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Research Article

In silico Molecular Docking of Some Isolated Compounds of *Piper-Sylvaticum* against Thrombolytic Activity

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Abstract

The aim of this study is to performed molecular docking studies to identify potential binding affinities of the phytocompounds from compounds **Piperine, Piperlonguminine, β-sitosterol. N-isobutyl deca-Q*trans*-2-*trans*-4-dienamide** for searching of lead molecule for thrombolytic activity.

Docking can be utilized to perform virtual screening on expansive libraries of mixes, rank the outcomes, and propose auxiliary speculations of how the ligands restrain the objective, which is significant in lead advancement. We used molecular docking method to interact the small molecules of given compounds and a protein at the atomic level, which allow us to characterize the behavior of compounds in the binding site of target proteins as well as to evaluate its activity on the target site. A wide range of docking score found during molecular docking by Schrodinger. Compounds **Piperine, Piperlonguminine, and β-sitosterol. N-isobutyl deca-trans-2-trans-4-dienamide showed the docking 4.607, 4.459, 3.152, and 1.088** respectively. Among all the compounds Pipeline showed the best docking score.

So, **Piperine** is the best compounds for thrombolytic activity, as it possessed the best value in Molecular docking. Further in vivo investigation need to identify the thrombolytic activity of isolated compounds from ***Piper-sylvaticum.***

INTRODUCTION

Blood clusters can happen in any vascular bed; it may occur when they happen in coronary, cerebral or aspiratory vessels, they can be instantly dangerous - coronary thrombi are the reason for myocardial areas of dead tissue, cerebrovascular thrombi deliver strokes, and pneumonic thromboembolic can prompt respiratory and heart disappointment [1]. Clumps can happen in veins or courses, which are vessels that are a piece of the body's circulatory framework. While the two sorts of vessels enable transport blood throughout the body they each capacity in an unexpected way. Veins are low-weight vessels that divert deoxygenated blood from the body's organs and back to the heart. An anomalous coagulation that occurs in a vein may confine the arrival of blood to the heart and can bring swelling as the blood accumulates behind the coagulation. Profound vein thrombosis (DVT) is a sort of cluster that structures in a noteworthy vein of the leg or, less ordinarily, in the arms, pelvis, or other huge veins in the body. Again coagulation in a vein may segregate from its purpose of root and go through the heart to the lungs where it ends up noticeably wedged, counteracting satisfactory blood stream. This is known as an aspiratory (lung) embolism (PE) and can be to a great degree hazardous.

Thrombolytic treatment is the organization of medications called lytics or "clump busters" to break down blood clusters that have intensely (all of a sudden) obstructed your significant conduits or veins and posture conceivably genuine or perilous ramifications. To be successful, the treatment should be started as quickly as time permits, before perpetual harm has happened [2-6]. Thrombolytic drugs break up blood clusters by actuating plasminogen, which frames a separated item called plasmin. Plasmin is a proteolytic catalyst that is equipped for breaking cross-interfaces between fibrin particles, which give the basic

uprightness of blood clumps. As a result of these activities, thrombolytic drugs are likewise called "plasminogen activators" and "fibrinolytic drugs.

In silico molecular docking is a settled computational system which predicts the cooperation vitality between two particles. This system mostly incorporates algorithms like molecular dynamics, stimulation, and fragment based method technique. Studying of molecular docking are utilized to decide the communication of two particles and to locate the best introduction of ligand which would shape a complex with general least vitality [7-10].

Traditionally healthful plants have served to be efficient thrombolytic agents for ages because of their wealthy diversity of photochemical. ***Piper-sylvaticumRoxb***.is an economically and ecologically important genus in the family **Piperaceae**. It can be found in Bangladesh, Burma, China (Yunnan) and India. The Piperaceae, also known as the pepper family, is a large family of flowering plants. The group contains roughly 3,600 currently accepted species in 13 genera.

Its seeds contain Alkamides, Sylvetin, piperic acid, Flavon, Sesamine, Lignon, and Piperine. Roots contain Piper longamine, and the whole plant contains Sylvon. The root yielded a lignin, sesamin, amides (including piperine, piperlongumine) and beta-sitosterol. It's used in hepatomegaly, splenomegaly, asthma, chronic cough, cold, headache, piles, diarrhea, and tuberculosis, wounds in lungs, indigestion, dyspepsia, and rheumatism [11,12]. Our aim is to discover a potent thrombolytic drug by *in silico* docking study.

MATERIALS AND METHODS

Protein preparation

Three-dimensional crystal structure of tissue plasminogen activator (PDB id: 1A5H) was downloaded in PDB format from the protein data bank [13]. After that, the structure was prepared and refined using the Protein Preparation Wizard of Schrödinger-Maestro v10.1. Charges and bond orders were assigned, hydrogens were added to the heavy atoms, selenomethionines were converted to methionines, and all waters were deleted. Using force field OPLS_2005, minimization was carried out setting maximum heavy atom RMSD (root-mean-square-deviation) to 0.30 Å.

