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In Silico Evaluation of Analgesic Activity of Ethnomedicinally Important Plant *Martynia annua* L.

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Abstract: Secondary metabolites which are potential source of drugs have long been documented as an important source of therapeutically medicines made from plants from several years. *Martynia annua* L. is well known small herbaceous annual plant. It is commonly known as Devil's claw or Cat's claw denotes to the inner woody capsule which splits open at one end into two curved horns or claws. In Ayurveda, the plant is known as Kakanasika in Sanskrit. In Hindi it is called as Bichhu and in Gujarati it is known as Vinchudo, which is being used in Indian traditional medicines for epilepsy, inflammation and applied locally for tuberculosis glands of camel's neck. The present study was aimed to investigate biological properties and chemical profiling of the selected extracts of the plant *Martynia annua* L. Molecular docking of phytochemicals have been studied for analgesic activity for three phytochemicals which are Chlorogenic Acid, Apigenin-7-O-beta- D-glucuronide, Pelargonin.

IndexTerms **- Secondary metabolites, *Martynia annua* L, Molecular docking, Analgesic activity.**

I. INTRODUCTION

Martynia annua L. (Martyniaceae) is one of the medicinal herbs used by native people of Mexico since ancient time for numerous therapeutic purposes. The plant is inborn to Mexico but now well familiarised throughout India on waste lands. (Suryavwanshi and Tare, 2013) In India Martynia annua L. is well recognised small herbaceous annual plant. It is commonly known as Devil's claw or Cat's claw denotes to the inner woody capsule which splits open at one end into two curved horns or claws (Kenwat et al., 2013; Singhai and Lodhi, 2011). In Ayurveda, the plant is known as Kakanasika in Sanskrit.In Hindi it is called as Bichhu and in Gujarati it is known as Vinchudo, which is being used in Indian traditional medicines for epilepsy, inflammation and applied locally for tuberculosis glands of camel's neck (Dhingra et al., 2013).

During the past decade, the indigenous or traditional system has gained importance in the field of medicine. A large population dependent on the traditional practitioners, who are dependent on medicinal plants to meet their primary health care needs. Although, modern medicines are available, herbal medicine retained their image for historical and cultural reasons (Kumar et al., 2012).

Since the usage of these herbal medicines has increased, issues and motto regarding their quality, safety and efficacy in industrialized and developing countries are cropped up. In order to make sure the safe use of these medicines, a necessary first step is the reviewing the whole plant for its potential as a medicinal plant. *Martynia annua* L. is a wild herb distributed throughout India. Materiamedica of India provides lots of information on the folklore practices and traditional aspects of therapeutically important natural products (Kumar et al., 2012).

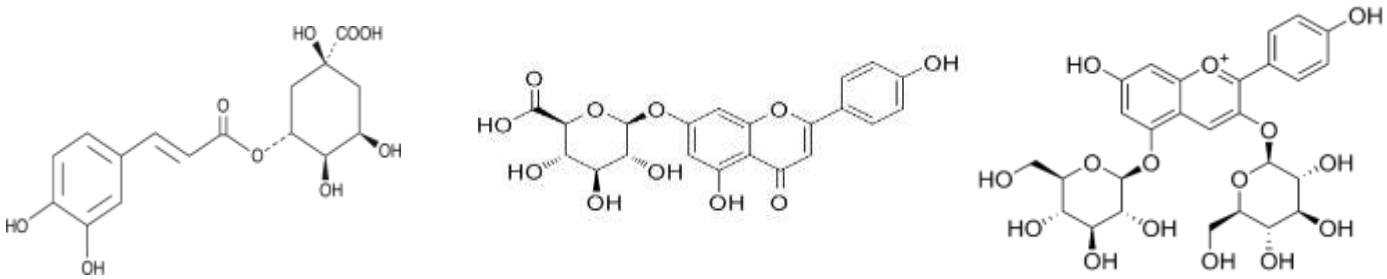
Bioinformatics occupies the organization of data created from experiments into databases, the development of new algorithms and software, using it for the interpretation and analysis of data. (Jasmine and Vanaja 2013)In the present study, few compounds from *Martynia annua* L. were analyzed by GC-MS and were identified. These secondary metabolites were screened with the database of available structures, and algorithms adapted from artificial intelligence applications to understand the applicability of the docking tool. The compounds thus screened with docking tools provide a preliminary data for refinement of the chemical structures or modification of the specific site on a target protein or nucleotide, enabling binding at the site that is being modelled computationally with several different techniques. The availability of the structural information aids in proper selection of target for inhibitor discovery as the binding sites of the molecules are identified (Nicola et al., 2008)

