.85, -220.24 and -144.07 respectively. The energy values obtained for Alpha-glucosidase with Fucosterol, Hexadecanoic acid and Hentriacontate were -56.31, -55.81 and -30.99 respectively. From this result it can be concluded that the complex with Fucosterol has less energy value and hence strong interaction with the enzymes when compared with Hexadecanoic acid and Hentriacontate.

Key words: Type II Diabetes mellitus, Sargassum wightii Grivelli ex J. Agardh, Docking, Energy value.

Introduction

Algae are capable of providing bioactive compounds for producing novel medical and pharmaceutical substances. Recent researches have revealed their potential as complementary medicine. Marine algae is a rich source of chemically diverse compounds with numerous biological activities. Presently, several lines of studies have proved insight into biological activities of marine algae including antioxidant, anticancerous, antiobesity, antidiabetic, antihypertensive, antihyperlipidemic, anticoagulant, anti-inflammatory, immunomodulatory, antiestrogenic, thyroid stimulating, neuroprotective, antifungal, antibacterial and tissue healing properties (Khalid *et al*., 2018).

Sargassum wightii Grivelli ex J. Agardh is a marine brown alga. A wide range of bioactive properties have been reported from this alga. Unnikrishnan *et al*., (2015) reported that the ethyl acetate and petroleum ether extract of *Sargassum wightii* showed significant inhibitory activity on Alpha- amylase and Alpha-glucosidase enzymes. These are the enzymes involved in carbohydrate metabolism. Alpha-glucosidase plays its part in the lysis of disaccharides and starch to produce glucose, whereas the Alpha- amylase causes the breakage of carbohydrates having long chains. These are considered as primary enzymes involved in digestion process and they play their part in the absorption within intestine. Inhibitors of these enzymes can slow down carbohydrate absorption by prolonging total carbohydrate absorption time, decreasing the rate of glucose absorption and subsequently reducing the post prandial plasma glucose increase. The

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present study is aimed to find the binding affinity of the compounds isolated from *Sargassum wightii* such as Hexadecanoic acid, Fucosterol and Hentriacontate with the targets Alpha - amylase and Alpha- glucosidase through computational docking by using Hex.

Materials and Methods

Offline tools like Protein Data Bank and PubChem as well as online tools like Rasmol, Hex, Swiss-PDB viewer are used for the study. Protein Data Bank is the central archive of experimentally solved molecular structures of large biomolecules like proteins and nucleic acids. In the present study, targets Alpha- amylase (2QMK) and Alpha- glucosidase (5GNN) retrieved from Protein Data Bank are used as three dimensional structures. The structure of compounds such as Hexadecanoic acid, Fucosterol and Hentriacontate are collected from the database called PubChem. PubChem provide easy access to all deposited data and individual data analysis tools (Sayers *et al*., 2010).

Rasmol is used as the structure visualization tool. The program reads the 3-D coordinates for the molecule using the pdb file format. It displays the molecule in various representations and allowed to rotate interactively. The molecules and proteins are viewed through this tool.

Hex is used as an interactive molecular graphics program for calculating and displaying feasible docking modes of pairs of protein and the compound. Hex is also used to calculate protein- ligand docking, assuming the ligand is rigid and it can superpose pairs of molecules using the knowledge of their 3-D shapes. The parameters used in Hex for docking purpose 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.

Swiss-PDB viewer is used for analysing several proteins at a time. The proteins are superimposed to deduce structural alignments and compared their active sites or any other relevant parts. Swiss-PDB viewer is then used to model the structure of complex obtained from Hex. Space fill model is used to find the interaction between target and compounds after docking.

Results and Discussion

Molecular docking has become an interestingly important tool for drug discovery. It is one of the most important method for finding the affinity between the compounds and the target protein (Gschwend *et al*., 1996). The molecular docking approach can be used to model the interaction between a small molecule and a protein at the atomic level, which allow us to characterize the behaviour of small molecules in the binding site of target proteins as well as to elucidate fundamental biochemical processes (Mc Conkey *et al*., 2002). Molecular docking methods can provide a relatively fast and economic alternative to standard experimental techniques (F Sousa. 2010). Modi *et al*., (2013) concerned the docking of the analogs of the drug BMS- 448044, which is a promising drug showing antiviral activity against HIV. The analogs were created with some useful modifications to this drug. The analogs were docked against GP 120 receptor which was the main interacting component of the virus. In this study -252.27, -263.29 were some of the energy values obtained and showed to be the best docking scores. Prakash *et al.,* (2010) conducted a docking experiment to find the best analog of the drug Progunalin for the treatment of malaria. These drug -

analogs were docked against the receptor 1MVT. The higher docking scores obtained using Hex were -200.81 for analog 1 and –201.92 for analog 2 where as the docking score obtained for Progunalin was -174.54. Based on this studies it is concluded that some of the modified drugs are better than commercial drugs available in the market. The docking was conducted using Hex software.

