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ARTICLE

In Silico Prediction in Binding Affinity of Compounds Isolated from *Sargassum wightii* with Tau Protein Associated with Alzheimer's Disease.

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Abstract

Alzheimer's disease is an irreversible neurodegenerative disease that slowly destroys memory and thinking skills and eventually the ability to carry out the simplest tasks. Recent statistical studies indicate that Alzheimer's disease rank third, just behind heart disease and cancer as a cause of death for older people. Tau protein forms neurofibrillary tangles, which start in the areas of the brain important for memory then march through the rest of the brain as symptoms progress. Algae can be used as a source of treatment against this. Sargassum wightii which is a brown marine macroalgae is having many therapeutic effects. Compounds isolated from this algae such as Di-isooctyl ester,1,2-benzenedicarboxylic acid and Sargaquinoic acid exhibit neuroprotective activity. These compounds have been taken for the present study. Docking is applied to perform the binding affinity of these compounds with tau protein by using Hex. This study reveals that the energy value observed for the three compounds with the target are- Di-isooctyl ester with energy value is -311.89, 1,2-benzenedicarboxylic acid with energy value -281.85 and Sargaquinoic acid with energy value -311.66. From this result it can be concluded that the compound Di-isooctyl ester and Sargaquinoic acid have less energy and hence strong interaction with Tau protein when compared with 1,2-benzenedicarboxylic acid. Further studies are required to find the interaction of the compound in in vivo and in vitro conditions.

Keywords: Alzheimer's disease, Sargassum wightii, Docking, Energy value

Introduction

Seaweeds are rich in soluble dietary fibers, proteins, minerals, vitamins, antioxidants, phytochemicals and polyunsaturated fatty acids with low caloric value. They are an excellent source of vitamins. Their aminoacid content is well-balanced and contains most of the essential aminoacids needed for life and health. Moreover, compounds isolated from seaweeds exhibit various anti-oxidant, anti-viral, anti-allergic, anti-inflammatory, anti-cancerous and anti-coagulant activities. Algae have been recognized as a rich energy source and thus have been utilized to produce many biofuels such as bioethanol, biodiesel and many more. These renewable fuels products are being termed as third generation fuels (Fayaz et al., 2005).

Sargassum, the marine macroalga belonging to the Class Phaeophyceae is widely distributed in tropical and temperate oceans. It belongs to the Order Fucales and Family Sargassaceae.

Alzheimer's disease is a progressive neurodegenerative disease resulting in the gradual decline of a person's memory and ability to learn. In Alzheimer disease abnormal aggregation of a microtubule-associated protein expressed in neurons is observed. This protein acts to stabilize microtubules in the cell cytoskeleton. Like most microtubule-associated proteins, it is normally regulated by phosphorylation. In Alzheimer's patients, hyperphosphorylated protein accumulates as paired helical filaments that in turn aggregate into masses inside nerve cell bodies forming neurofibrillary tangles. The main component of the tangles is one form of a protein called Tau protein. Tau protein has the ability to bind and stabilize the cell's internal skeleton called microtubule. In neuron cells that are healthy, microtubules form structures like train tracks, which guide nutrients and molecules from the centre of the cells down to the end of the axons. Tau protein normally forms the connector pieces of the microtubule tracks. In the cells which are affected by Alzheimer's, the train track structures collapses and the Tau protein is changed chemically so that it can no longer hold the pieces together (Gail and William, 2004).

Molecular docking has become an increasingly important tool for drug discovery. It is one of the most important method for finding the affinity between the compounds and the target protein. Programs based on different algorithms help to perform molecular docking studies, which have made docking an increasingly important tool in pharmaceutical research. The molecular docking approach can be used to model the interaction between a small molecule and a protein at the atomic level, which help to characterize the behaviour of small molecules in the binding site of tar-

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get proteins as well as to elucidate fundamental biochemical processes (Meenakshi, et.al 2009).

In the present work, three different compounds from the algae Sargassum wightii possessing regenerative capacity is studied. The compounds are Diisooctyl ester, Sargaquinoic acid and 1, 2- benzenedicarboxylic acid.

Materials and Methods

Different tools have been used for the prediction of binding affinity of the compounds with the Tau protein. The three dimensional structure of the protein was retrieved from the Protein Data Bank (PDB) and that of compounds from Pubchem. These are online tools and contained structural information of the macromolecules and compounds. For docking study, HEX was used. It was used to find the binding affinity between the compounds and the protein.