Molecular modeling evolved as modern medicinal chemistry technique which is used to evaluate the structure activity relationship (SAR) (Leonardo et al., 2015). Molecular docking is one of them which is being used for the examination of molecular recognition of receptor-ligand binding through structure based and ligand based approaches (Vasava et al., 2017).

II. MATERIALS AND METHODS

2.1Molecular Docking

The phytochemicals been extract from *Martynia annua* L. plant by GCMS method. Furthermore, the 2D structures (**Figure-1**) of these phytochemicals retrieved from PubChem database and converted into 3D form with MarvinSketch suite. These 3D structures prepared according to the software requirements including addition of hydrogen bonds, cleaning process and followed by energy minimization with Amber03 force field (Krieger et al, 2002 and Krieger et al, 2004).



Chlorogenic acid **Apigenin-7-O- beta-D- glucuronide** **Pelargonin**

Figure-1 2D representation of extracted phytoconsitutents

2.2 Protein Preparation

Three compounds from *Martynia annua* L. (Chlorogenic Acid, Apigenin-7-O-beta- D- glucuronide, Pelargonin) were taken for docking analysis on the protein 4RUZ based on the structural activity relationship which contains Analgesic activity. Three dimensional crystal structure of Carbonic anhydrase having resolution of 1.63 Å was retrieved from the RCSB (Research Collaboratory for Structural Bio-informatics).

Protein data bank under the PDB ID: 4RUZ chain A, crystal structure having 260 amino acids chain length with ligand 4-ethoxybenzenesulfonamide, which is useful in identification of its active binding sites which is used for the curation of mountain sickness, gastric and duodenal ulcers, neurological disorders and osteoporosis disease.

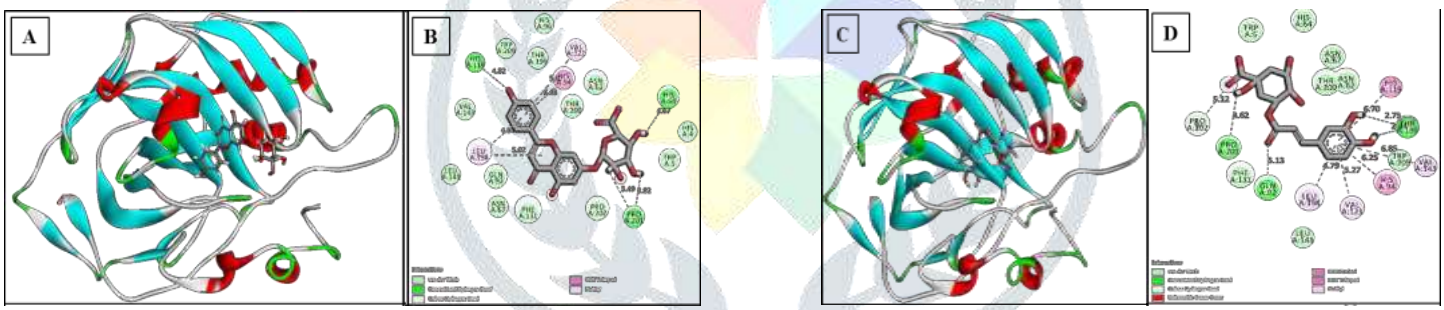
2.3 Molecular Docking

Based on the active site information, molecular docking of all phytochemicals has been performed with 4RUZ in YASARA software. It contains Amber 03 force field and provides best docked phytochemicals with binding energy, hydrogen bonds and contacting amino acid residues.

