Protein-Protein docking studies on Magnesium chelatase of *Ulva fasciata* against the human TSHR protein.

Abstract

The course and prognosis of hypothyroidism in humans are affected by the most common mutation in the hypothyroid protein, TSHR. In order to facilitate the potential mutant TSHR's interaction with *Ulva fasciata's* magnesium-chelatase, we utilize 3D *Insilico* drug docking approaches. The translated amino acid sequence and three-dimensional chemical compound were taken from the NCBI database in order to perform drug docking procedures. In post-docking tests, advanced 3D molecular visualization capabilities were utilized. In post-docking tests, advanced 3D molecular visualization capabilities were utilized. The findings of the docking investigation indisputably demonstrate that amino acid mutational sites are directly suppressed by magnesium chelatase. The H-bond interaction between TSHR and magnesium chelatase is shown in three dimensions by means of concepts from molecular dynamics techniques. Ultimately, we found that *Ulva fasciata's* pharmaceutical ingredient, magnesium chelatase, aids in the treatment of hypothyroidism. One of the main endocrine hormonal problems is hypothyroidism, and our research serves to demonstrate how well the sea weed *Ulva fasciata* works as a unique medicinal agent to treat this disorder.

Keywords: TSHR, *Ulva fasciata* , Protein –Protein Docking

Introduction

Thyroid-associated ophthalmopathy, also referred to as Graves' orbitopathy (GO), is a relatively uncommon condition, with an incidence of 2.67–3.3 cases/100,000/year in females and 0.54–0.9 cases/100,000/year in males [1]. The incidence of GO varies depending on the testing method used to diagnosis GO, such as clinical signs and symptoms, physical

examination, and imaging techniques, and affects approximately 25% to 50% of patients with Graves disease (GD). Eye discomfort, photophobia, hazy vision, increased tear production, and double vision are common signs of GO. One or both eyes may be affected by GO's periorbital oedema, exophthalmos, eyelid recession, and alterations in eye motility. A significant portion of GO patients—roughly 5–6%—have compressive optic neuropathy or potentially blinding corneal ulcerations; these individuals may go blind. Although GO can occur at any age, it most frequently affects women between the ages of 30 and 50 [2]. However, men and individuals who receive a diagnosis later in life tend to have more severe cases of GO [3]. Smoking, high cholesterol, thyroid dysfunction, radioiodine therapy, low thyroid peroxidase antibodies (TPOAbs), high thyrotropin receptor antibodies (TRAbs), and low thyroglobulin antibodies (TgAbs) are traditional risk factors for GO. High thyroglobulin (Tg) [4], a selenium deficit, an imbalance in the intestinal flora, and elevated levels of Yersinia enterocolitica and Escherichia coli in the digestive tract are new risk factors for GO [5].

The biological and chemical potential of seaweeds has been covered in other papers [6, 7, 8, 9]1, 2, 3, 4]. Global seaweed aquaculture has generated about 30 million tons of fresh biomass in the last few decades, with a projected market value of over $13.3 billion. More than 95% of the seaweed produced worldwide is farmed by *Laminaria/Saccharina (35.4%), Kappaphycus and Eucheuma (33.5%), Gracilaria (10.5%), Porphyra (8.6%), and Undaria (7.4%)* [10]. Seaweeds therefore represent a prospective millennium market with a number of social, economic, and ecological advantages [5, 6]. Coral reefs have lost up to 67% of their historical global range, making them one of the planet's most threatened ecosystems. Furthermore, human activity and the consequences of climate change pose a threat to the remaining intact coral reef systems, as reported in a recent report by the Global Coral Reef Monitoring Network [11, 12]. Prior studies in the literature suggest that coral's secondary metabolites may have cytotoxic, anti-inflammatory, antifouling, and antimicrobial properties in addition to benefits for bone repair and the nervous system [13, 14, 15, and 16].

