EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 11
Issue: 10
247-254
Year: 2024

ANTI INFLAMMATORY EFFECT OF SIDDHA HERBAL DRUG AZHAVANAM VERPATTAI CHOORNAM USING IN SILICO MODEL. A COMPUTATIONAL STUDY TO PREDICT ITS EFFICACY IN TREATING MENORRHAGIA

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Article Received on 12/08/2024 **Article Revised on 02/09/2024** **Article Accepted on 23/09/2024**

ABSTRACT

Background: Siddha medicine is a form of traditional medicine originating in southern India. It is one of the oldest systems of medicine in India. Siddhars have classified disease into 4448 types. In this modern mechanical world, now-a-days people are suffering from various disease. Especially females are the majority of sufferers due to their dual role both in family as well as society. One among the diseases in menstrual disorders is the "Perumbadu''. Sage Yugi classified 'Perumbadu' in his Yugi Vaidhya Chinthamani into 4 types. Of these Vatha Perumbadu is one of them. Perumbadu in Siddha can be compared with Menorrhagia. The present study focus on Azhavanam ver pattai choornam, a herbal formulation recommended for Menorrhagia treatment as mentioned in Gunpadam-Mooligai. The Primary objective of this research is to investigate the in-vitro anti Inflammatory activity and biochemical properties of Azhavanamverpattai choornam. **Aim**: The aim of the study is to analyze the in-vitro Anti Inflammatory activity of Azhavanam verpattai choornam. **Methodology:** This study investigates theAnti inflammatory potential of Azhavanam verpattai choornam by examining how its phytocomponents bind to specific aminoacids (His70, Asp71, Ser72, Val91, Pro117,Ser119,Thr120,Pro121,Ser122,Thr124,Thr125) of the target by forming hydrogen bond will hinder the function of the inflammatory cytokine IL6(Interleukin6) with PDB-1N26. These amino acid residues are functionally responsible for binding of substrate and inhibitors. There by Phytocomponents which inhibit the target IL6(Interleukin 6) may act as a potential therapeutic agent for management of inflammation. **Result:** The study result of Azhavanam verpattai choornam has significant Anti-inflammatory activity.

KEYWORDS: Perumbadu, Menoirrhagia, Azhavanam verpattai choornam, Anti-inflammatory activity.

INTRODUCTION

Menorrhagia is seen in women with increased uterine vascularity such as Chronic Pelvic inflammatory disease, Pelvic endometriosis. The vascular changes in the endometrium and amount and duration of the menstrual bleeding is controlled by the interaction of different prostaglandins secreted by the endometrium. PGI 2 (Prostacyclin) responsible for muscle relaxation and vasodilatation. PGI 2 causes menorrhagia. Hence this study aims to investigate the Antiinflammatory properties of Azhavanam verpattai choornam using in-vitro assay.

MATERIALS AND METHODS

Drug Selection

The Siddha Herbal formulation Azhavanam verpattai choornam is mentioned in Siddha classical literature Gunapadam- Mooligai part I.

INGREDIENTS OF AZHAVANAM VERPATTAI CHOORNAM

A single drug is used here
Azhavanam verpattai powder -1g-Lowsonia inermis.

PROCESS OF DRUG PREPARATION

The Above mentioned trail drug was purified According to proper method described in Siddha classical literature. The purified drug was powdered, and stored in a tight container.

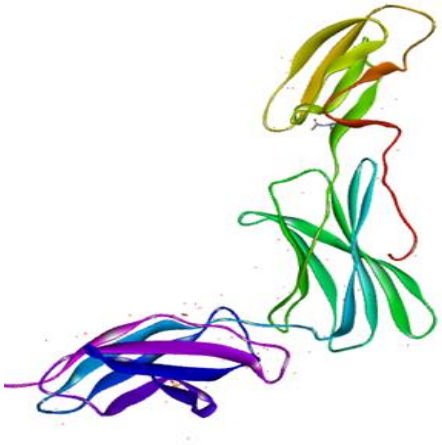
ANTI INFLAMMATORY ACTIVITY EVALUATION OF AZHAVANAM VERPATTAI CHOORNAM

Docking calculations were carried out for retrieved phytocomponents against target protein. Essential hydrogen atoms, Kollman united atom type charges, and solvation parameters were added with the aid of AutoDock tools (*Morris, Goodsell et al., 1998*). Affinity (grid) maps of ×× Å grid points and 0.375 Å spacing were generated using the Autogrid program (*Morris, Goodsell et al., 1998*). AutoDock parameter set- and distance-dependent dielectric functions were used in the calculation of the van der Waals and the electrostatic terms, respectively. Docking simulations were performed using the Lamarckian genetic algorithm (LGA) and the Solis & Wets local search method (*Solis and Wets, 1981*). Initial position, orientation, and torsions of the ligand molecules were set randomly. All rotatable torsions were released during docking. Each docking experiment was derived from 2 different runs that were set to terminate after a maximum of 250000 energy evaluations. The population size was set to 150. During the search, a translational step of 0.2 Å, and quaternion and torsion steps of 5 were applied.

