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ARTICLE

Molecular Docking to Elucidate the Binding Affinity of Psoriasin with Antifungal Compounds Isolated from *Ulva lactuca* Lin.

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Abstract

Fungal infections currently remains as a common problem in human health. The spread of multi-resistant strains of fungus and the reduced the number of drugs available, make it necessary to discover new classes of antifungal compounds. This has led to the search of antifungal compounds from natural sources. Ulva lactuca is a macroalga belonging to the Class Chlorophyceae. Methanolic extract of this alga contains certain compounds such as Palmitic acid, Squalene, Phthalic acid and Stigmasterol having antifungal activities. The present study was carried out to predict the binding affinity of these compounds with the protein Psoriasin. The 3D structure of Psoriasin is retrieved from PDB. The protein and the compounds were docked through Hex. The stability of the docked complex were established. The highly stable docked complex have least energy values. The compound Squalene is highly stable. The interaction study revealed that the compound Palmitic acid neither bound to the calcium nor zinc domain of the protein. While the compound Phthalic acid bound to the Calcium domain of the protein Psoriasin the other compounds Squalene and Stigmasterol bound to the Zinc domain of the Psoriasin protein and hence have high affinity towards the antifungal activity.

Keywords: Antifungal, *Ulva lactuca*, Palmitic acid, Phthalic acid, Squalene, Stigmasterol, Psoriasin, Docking, Hex

Introduction

Algae with their increasing popularity due to their versatility are finding applications in many emerging spheres as nutritional supplement, fertilizer, stabilizing agents, neutraceutical, pharmaceutical and in medical fields. Algae have been recognized as a rich energy source. Green algae have been extensively used under research for the last two decades. The green algae Ulva lactuca have been found to have antimicrobial (Oranday et.al., 2004), antibacterial, preservative, anticoagulant, antiperoxidative, antihyperlipidemic, hepatoprotective, anti-inflammatory, antiprotozoal (Orhan et al., 2006), antiviral activities and also employed as dietary fibers in many area around the world (Arumugam et al., 2008). Psoriasin is a protein present in man whose overexpression cause suppression of psoriasis in human. Bioinformatics is an interdisciplinary field that develops methods and software tools for understanding biological data. As an interdisciplinary field of science bioinformatics combines computer science, statistics, mathematics and engineering to analyze and interpret biological data. Bioinformatics has been used for in silico analysis of biological queries using mathematical and statistical techniques. Bioinformatics is the symbiotic relationship between computational sciences. Bioinformatics has become an important part of many areas of biology. Docking is an in silico technique of determining the molecular structure of complexes formed by two or more molecules without the need for experimental measurement. Docking is an invaluable tool for drug designing. In this study,docking was done with a protein and four compounds from Ulva lactuca to find out their affinity and hence establish their antifungal impact in Psoriasis

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Materials and Methods

From literature survey it was identified that methanol extract of Ulva lactuca contains compounds such as Palmitic acid, Phthalic acid, Squalene and the Ethyl acetate extract contain the compound Stigmasterol. These four are compounds having antifungal activity. In the present study, many online as well as offline databases and tools were used.
Protein Data Bank (PDB)

PDB is a crystallographic database for the three-dimensional structural data of large biological molecules, such as proteins and nucleic acids. This is freely accessible on the internet via the websites of its member organization. In the present study, the three dimensional structure of the protein was downloaded from PDB.

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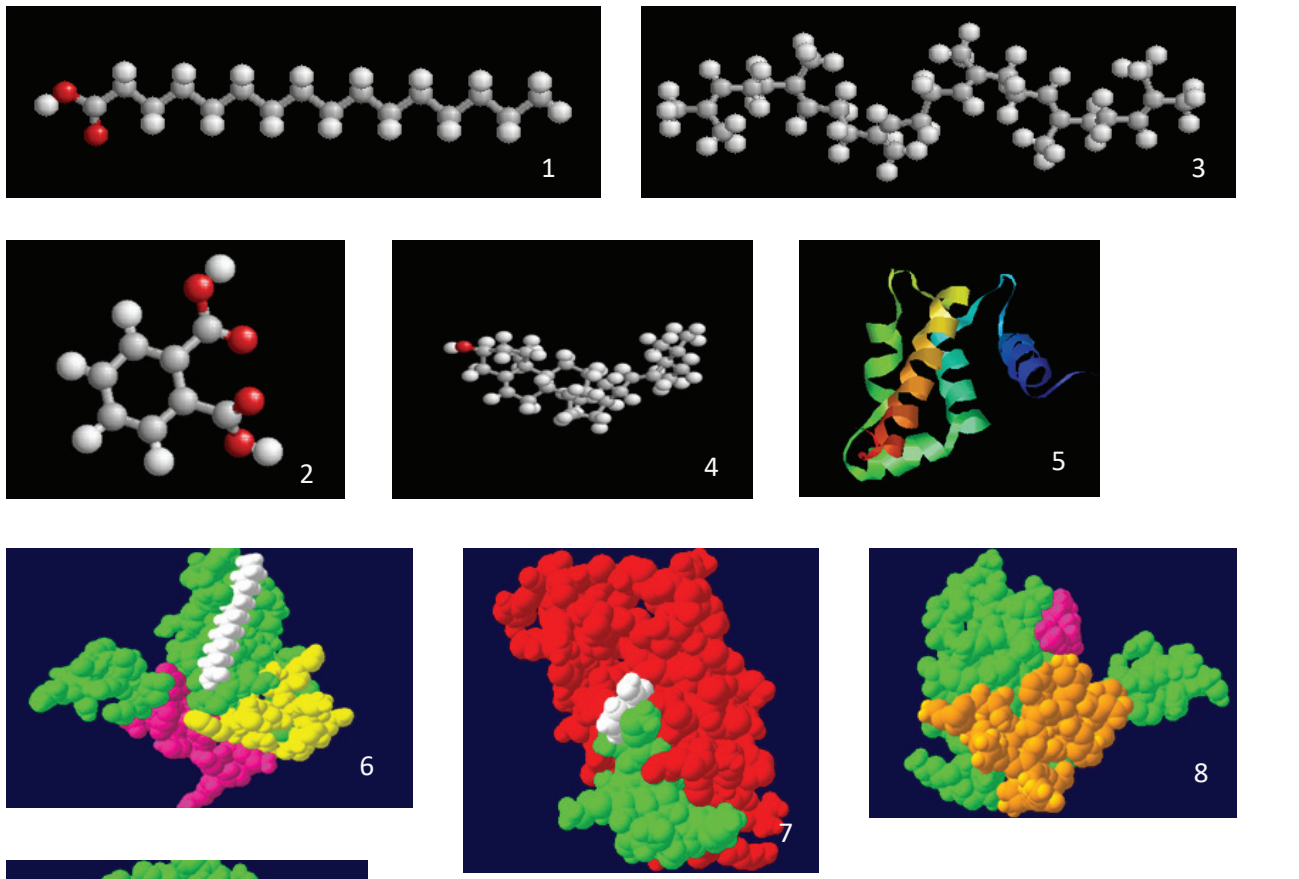

