ESTROGEN RECEPTOR COMPARED WITH SYLIBIN AS A TARGET FOR POSTMENOPAUSAL SYMPTOMS VIA MOLECULAR DOCKING

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ABSTRACT

Natural products from plants are high in demand due to their low toxicity and easy availability. Molecular docking helps in identifying the best target suitable for the selected drug. This study aimed to evaluate molecular interactions of selected estrogen targets with bioactive compounds of *Anastatica hiruchuntica i.e.* sylibin. The biological effects of estrogen are mediated by two distinct estrogen receptors (ERs), ERα and ERβ. ER subtype-selective agonists have potential roles in bone and metabolic homeostasis, depression, vasomotor symptoms, neurodegenerative diseases, and cancer. Clinical studies are necessary to validate these compounds as agents for the prevention and treatment of diseases.

Keywords: Estrogen receptor, *Anastatica hiruchuntica*

I] INTRODUCTION (1,2)

A type of bioinformatic modeling called molecular docking includes the interaction of two or more molecules to produce a stable adduct. It makes predictions about the three-dimensional structure of any complex based on the binding characteristics of ligand and target. Different potential adduct structures are generated by molecular docking and are ranked and categorized using the software's scoring function. Based on the system's overall energy, docking simulations forecast an optimum docked conformer. Despite all viable strategies, the difficulties still lay in ligand chemistry (tautomerism and ionisation), receptor flexibility (single conformation of stiff receptor), and scoring function (differentiate actual binding mode). This article briefly discusses a number of significant features of molecular docking, including its techniques, kinds, applications, and problems.

The estrogen receptor subtypes alpha (ER) and beta (ER) play a significant role in modulating the physiological actions of estrogenic substances. By binding to related DNA regulatory regions, these proteins exert their effects in the cell nucleus, controlling the transcription of particular target genes. Both receptor subtypes are expressed in numerous cells and tissues in humans, and they regulate important physiological processes in a number of organ systems, including the reproductive, skeletal, cardiovascular, and central neurological systems, as well as in particular tissues (such as breast and sub-compartments of prostate and ovary). Male reproductive organs (testes and epididymis), bone, mammary gland, uterus, ovary (thecal cells), prostate (stroma), liver, and adipose tissue are the main locations where ER is found. In contrast, ER is mostly located in the ovary (granulosa cells), bladder, colon, prostate, and bladder epithelium.

II] EXPERIMENTAL

Molecular docking simulations were performed using PyRx-Virtual Screening Tool [3]. The structure of Silybin (in .sdf File format) was downloaded from National Center for Biotechnology Information PubChem database (https://pubchem.ncbi.nlm.nih.gov/). The energy minimization (optimization) was performed by MMFF94. Estrogen Receptor Alpha Ligand Binding Domain in Complex with Estradiol and SRC2-LP1 (PDB ID: 5WGD), https://www.rcsb.org/structure/5WGD) was obtained from Protein Data Bank (PDB) www.rcsb.org.Autodock vina 1.1.2 in PyRx 0.8 having grid X: 62.7044, Y: 47. 4137, Z: 25.00 was used to perform the MD studies of all the selected drugs against the Estrogen Receptor Alpha Ligand Binding Domain in Complex with Estradiol and SRC2-LP1. In silico ADME was performed using swiss ADME (http://www.swissadme.ch/index.php)

III] RESULTS AND DISCUSSION

Silybin found to be forming a stable complex with Estrogen Receptor Alpha Ligand Binding Domain via -8.9 kcal/mol binding energy and formed 3 hydrogen bonds conventional hydrogen bond with GLN 502 and carbon hydrogen bond with GLN506, ARG 503, Pi-alkyl with ALA493, Pi Sigma with LEU 495, Pi Cation with ARG503, Vander wall interaction with ARG434. GLU443, LEU489, GLN441, GLU444, MET490, ASN439, GLN499, MET438. As shown in following figures.

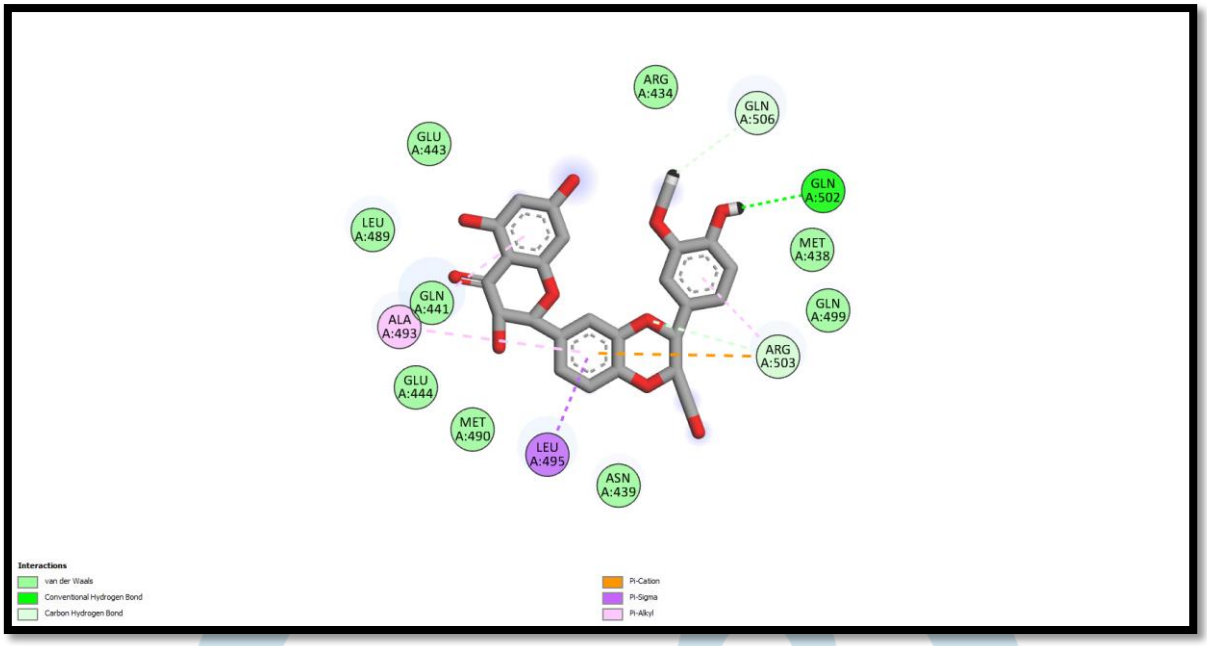

Figure 1: Silybin found to be forming a stable complex with Estrogen Receptor.

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