Ligand preparation

Compounds were retrieved from PubChem databases, i.e**. Piperine** (compound ID: 638024), **Piperlonguminine** (compound ID: 5320621), **β-sitosterol** (compound ID: 222284), **N-isobutyl deca-*trans*-2-*trans*-4-dienamide** (compound ID: 5318516). The 3D structures for these were built by using Ligprep2.5 in Schrödinger Suite 2015 with an OPLS_2005 force field. Their ionization states were generated at pH7.0 ± 2.0 using Epik2.2 in Schrödinger Suite. Up to 32 possible stereoisomers per ligand were retained.

Receptor grid generation

Receptor grids were calculated for prepared proteins such that various ligand poses bind within the predicted active site during docking. In Glide, grids were generated keeping the default parameters of van der Waals scaling factor 1.00 and charge cutoff 0.25 subjected to OPLS 2005 force field. A cubic box of specific dimensions centered around the centroid of the active site residues (Reference ligand active site) was generated for the receptor. The bounding box was set to 14 Å × 14 Å × 14 Å for docking experiments.

Glide Standard Precision (SP) ligand docking

To find out the accurate binding model for the active site of tubulin, molecular docking analysis was performed using ligand fit of GLIDE software from Schrodinger [9,14]. Molecular docking analysis was performed using crystal structure of plasminogen activator (PDB id: 1A5H). The structure of crystal structure of tissue plasminogen activator (PDB id: 1A5H) were obtained from Protein Data Bank (http://www.rcsb.org). The mechanism of ligand position is based on the fitting points. Fitting points are incorporated into the hydrogen bonding groups on the ligand and the proteins. The ligand fit module from GLIDE software was utilized to execute the molecular docking analysis, based on shape-based searching and Monte Carlo methods. At the time of docking, variable trials Monte Carlo conformation was applied where the number of steps depends on the number of rotatable bonds present in the compounds/ ligands. By default the torsion number is 2, the maximum minimizations steps are 300 and maximum successive failure is 110. During the docking process, the top ten conformations were engendered for each of the compounds after the minimization of the energy.

RESULTS

In order to study the interaction of the compounds **Piperine**, **Piperlonguminine**, **β-sitosterol**.**N-isobutyl deca-*trans*-2-*trans*-4-dienamide** with 1A5H, we performed Glide docking analysis by Schrodinger suite v10.1, where among of these compounds N-isobutyl deca-*trans*-2-*trans*-4-dienamideshows highest docking score shown in Table 1. The negative and low value of Piperine glide energy of binding demonstrates a strongly favorable bond between 1A5H and in most favorable conformations. The results of docking analysis were described in Table 1 and Figure 1.

DISCUSSION

From the earliest starting point of progress, human are tried and true on plants for the treatment of numerous diseases. Nowadays psychopharmacological examination has made another field to revelation plant subsidiary medications, which are viable in therapeutic of specific infections, and reestablished the consideration in natural prescriptions. It is evaluated that 30% of the pharmaceuticals are set up from plants subordinates. Bangladesh is an extraordinary asset with a bunch of restorative plants that are yet to be completely investigated. Since various research works have been directed to find the plants and common nourishment sources and their supplements having antithrombotic (anticoagulant and antiplatelet) impact and there is sign that expending such sustenance prompts counteractive action of coronary occasions and stroke. The objective of molecular docking is the precise expectation of the structure of a ligand inside the requirements of a receptor restricting site and to accurately assess the quality of official. The coupling

Table 1: Docking results of Piperine, Piperlonguminine, β-sitosterol, N-isobutyl deca-*trans*-2-*trans*-4-dienamidewith tissue plasminogen activator (PDB: 1A5H).

Compound Name	Compound ID	Docking Score	Glide e model	Glide Energy
Piperine	638024	-4.607	-44.58	-36.211
Piperlonguminine	5320621	-4.453	-40.959	-32.621
β-sitosterol	222284	-3.152	-36.749	-31.821
N-isobutyl deca-*trans*-2-*trans*-4-dienamide	5318516	1.088	-7.322	-8.871

