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IN SILICO STUDY OF *BOSWELLIA SERRATA* ROXB. EX COLEBR: A WILD ETHNOMEDICINAL PLANT FOR THERAPEUTIC PURPOSE

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ABSTRACT

Boswellia serrata Roxb. ex Colebr. is a deciduous tree in the Burseraceae family. It is native to India and Pakistan. *Boswellia serrata* is in the same botanical Burseraceae family as the tree from which myrrh is harvested. In India, frankincense from the tree is called "salai guggal". In biomedical arena, computer-aided or *in silico* design is being utilized to expedite and facilitate hit identification, hit-to-lead selection, optimize the absorption, distribution, metabolism, excretion and toxicity profile and avoid safety issues. There are over a hundred chemical substances that have been derived from plants for use as drugs and medicines. Medicinal plants containing natural and its synthesize chemical compound belonging to two research targets (Mitogen-activated protein kinase for cancer and Thymidine monophosphate kinase for TB) and two successful targets (HIV protease for HIV and Enoyl-ACP reductase for malaria). Beside that ligand library compounds were also examined for druglikeness. Molecular docking studies were carried out with docking programmed. The virtual screening from ligand library point towards the best score and efficient binding of the ligand 2-ethenyl-6-methylhept-5-en-1-yl acetate with two research target and two successful targets from the ligand library included in study. The synthesize chemical compound having best score comparison to the natural chemical compound present in the *Boswellia serrata* Roxb. ex Colebr wild medicinal plant.

Keywords: Medicinal Plants, Mitogen-activated protein kinase, Thymidine monophosphate kinas, HIV protease, Enoyl-ACP reductase, docking.

INTRODUCTION

Boswellic acids are the major constituents of the gum derived from the plant *Boswellia serrata* Roxb. ex Colebr. (Family Burseraceae, Syn. *B. glabra*). The gum resin comprises of β-boswellic acids as the main triterpenic acid along with 11-keto-β-boswellic acids and their acetates [1-2]. The gum exudate is known for its anti-inflammatory properties in the Ayurvedic system of medicines [1, 3-4]. The alcoholic extract of the gum is used for the treatment of adjuvant arthritis [1,5]. It has synergistic effect with glucosamine, an anti-inflammatory and anti-arthritic agent [1,6]. Acetyl-11-keto-β-boswellic acid (AKBA), a component of the gum exudate is a pentacyclic terpenoid and is reported to be active against a large number of inflammatory diseases [1,7-8] including cancer, arthritis, chronic colitis, ulcerative colitis, Crohn's disease, and bronchial asthma [1,9-11].

MATERIALS AND METHODS

More than 100 natural and synthesize chemical compound were selected from PubChem compound database for creation of ligand library [12].

Expert system for calculation of druglikeness score based on qualifies scoring was used as described from on line server molinspiration [13].

Various successful and research target were selected from literature survey and 3D protein structure of target was downloaded from the protein data bank [14].

Targets were analyzed for active site details and hydrogen was added for docking. Docking was done by using GOLD 3.2 software [15]. Scoring was done by gold score and chem score method. Conesus scoring was done by collative score from Gold docking program.

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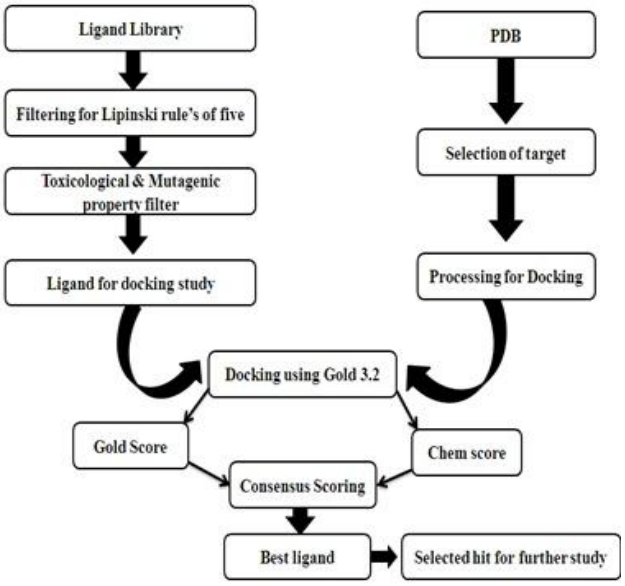
Consensus scoring of the both docking programmed was done to find out the best lead among all the hit included in the study.