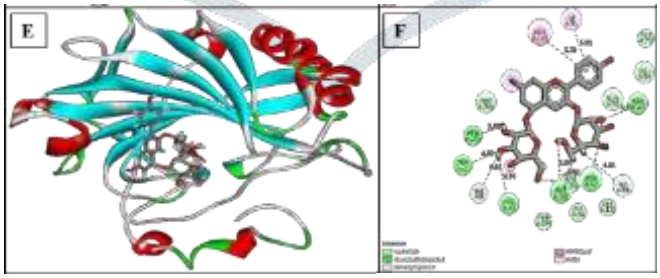
III. RESULTS OF MOLECULAR DOCKING

3.1 Docking validation

Native ligands of downloaded proteins have been re-docked for the experimental proof and positive references which confirms the formation of docking complexes. On the basis of the docking score and interacting profiles of various conformations considered for further docking experiments.



(A&B) Chlorogenic Acid **(C&D) Apigenin-7-O-beta- D- glucuronide**



(E&F) Docked pose of Anhydrase with Pelargonin

Figure-2 (A,C&E) Docked pose of Anhydrase with Chlorogenic Acid, Apigenin-7-O-beta- D- glucuronide, Pelargonin, (B,D&F)Protein–ligand interaction maps developed from Discovery Studio Visualizer (Hydrogen- green color, van der Waals interactions-light green color, Pi-Pi-Stacked-dark pink color, Pi-Pi T-shaped- dark pink color and Pi-Alkyl- light pink color).

3.2. Docking Results analysis

Active site of the docked complex of 4ruz has been considered for the further docking analysis which includes the library of optimized phytochemicals for docking experiments. Among them, Chlorogenic Acid, Apigenin-7-O- beta- D- glucuronide and Pelargonin were found as best docked ligands with the energy of 7.9, 7.819, and 7.363 kcal/mol (Figure-1). In addition, Trp 5, Asn 62, His 64, Asn 67, Gln 92, His 94, His 119, Val 121, Phe 131, Leu 198, Thr 199, Thr 200, Pro 201, Pro 202 were the reported amino acids residues, which remains common in all docked ligands (Table-1)

Table-1 Docking score, binding energy, Hydrogen bonds, and contacting receptor residues of 4RUZ ligand for Analgesic Activity

Ligands	Binding energy	Hydrogen bonds	Contacting receptor residues
Chlorogenic Acid	7.9	4	Trp 5, Asn 62, His 64, Asn 67, Gln 92, His 94, His 119, Val 121, Phe 131, Leu 141, Val 143, Leu 198, Thr 199, Thr 200, Pro 201, Pro 202, Trp 209
Apigenin-7-O-beta-D- glucuronide	7.819	3	His 4, Trp 5, Asn 62, His 64, Asn 67, Gln 92, His 94, His 96, His 119, Val 121, Phe 131, Leu 141, Val 143, Leu 198, Thr 199, Thr 200, Pro 201, Pro 202, Trp 209
Pelargonin	7.363	7	His 4, Trp 5, Asn 62, His 64, Asn 67, Glu 69, Phe 70, Ile 91, Gln 92, His 94, His 96, Val 121, Phe 131, Leu 198, Thr 199, Thr 200, Pro 201, Pro 202

These binding potency shows the higher affinity towards the receptor which confirms that these ligands can be used for in vitro as well as in vivo analysis and possible inhibitors for the anhydrase as Analgesic agents.

IV. Discussion

In any pharmacological activity, nowadays virtual screening has a positive impact on the discovery of new drugs through advanced computational techniques. Ramalho et al, 2013 discussed the advantage of virtual screening that, it utilizes the docking and scoring of each compound from a dataset and the system used is based on predicting the binding modes and binding affinities of each component in the dataset by means of docking to an X-ray crystallographic structure. Liu et al, 2014 considered that, current studies have focused on definite features such as the size and diversity of the ligand dataset, extensive range of targets and the estimation of docking programs. In this study total three Ligands were taken i.e. Chlorogenic Acid, Apigenin-7-O-beta- D- glucuronide and Pelargonin of martynia annua plant were docking into the active site of 4ruz enzyme for analgesic activity. In this study total 3 compound were docked among them chlorogenic acid shows the highest binding energy 7.9 with 4 hydrogen and the binding energy of Apigenin-7-O-beta-D-glucuronide was 7.819 with 3 hydrogen bond, while in Pelargonin binding energy was 7.363 with highest 7 hydrogen bond.

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