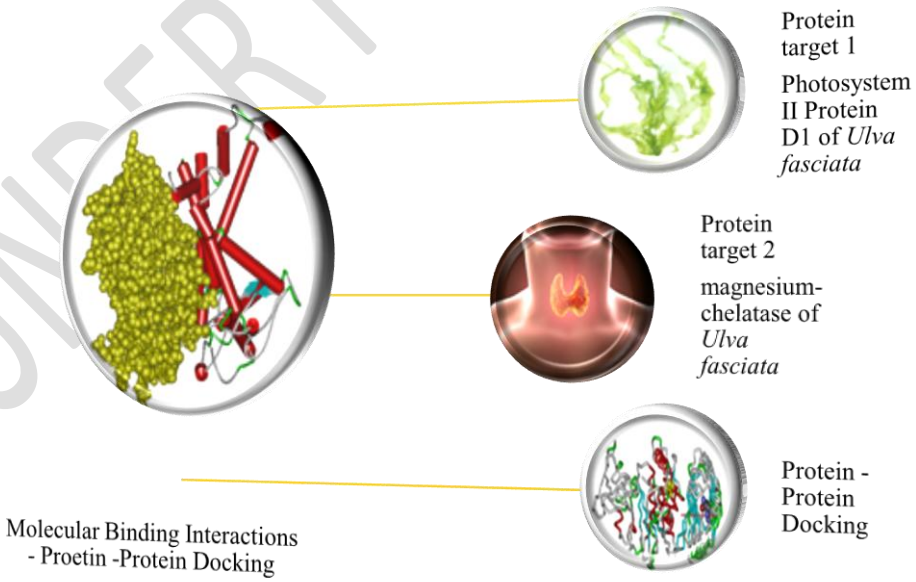
Our investigation analysed in detail the molecular interactions between the sea weed protein of Ulva fasciata and the human Thyroid Stimulating Hormone Receptor (TSHR). The final results clearly showed the mechanism of inhibition of magnesium chelatase with the Thyroid Stimulating Hormone Receptor.

Methodology

Target selection: Data from the NCBI Genpept database (YP_009220447.1 magnesium-chelatase (*Ulva fasciata*) and (AAI20973.1 TSHR protein (Human) were utilized to conduct a molecular drug docking study. A powerful molecular visualization application called Discovery Studio was used to anticipate three-dimensional structures.

Protein Docking: HDOCK, an automated molecular drug docking service (http://hdock.phys.hust.edu.cn/), has been used in molecular drug docking research. [17]. Using a 3D molecular dynamics method, the molecular affinities of TSHR protein and YP_009220447.1 magnesium-chelatase (*Ulva fasciata*) in human hypothyroidism were ascertained.

Protein –Protein docking: Experiments involving post-docking were conducted with the Discovery Studio software. Using the molecular dynamics concept, a thorough analysis of the three-dimensional image based on the docking score (3D H-bond/Electrostatic interactions) was carried out.



Pic 1. Diagrammatic representations of the overview of the *Insilico* research work

Results and Discussion

>YP_009220447.1 magnesium-chelatase subunit ChlI (chloroplast) [Ulva fasciata]
MSEKIELESRPVFPFTSIVGQEEMKLALILNVIDPKIGGVMVMGDRGTGKSTTVRALSDLLPDMKVVAND
PFNSDPNDPELMSDEVADKIKNNKTLEIETKKIPMIDLPLGATEDRVCGTIDMEKALTEGIKAFEPGLLA
SANRGILYVDEVNLLDDHLVDVLLDSAASGWNTVEREGISISHPARFILVGSGNPEEGELRPQLLDRFGM
HAEIRTVKEPDLRVQIVEQRAAFDSDPIEFRNNYSESQKTLSEKIVKARELLKEVDLNYEFRIKISQICS
ELNVDGLRGDIVTNRAAKALTAFEGRNEVTAQDIFRVIPLCLRHRLRKDPLETIDSGDKVRDIFKKIFS

Fig.1: Amino acid sequence of the sea weed, Ulva fasciata

>AAI20973.1 TSHR protein [Homo sapiens]
MRPADLLQLVLLLDLPRDLGGMGCSSPPCECHQEEDFRVTCKDIQRIPSLPPSTQTLKLIETHLRTIPSH
AFSNLPNISRIYVSIDVTLQQLESHSFYNLSKVTHIEIRNTRNLTYIDPDALKELPLLKFLGIFNTGLKM
FPDLTKVYSTDIFFILEITDNPYMTSIPVNAFQGLCNETLTLKLYNNGFTSVQGYAFNGTKLDAVYLNKN
KYLTVIDKDAFGGVYSGPSLL