PDB	Name of the Target
1N26	IL6 (Interleukin 6)

RECEPTOR STRUCTURE

Crystalline structure of the target protein IL6 was retrieved from protein data bank and protein clean-up process was done and essential missing hydrogen atom were being added. Different orientation of the lead molecules with respect to the target protein was evaluated by Autodock program and the best dock pose was selected based on the interaction study analysis.

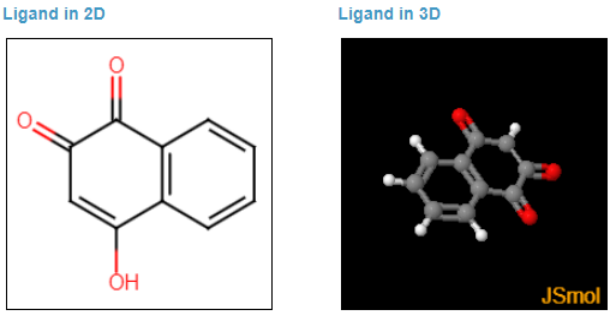


2D and 3D Structure of Phytocomponents

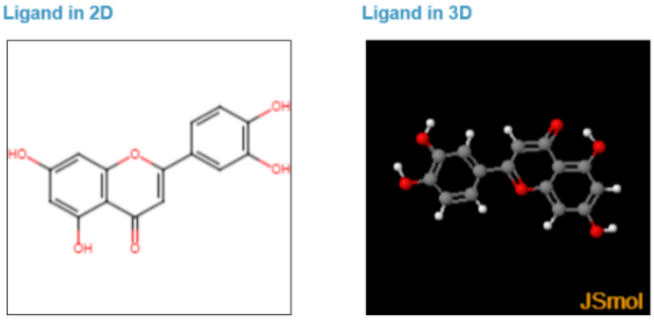
List of Phytocomponents Selected for docking

Herbs	Phytochemicals
Lawsonia inermis	Lawsone Luteolin Apigenin Scopoletin

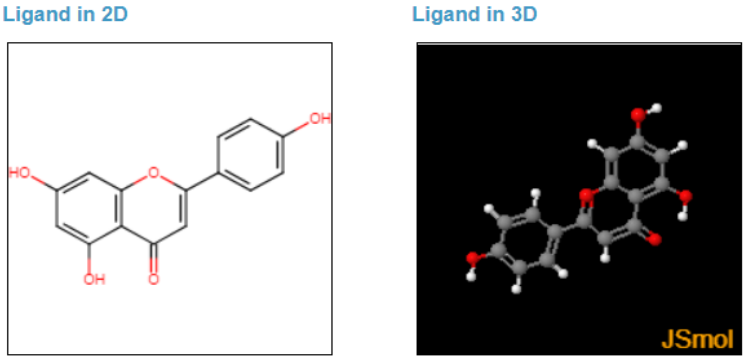
Lawsone



Luteolin



Apigenin



Scopoletin

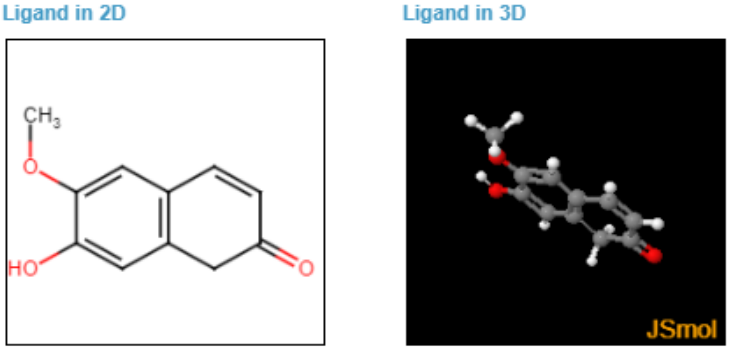


Table 1: Ligand Properties of the Compounds Selected for Docking Analysis.

Compound	Molar weight g/mol	Molecular Formula	H Bond Donor	H Bond Acceptor	Rotatable bonds
Lawsone	174.15 g/mol	$C_{10}H_6O_3$	1	3	0
Luteolin	286.24g/mol	$C_{15}H_{10}O_6$	4	6	1
Apigenin	270.24 g/mol	$C_{15}H_{10}O_5$	3	5	1
Scopoletin	192.17 g/mol	$C_{10}H_8O_4$	1	4	1

RESULTS

Table 2: Summary of the molecular docking studies of compounds against IL6 (Interleukin 6) (1N26).

