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MOLECULAR DOCKING STUDY ON *ANISOMELES INDICA* LINN. WILD ETHNOMEDICINAL PLANT FOR THERAPEUTIC PURPOSE

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ABSTRACT:

There is a growing focus on the importance of medicinal plants and traditional health systems in solving the health care problems of the world. Because of this awareness, the international trade in plants of medical importance is growing phenomenally, often to the detriment of natural habitats and mother populations in the countries of origin. There are over a hundred chemical substances that have been derived from plants for use as drugs and medicines. Herbal drugs constitute a major share of all the officially recognised systems of health in India *viz*. Ayurveda, Yoga, Unani, Siddha, Homeopathy and Naturopathy, except Allopathy. More than 70% of India's 1.1 billion populations still use these non-allopathic systems of medicine. Currently, there is no separate category of herbal drugs or dietary supplements, as per the Indian Drugs Act. *Anisomeles indica* Linn. (Family: Lamiaceae / Labiatae) is found throughout tropical and subtropical region of India. The plant is used in folk medicine as a cure in gastric catarrh and intermittent fever. Essential oil present in herb is used in uterine affection. *A. indica* Linn. is reported to have antipyretic, analgesic, anti-inflammatory activity and it also acts as natural herbicide in wheat fields. It is also reported that the leaves of *A. indica* consists of diterpenoids, ovatodiolide and its derivatives that are used as HIV inhibitors. Roots contain stigmasterol, K-sitosterol, paraffins and fatty acids. In India, the plant is used as a carminative and as aromatics. As a result of indiscriminate use of antimicrobial drugs in the treatment of infectious diseases, microorganisms have developed resistance to many antibiotics. There is need to develop alternative antibiotic drugs from plants. One approach is to screen local medicinal plants, which represent rich source of novel antimicrobial agents. In present work an attempt has been carried out to evaluate anti-HIV, anti-malarial, anti-cancer and anti-TB action of such species. 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 drug likeness. Molecular docking studies were carried out with docking programmed.

KEY WORD: *Molecular, Docking, Anisomeles Indica, Wild, Ethnomedicinal, Plant, Therapeutic.*

INTRODUCTION:

Anisomeles indica Linn. (Family: *Lamiaceae*) is found throughout tropical and subtropical region of India. It is wildly found common at road sides and in North Gujarat forest areas of Aravalli hills. The plant is used in folk medicine as a cure in gastric catarrh and intermittent fever and essential oil present in herb is used in uterine affection. (Kirtikar *et.al.* 1999, Anonymous, 2003) *A. indica* Linn. is reported to have antipyretic, analgesic, anti-inflammatory activity and it also acts as natural herbicide in wheat fields(Dharmasiri *et.al.* 2000 and 2003). The leaves of *A. indica* consist of diterpenoids, ovatodiolide and its derivatives that are used as HIV inhibitors(Alam *et.al.* 2000). Roots contain stigmasterol, K-sitosterol, paraffins and fatty acids. In India, the plant is used as a carminative and as aromatics (Anonymous, 1965-1981). As a result of indiscriminate use of antimicrobial drugs in the treatment of infectious diseases, microorganisms have developed resistance to many antibiotics. There is need to develop alternative antibiotic drugs from plants. One approach is to screen local medicinal plants, which represent rich source of novel antimicrobial agents. In present work an attempt has been carried out to evaluate anti-HIV, anti-malarial, anti-cancer and anti-TB action of such species. 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 drug likeness. Molecular docking studies were carried out with docking programmed.

MATERIAL AND METHODS:

Forest areas and villages of research area (North Gujarat, Aravalli Hill range Forest areas) were frequently visited, to collect the information about the forest wealth and uses of wild plant species were noted. Village wise men, experienced informants, elderly people, head man of the hamlets, tribal medicine men, were contacted and by repeated queries data was gathered. This is the original and ancient knowledge, which

was not documented systematically earlier but from last few decades several ethnobotanical workers have been worked on this subject. Screening of these ethnomedicinal species and select interested plants for further study.