Fig.2: Amino acid sequence of human TSHR protein

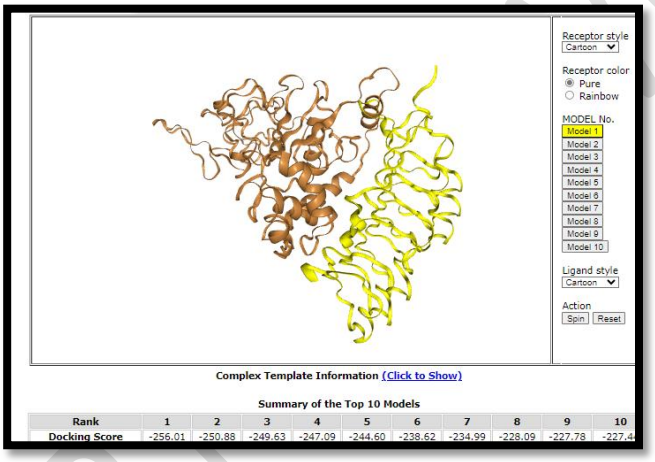


Fig.3: Complex form of human TSHR protein and YP_009220447.1 magnesium-chelatase of *Ulva fasciata* viewed using H-Dock server with respective binding scores.

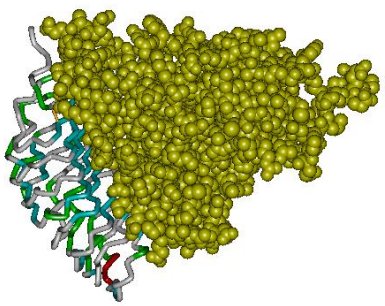


Fig.5: Complex form of human TSHR protein and YP_009220447.1 magnesium-chelatase of *Ulva fasciata* viewed using Discovery Studio Software. Yellow coloured structure represents the TSHR protein.

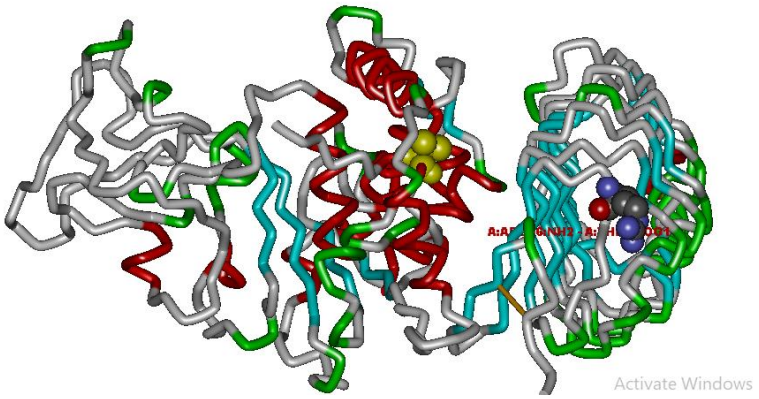


Fig.6: 3D Complex form of human TSHR protein and magnesium-chelatase of *Ulva fasciata* viewed using Discovery Studio software (Binding Interaction Mode).

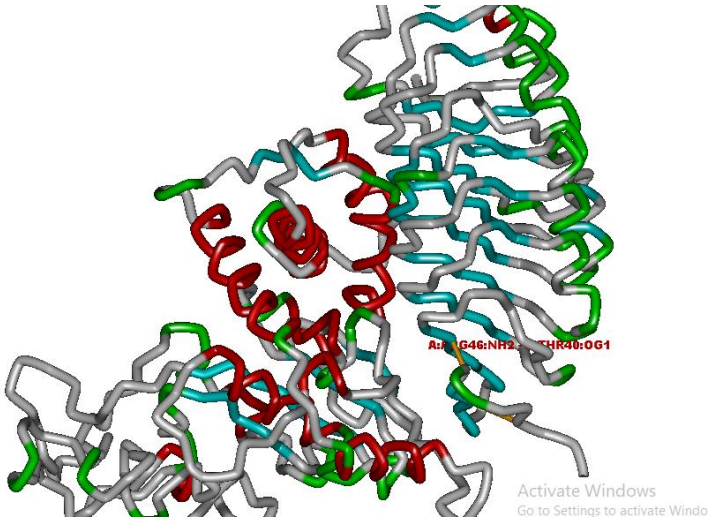


Fig.7: 3D Complex form of human TSHR protein and magnesium-chelatase protein of *Ulva fasciata* viewed using Discovery Studio software (Binding Interaction Mode with respective amino acid labels/positions).