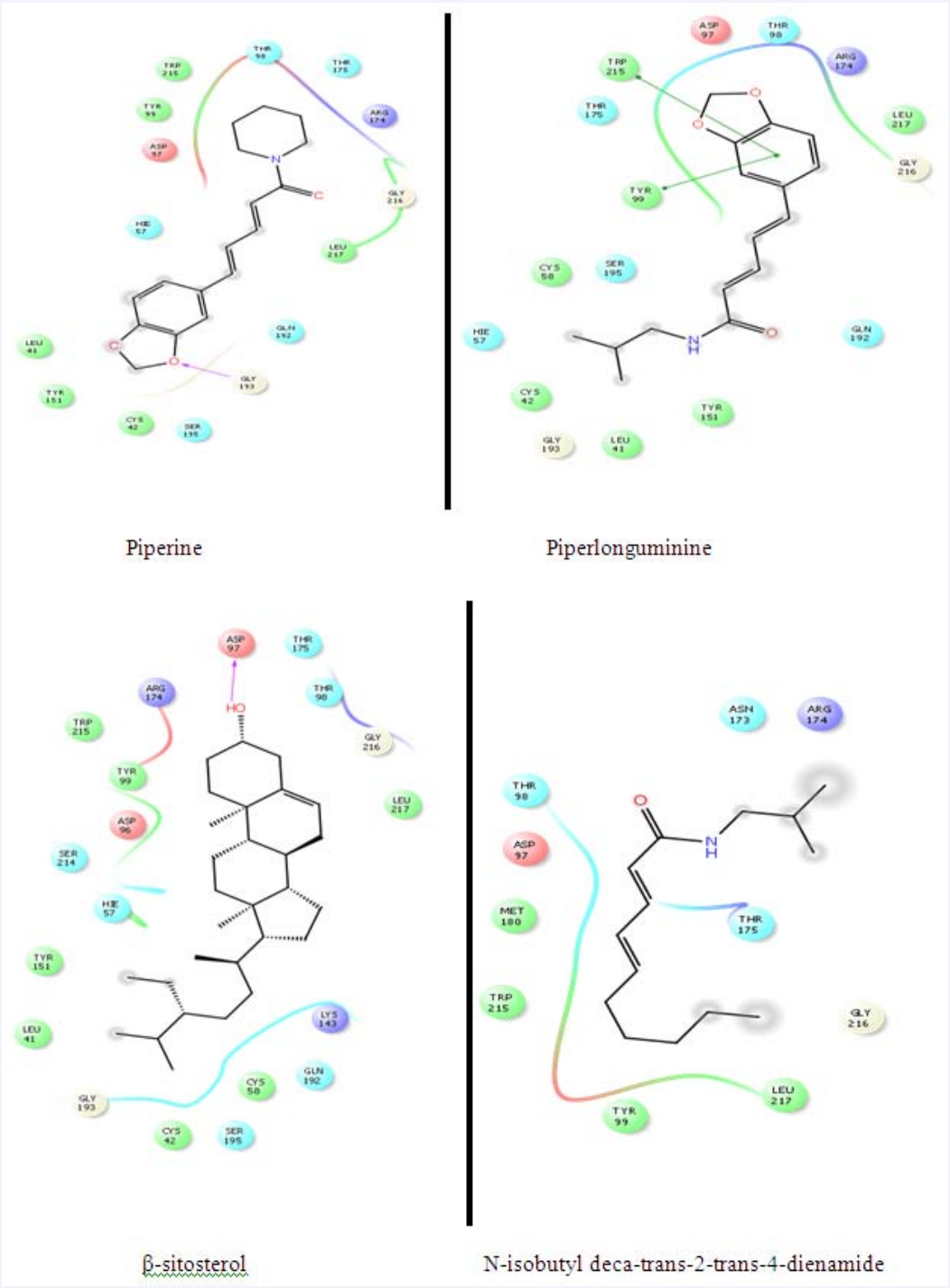

Figure 1 Docking results of Piperine, Piperlonguminine, β-sitosterol and N-isobutyl deca-trans-2-trans-4-dienamide with tissue plasminogen activator (PDB: 1A5H).

method of tissue plasminogen activator was examined by doing computational examination glide docking both glide standard (SP) had been introduced. The aftereffects of docking investigation were portrayed in Table 1 and the docking figure appeared in Figure 1. Among every one of the mixes, **Piperine** demonstrated the well docking score, glide emodel and glide energy. Since the negative and low estimation of glide energy of strongly favorable bond is preferable for best docking study. And unequivocally positive bond is ideal for best docking examination. So the docking score in the vicinity of 1A5H and in **Piperine** is most great compliances [15-20].

CONCLUSION

From the above study we can say that the compound ***Piper-sylvaticum*** could be an incredible medication for the thrombolytic treatment. Along these lines, we can state that every one of the mixes aside from give negative outcome but **Piperine** was the best thrombolytic action as indicated by the docking score. Since it also can be found from medicinal plant we can expect less side effects. In this way, we can do further in vivo examination need to distinguish the thrombolytic movement of separated mixes from **Piperine**.

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