The three compounds Hexadecanoic acid, Fucosterol and Hentriacontate derived from *Sargassum wightii* Greville are docked with receptor Alpha- amylase and Alpha-glucosidase and computed the energy values using Hex. The energy value of Alpha-amylase -Hexadecanoic acid complex was -220.24, Alpha-amylase - Fucosterol was -268.85 and Alpha- amylase -Hentriacontate was -144.07. So the energy values obtained are found to vary between -269 and -144. Hentriacontate showed high energy value and hence exhibited less stability, where as Fucosterol and Hexadecanoic acid possessed less energy values and therefore high stabilities. Simlarly Alpha-glucosidase -Hexadecanoic acid complex was -55.01, Alpha -glucosidase - Fucosterol was -56.85 and Alpha-glucosidase -Hentriacontate was -30.99. Here the energy values obtained are found to vary between -56 and -30. Based on energy values, Fucosterol can be considered as the best compounds among the three. They showed good binding affinity towards the receptor. The result shows that Fucosterol can be considered as a promising anti-diabetic compound.

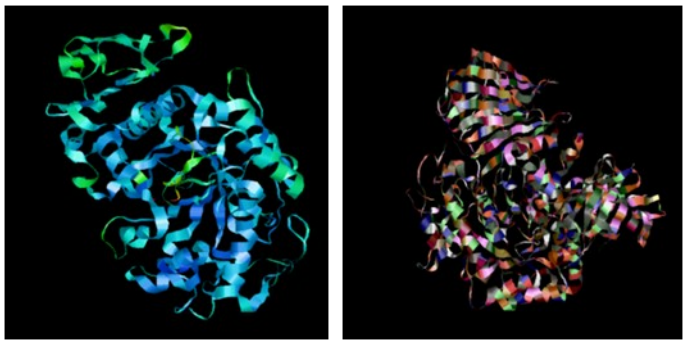
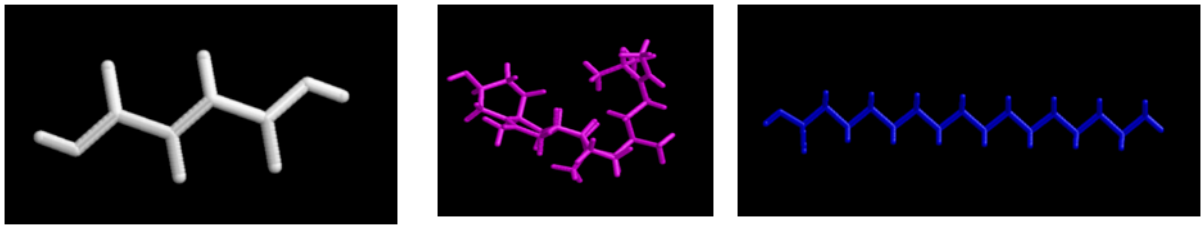
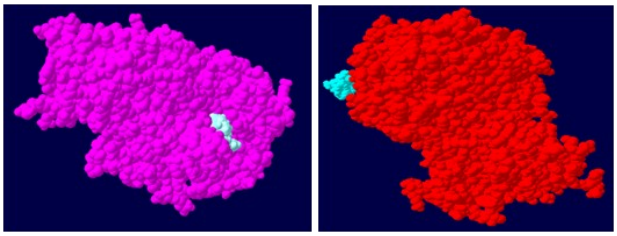


Figure 1. Secondary structure of (a) Alpha- amylase, (b) Alpha- glucosidase



(a) **(b)** **(c)**

Figure 2. Secondary structure of (a) Hexadecanoic acid (b) Fucosterol and (c) Hentriacontate



(a) **(b)**

Figure 3. Docked complexes (a) Fucosterol bound to Alpha- amylase (b) Fucosterol bound to Alpha- glucosidase

Conclusion

This study is carried out to establish the affinity of the compounds isolated from algae *Sargassum wightii* Grivelli ex J. Agardh with Alpha- amylase and Alpha- glucosidase enzymes through docking. Among the three compounds from the algae, Hexadecanoic acid, Fucosterol and Hentriaconate, Fucosterol showed excellent binding affinity against Alpha- amylase and Alpha- glucosidase and found to be a good anti-diabetic compound.

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