***IN SILICO* WORKFLOW DIAGRAM**



RESULTS

More than 100 natural and synthesize chemical compound were included in study. The entire compound filtering for the Lipinski rule of five. Out of total 102 compounds only 68% compounds were found to meet the Lipinski's Rule of Five. Then filtering of the entire compound for the Mutagenicity Negative & Developmental NON-toxicant. Out of total 69 compounds only 86% compounds were found to Mutagenicity Negative & only 8% compounds were found to Developmental NON-toxicant. Initial filtering of the entire compound for the Lipinski rule of five, Mutagenicity Negative & Developmental NON-toxicant lead set of only 2 compounds which used in the further study.

Virtual screening of filtered 2 compounds was done against PDB structure of two research targets (Mitogen-activated protein kinase for cancer [3ORN] and Thymidine monophosphate kinase for TB [1G3U]) and two successful targets (HIV protease for HIV [1AID] and Enoyl-ACP reductase for malaria [1NHG]). [Table: 1]

For the first research target 3ORN maximum gold score and chem score were observed for ligand CID:109340 followed by ligand CID:14235. [Fig. 1]

In case of second research 1G3U target included in study best gold score and chem score were observed for ligand CID:109340 followed by ligand CID:14235. [Fig. 2]

The successful target 1AID was scored best gold score and chem score for ligand CID: 109340 followed by ligand CID: 14235. [Fig. 3]

The second successful target 1NHG was found to have best gold score for ligand CID: 109340 followed by ligand CID: 14235. [Fig. 4]

In the second step to compile the result of two docking programmed were compiled to gather with consensus scoring method. On performing the consensus scoring for target 3ORN for ligand CID: 109340 followed by ligand CID: 14235.

For target 1G3U for ligand CID: 109340 followed by ligand CID: 14235.

The ligand CID: 109340 were best scored for target 1AID followed by ligand CID: 14235. For target 1NHG ligand CID: 109340 were found best followed by ligand CID: 14235.

The best scored ligand CID: 109340 were selected for further study.

Fig.1: Docking score of Mitogen-activated Protein kinase (3ORN)

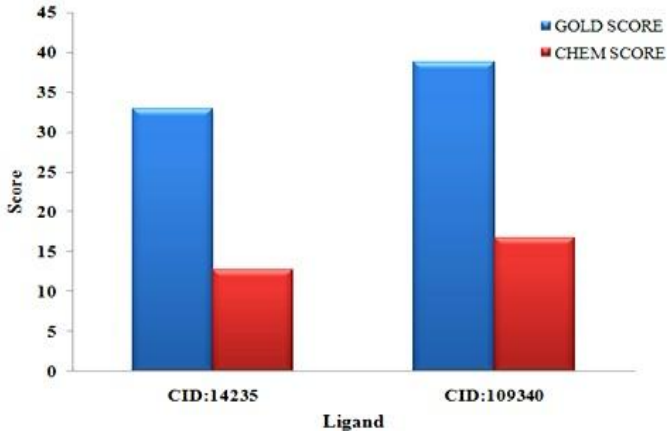
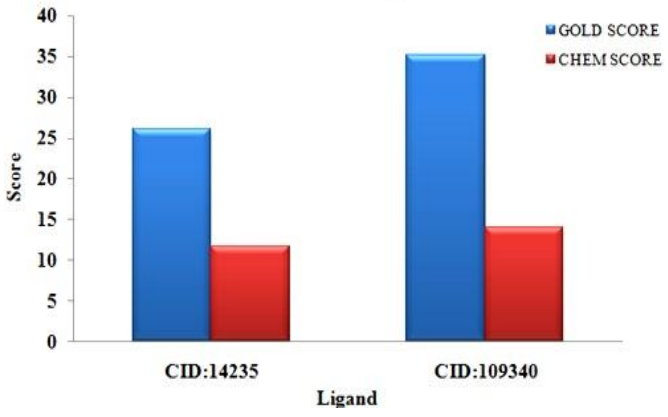
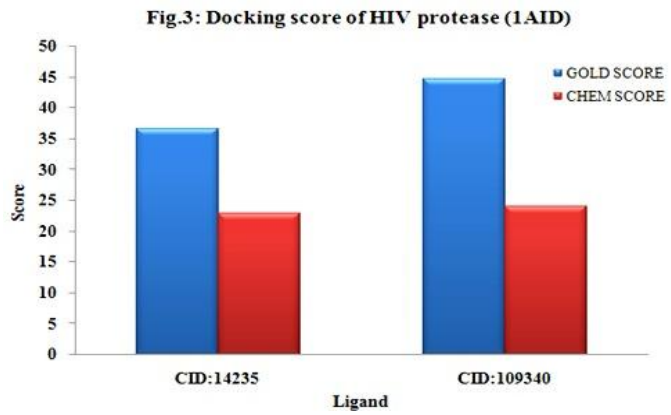