More than 450 natural and synthesize chemical compound were selected from PubChem compound database for creation of ligand library (Wang *et.al.* 2009). Expert system for calculation of drug likeness score based on qualifies scoring was used as described from on line server molinspiration. (www.molinspiration.com) (Rajasekaran *et.al.* 2010). Various successful and research target were selected from literature survey and 3D protein structure of target was downloaded from the protein data bank. (Abola *et. al.,* 1996)

Targets were analyzed for active site details and hydrogen was added for docking. Docking was done by using GOLD 3.2 software (Verdonk *et. al.,* 2003). Scoring was done by gold score and chem score method. Conesus scoring was done by collative score from Gold docking program. Consensus scoring of the both docking programmed was done to find out the best lead among all the hit included in the study.

RESULT AND DISCUSSION:

More than 450 natural and synthesize chemical compound were included in study. Initial filtering of the entire compound for the Lipinski rule of five and mutagenicity lead set of 15 compounds which used in the further study.

Virtual screening of filtered 15 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 were observed for ligand CID_5280960 followed by ligand CID_18721 and CID_5280442. Whereas best Chem score was Ligand CID_44257884 found best followed by ligand CID_5280960 and CID_5281617. [Fig 2]

The second successful target 1NHG was found to have best gold score for ligand CID_18721 followed by ligand CID_5281601 and CID_5280442. Whereas best Chem score was ligand CID_79730 found best followed by ligand CID_5281617 and CID_5281601. [Fig 3]

In case of second research 1G3U target included in study best gold score was for Ligand CID_11337269 followed by ligand CID_18721 and CID_272741; whereas best Chem score was Ligand CID_5280442 found best followed by ligand CID_5281617 and CID_5281601. [Fig 4]

The successful target 1AID included in study best gold score was for Ligand CID_11337269 followed by ligand CID_18721 and CID_79730; whereas best Chem score was Ligand CID_145659 found best followed by ligand CID_5281601 and CID_31161. [Fig 5]

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 ligand CID_5280960 found best followed by ligand CID_5280442 and CID_79730.

For target 1G3U ligand CID_5280442 was best scored followed by ligand CID_5281601 and CID_11337269.

The ligand CID_145659 was best scored for target 1AID followed by ligand CID_18721 and CID_5281601. For target 1NHG ligand CID_5281601 was found best followed by ligand CID_79730 and CID_5281617.

The best scored ligand CID_5281601 and CID_79730 were selected for further study.

CONCLUSION:

The virtual screening from ligand library point towards the best score and efficient binding of the ligand 5-hydroxy-7-methoxy-2-(4-methoxyphenyl)-4*H*-chromen-4-one and 5,7-dimethoxy-2-(4-methoxyphenyl)-4*H*-chromen-4-one 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_5281601 and CID_79730 and as best from library for further study. The synthesize chemical compound having best score comparison to the natural chemical compound present in the *Anisomeles indica* Linn. wild medicinal plant.

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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