Results and Discussion

Bioinformatics is multidisciplinary field that develops and improves on methods for storing, retrieving, organizing and analyzing biological data. A major activity in bioinformatics is to develop software tools to generate useful biological knowledge. There are several computational approaches present in bioinformatics for analyzing the diversity of compounds. Docking is one of important tool to find out bioactive compounds. It is one of the most relevant tools for predicting the mechanism of compound-target interaction. Figure 1 represents the secondary structure of the Tau protein which is required for the preparation of docking. It contains the helices and sheets. The Stick Model of three different compounds such as Diisooctyl ester, 1,2-benzendicarboxylic acid and Sargaquinoic acid from Sargassum wightii are shown in Figure 2, 3 and 4 respectively.

The three compounds present in Sargassum wightii -Diisooctyl ester, 1,2-benzendicarboxylic and Sargaquinoic acid were docked with receptor Tau and the energy values were calculated by using Hex. The energy values of 3 compounds were- Diisooctyl ester: -311.89, 1, 2-benzendicarboxylic: -281.85, Sargaquinoic acid: -311.66. Of the different species, Sargassum wightii is with a wide range of bioactive properties. These bioactive compounds and various extracts showed significant therapeutic potential and could be introduced for the preparation of novel functional ingredients in pharmaceuticals for the treatment or prevention of several disorders (Adaikala Raj, 2014).

All the three compounds were loaded in the HEX docking tool along with Tau protein one by one to perform docking and hence foun out the compound which is exhib-

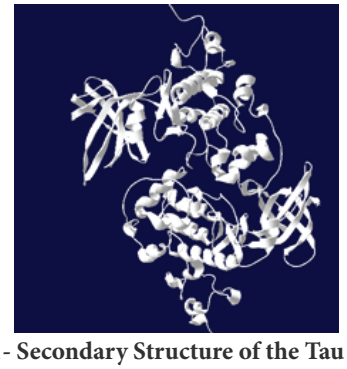

Figure 1- Secondary Structure of the Tau protein

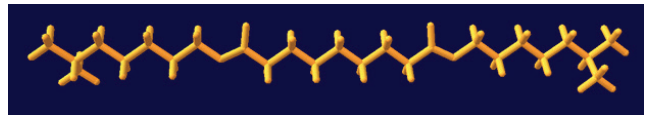

Figure 2- Stick Model of Diisooctyl ester

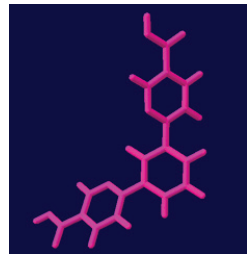

Figure 3- Stick Model of 1, 2-benzendicarboxylic acid

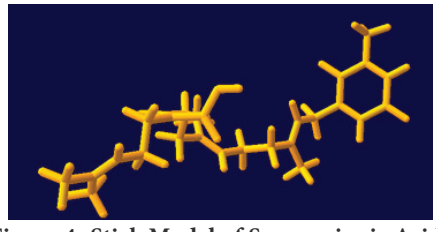

Figure 4- Stick Model of Sargaquinoic Acid

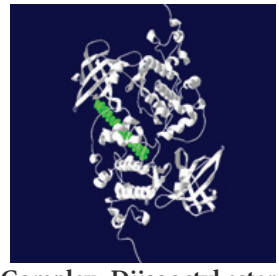

Figure 5- Docked Complex- Diisooctyl ester bound with the active site of Tau protein

Figure 6- Docked Complex- Sargaquinoic acid bound with the active site of Tau protein

iting good binding affinity towards the target. Figure 5 & 6.

The energy value observed for the three compounds present in Sargassum wightii with the target are- Di-isooctyl ester with energy value is -311.89; 1,2-benzenedicarboxylic acid with energy value -281.85 and Sargaquinoic acid with energy value -311.66. From this result it can be concluded that the compounds Di-isooctyl ester and Sargaquinoic acid have less energy and hence strong interaction with Tau protein when compared with 1,2-benzenedicarboxylic acid. So these compounds can be used to discover drugs against Alzheimer's disease. Further studies are required to find the interaction of the compound in in vivo and in vitro conditions.

Conclusion

Seaweeds are rich in nutrients and vitamins. Many of the marine algae have shown to possess bioactive effects. Therefore, recently a new trend has been arisen to isolate novel bioactive compounds from edible seaweeds. These compounds have great medicinal value and have been extensively used in the drug and pharmaceutical industry. Alzheimer's disease is the most common cause of dementia among older adults. The compounds Di-isooctyl ester and Sargaquinoic acid present in Sargassum wightii have less energy and hence strong interaction with Tau protein when compared with 1,2-benzenedi carboxylic acid. So these compounds can be used to discover drugs against Alzheimer's disease.

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