Fig.2: Docking score of Thymidine monophosphate kinase (1G3U)





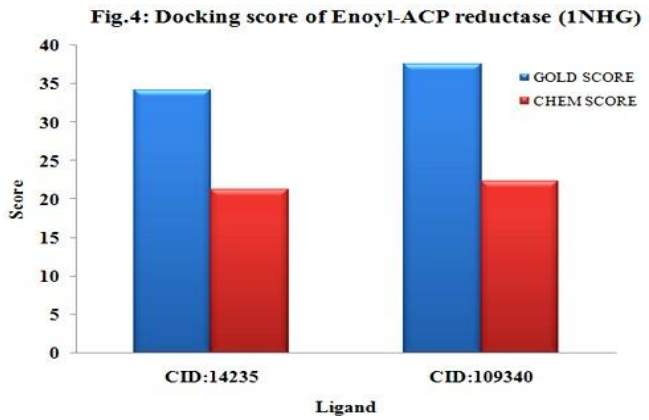


Table 1. Details of Receptors

Disease	Target name	Target type	PDB ID
Cancer	Mitogen-activated protein kinase	Research target	3ORN
HIV	HIV protease	Successful target	1AID
Malaria	Enoyl-ACP reductase	Successful target	1NHG
TB	Thymidine monophosphate kinase	Research target	1G3U

DISCUSSION

According to Tona *et al.*, 1998 Plants are important source of potentially useful structures for the development of new chemotherapeutic agents [16]. The first step towards this goal is the *in vitro* antibacterial activity assay. Many reports are available on the antiviral, antibacterial, antifungal, anthelmintic and anti-inflammatory properties of plants [17-23]. Some of these observations have helped in identifying the active principle responsible for such activities and in the developing drugs for the therapeutic use in human beings.

The ethanomedicinal plant *Boswellia serrata*, 3-O-Acetyl-11-keto-beta-boswellic acid (AKBA) is the most active compound of *Boswellia* extract and is a potent inhibitor of 5-lipoxygenase (5-LOX), a key enzyme in the biosynthesis of leukotrienes from arachidonic acid in the cellular inflammatory cascade [24-25].

CONCLUSION

The virtual screening from ligand library point towards the best score and efficient binding of the ligand 2-ethenyl-6-methylhept-5-en-1-yl acetate with two research target Mitogen-activated protein kinase, Thymidine monophosphate kinase and two successful target HIV protease, Enoyl-ACP reductase from the ligand library included in study. The result indicates ligand CID: 109340 as best from library for further study. The synthesize chemical compound having best score comparison to the natural chemical compound present in the *Boswellia serrata* Roxb. ex Colebr wild medicinal plant.

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