Fig.1: *In silico* Workflow Diagram

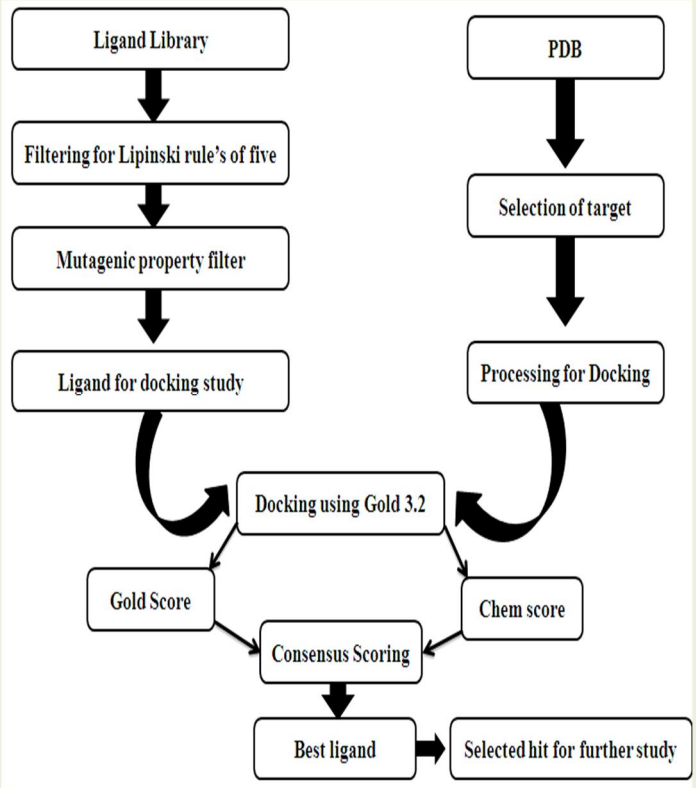

Fig.2: Docking score of Mitogen-activated Protein kinase (3ORN)

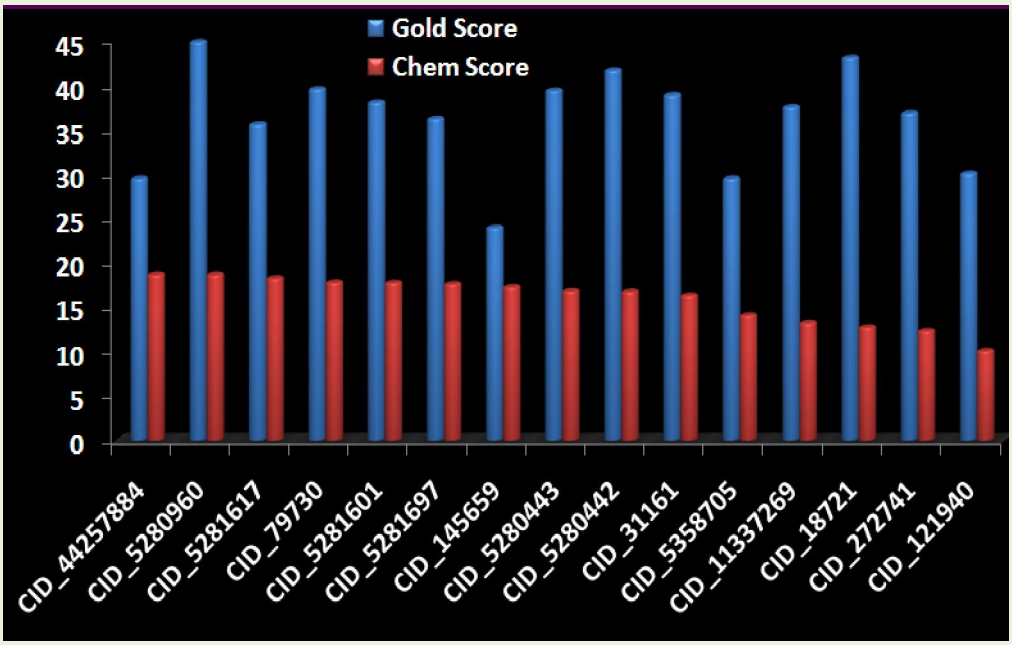

Fig.3: Docking score of Enoyl-ACP reductase (1NHG)