Figure 1- Palmitic acid
Figure 2- Phthalic acid
Figure 3- Squalene
Figure 4- Stigmasterol
Figure 5- Secondary structure of Psoraisin
Figure 6- Interaction between Palmitic acid and Domain of the protein Psoriasin
Figure 7- Interaction between Phthalic acid and the Calcium domain of the protein Psoriasin
Figure 8- Interaction between Squalene and domain of the protein Psoriasin
Figure 9- Interaction between Stigmasterol and domain of the protein Psoriasin

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PubChem

PubChem is a database of chemical molecules and their activities against biological assays. PubChem contains its own online molecule editor with SMILES/SMARTS and InChI, support that allows the import and export of all common chemical file formats to search for structures and fragments. In the present study, the smiles of the compounds were retrieved from Pubchem and subjected for its conversion to three dimension.

Swiss-pdb viewer

Swiss-pdb viewer is an application that provides a user friendly interface allowing to analyze several proteins at the same time. The proteins can be superimposed in order to deduce structural alignments and compare their active sites or any other relevant parts. Aminoacid mutations, H-bonds, angles and distances between atoms are easy to obtain. Moreover, Swiss-pdb viewer is tightly linked to

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Results and Discussion

In the field of molecular modeling, docking is a method which predicts the preferred orientation of one molecule to a second when bound to each other to form a stable complex. In the present study, the protein Psoriasin taken as receptor and the ligands are the compounds from Ulva lactuca especially Palmitic acid, Phthalic acid, Squalene and Stigmasterol. These molecules were subjected to docking in Hex. The default grid dimension was set as 0.75 and activate docking. Then a small hex progression box opened in the middle of the window, and this box shows the progressing of docking, within few minutes docking process were completed. This protocol was repeated with all the four compounds.

In the present study, four compounds isolated from Ulva lactuca were docked with a protein called Psoriasin. The docked complex was then analyzed for motif orientation. The docked complex of protein Psoriasin and Palmitic acid is shown in the Figure 6. The energy value of this complex structure is -253.02. When the target molecule subjected for docking with the second compound Phthalic acid, energy value obtained is -186.02. The same protocol was applied for Squalene and Stigmasterol. The energy value obtained were recorded as -325.90 and -314.61 respectively. From the variation in energy values of the docked complexes the stability of the compound can be predicted. Among the four compounds, Phthalic acid when docked with the receptor showed the lowest and Squalene exhibited the highest energy value.

The interaction between Palmitic acid and the domain of the protein Psoriasin was also checked through Swiss pdb viewer. There are two important functional parts in the given target such as Calcium coordinating residues, whose sequence of aminoacid was "KDKNEDKKIDFSEF" and Zinc coordinating residue consist of "GMIDMFQHKYTRRDDKIDKPS".

Figure 6 showed that the compound Palmitic acid in white colour neither bound to zinc (yellow shade) nor calcium domain (pink) of the Psoriasin. In Figure 7, white coloured Phthalic acid bound only to calcium domain of the protein Psoriasin which is green in colour.

In the present study, docked complex of protein and compound Squalene is represented in the Figure 8. In this figure the Zn active site of the protein is indicated by orange colour. The pink colour represented the compound Squalene and the green colour by the other part of protein Psoriasin. The image clearly figure out that the compound Squalene bound to the zinc coordinating domain of Psoriasin.

The docked complex of Psoriasin with Stigmasterol is shown in the figure 9. Here, the Zinc domain of the protein is represented in white colour. The compound Stigmasterol represented by pink colour. From the figure it can be that the compound Stigmasterol is bound to the zinc domain of the Psoriasin.

Conclusion

In the present study, docking was carried out to find the interaction between antifungal compounds isolated from Ulva lactuca with protein Psoriasin. Docked results revealed that the compounds have affinity towards either Zn2+ or Ca2+ domain of the Psoriasin protein. Among the four compounds taken for the study, Palmitic acid neither bound to Zn2+ nor Ca2+ domain of the Psoriasin, whereas Phthalic acid bound only to Ca2+ domain of the targeted protein. Squalene and Stigmasterol bound to the Zn2+domain of the protein Psoriasin.

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