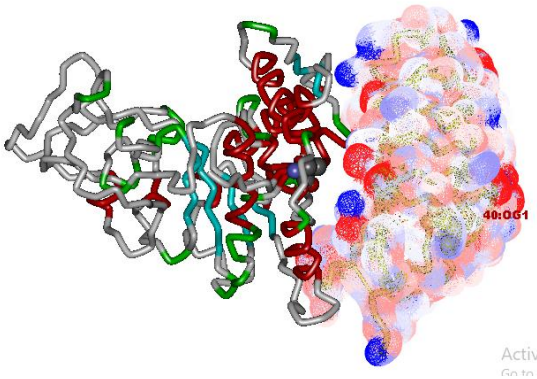


Fig.8: 3D Complex form of human TSHR protein and magnesium-chelatase protein of *Ulva fasciata* viewed using Discovery Studio software (Amino acids interacting at Domain and Motif).

The amino acid sequences corresponding to the gene-coded proteins of photosystem II protein D1 (*Ulva fasciata*) and TSHR are 349 aa and 231 aa, respectively (Fig: 1 and 2). In our research work, we use the potential inhibitor derived from algae (*Ulva fasciata*).

Marine macroalgae are eukaryotic, macroscopic, multicellular, photosynthetic organisms that are classified as belonging to the order Plantae. Seaweed is another name for these creatures. In addition to the seabed or solid rock strata beneath it, these salt-loving marine plants can also be found on the surfaces of rocks, corals, shells, pebbles, and other plants. In oceanic places where light is most abundant, marine algae typically thrive in the tidal and subtidal zones. Because of their easy response to physiological changes by creating stress-tolerant chemicals, they can endure extreme temperatures, cold temperatures, UV radiation, salinity, and desiccation. A multitude of primary and secondary metabolites are produced by them as a result of their survival. Numerous physiologically active substances with a range of therapeutic advantages can be found in marine algae [18, 19].

The complex form of the TSHR protein retrieved via the H-Dock server and photosystem II protein D1 have a 3D docking score of -256.01 *kcal/mol*, (Fig :3) as illustrated in Fig. (1). Using Discovery Studio software, the H-bond interactions between photosystem II protein D1 and the TSHR protein are displayed in detail (Fig: 4, 5, 6, 7, 8). It is clear from this image that the TSHR protein and the photosystem II protein D1 protein structure have interacted non-covalently. Therefore, it may be said that, as demonstrated by

earlier research, the TSHR protein will be downregulated. Our docking studies are consistent with a number of prior investigations [17, 18, 19, 20, 21, 22].

Our retrieved protein's functional domain area is the *Ulva fasciata* 46 SER (44-51) *ATP/GTP-binding site motif A (P-loop* (PS00017). Our research demonstrates that gentamicin, an antibiotic, interacts directly with the domain areas. Our study unequivocally demonstrated that the following amino acids are present at the drug-protein binding region: ARG:46,THR:40,ARG:241,GLU:34,TYR:244,GLN:33

Conclusion

Our study unequivocally demonstrates the interaction between the seaweed protein and the human hypothyroidism protein, TSHR. The *Ulva fasciata* magnesium-chelatase binds efficiently to the TSHR protein's functional domain area, as demonstrated by our clear docking data. The H-bond interaction is clearly defined by the binding relationship between magnesium-chelatase and TSHR protein, as assessed by docking scores. Therefore, we conclude that *Ulva fasciata* seaweed protein functions as a possible Endocrinological medication that lessens the symptoms of hypothyroidism in humans. Our *Insilico* study clearly shows that the human TSHR protein may be pharmacologically affected by magnesium-chelatase.

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