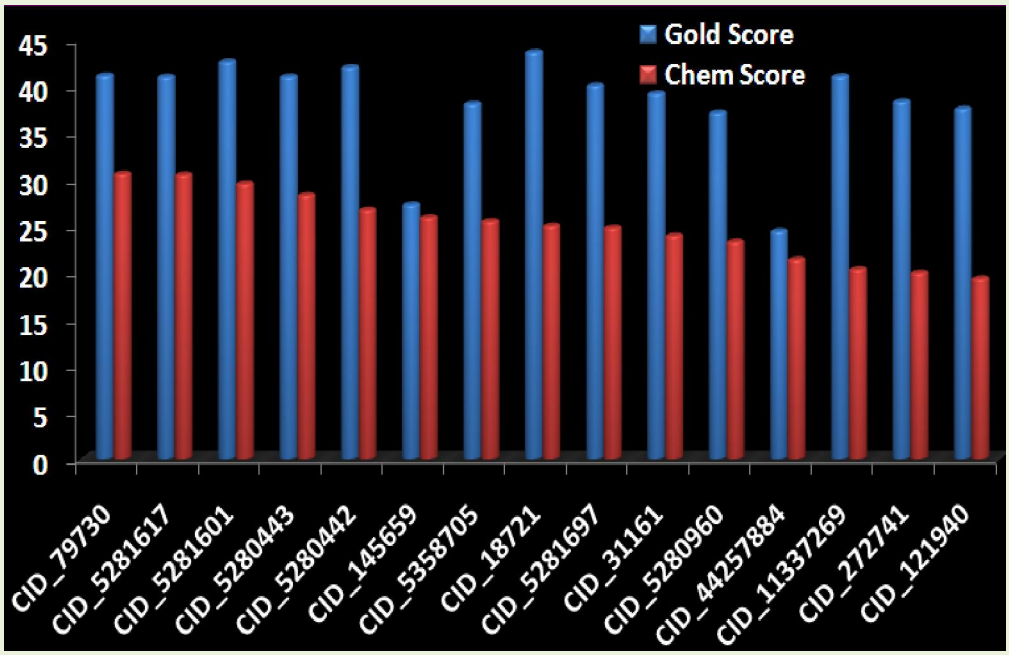

Fig.4: Docking score of Thymidine monophosphate kinase (1G3U)

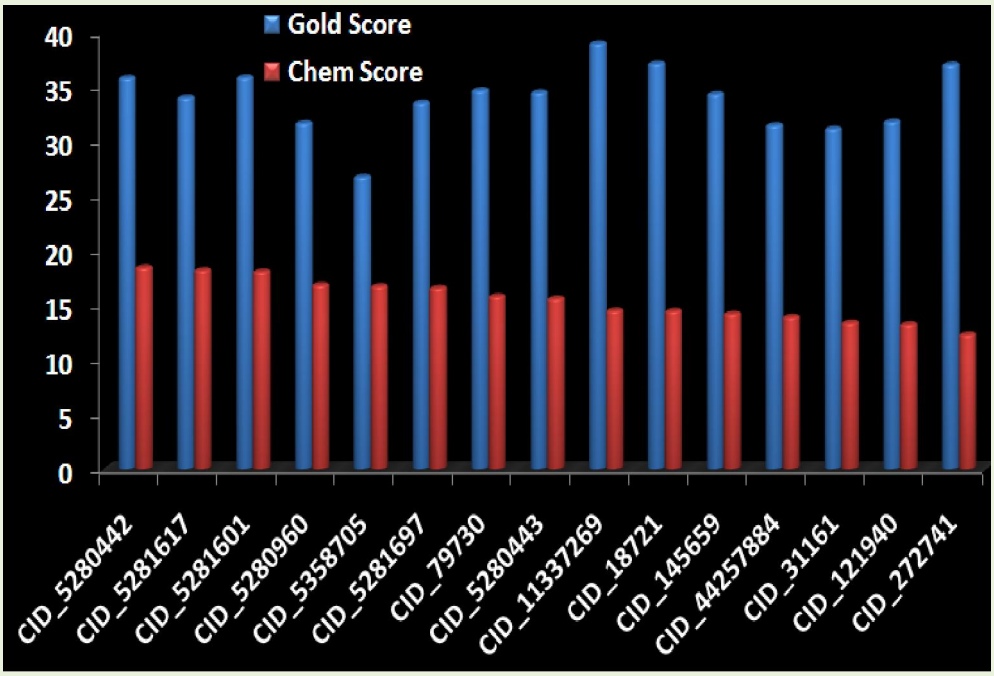

Fig.5: Docking score of HIV protease (1AID)