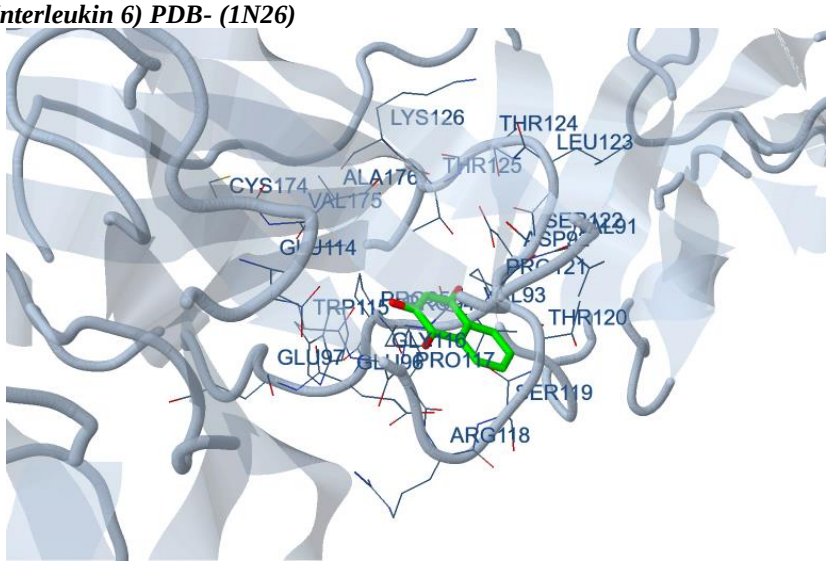
Compounds	Est. Free Energy of Binding	Est. Inhibition Constant, Ki	Electrostatic Energy	Total Intermolec. Energy	Interact. Surface
Lawsone	-5.66 kcal/mol	70.40 uM	-0.31 kcal/mol	-5.66 kcal/mol	427.564
Luteolin	-6.13 kcal/mol	32.34 uM	-0.09 kcal/mol	-5.84 kcal/mol	570.928
Apigenin	-5.14 kcal/mol	169.55 uM	-0.11 kcal/mol	-6.61 kcal/mol	548.417
Scopoletin	-5.77 kcal/mol	59.10 uM	-0.09 kcal/mol	-5.59 kcal/mol	477.164

Table 3: Amino acid Residue Interaction of Lead against IL6 (Interleukin 6) PDB- (1N26).

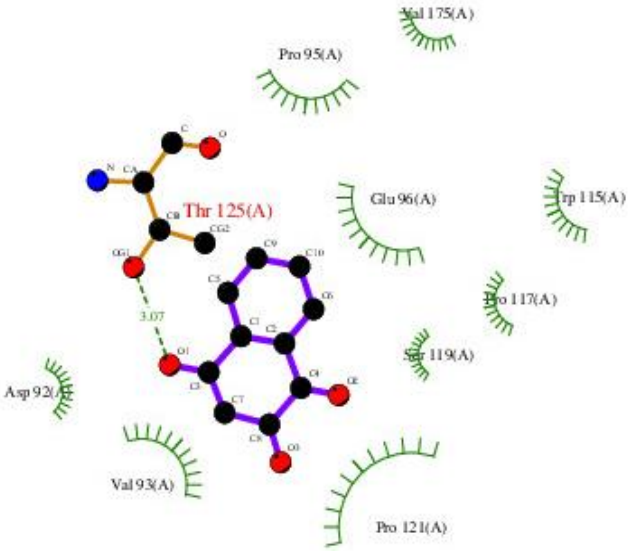
Compounds	Interactions	Amino acid Residues									
Lawsone	4	92	93	95	96	115	117	119	121	125	175
		ASP	VAL	PRO	GLU	TRP	PRO	SER	PRO	THR	VAL
Luteolin	0	123	126	147	148	150	155				
		LEU	LYS	GLN	TYR	GLN	PHE				
Apigenin	5	93	95	96	115	117	119	121	122	125	175
		VAL	PRO	GLU	TRP	PRO	SER	PRO	SER	THR	VAL
Scopoletin	3	69	93	96	115	119	121	125			
		LEU	VAL	GLU	TRP	SER	PRO	THR			

DOCKING POSE

Lawsone with IL6 (Interleukin 6) PDB- (1N26)



2D Interaction Plot Analysis



Key

Ligand bond

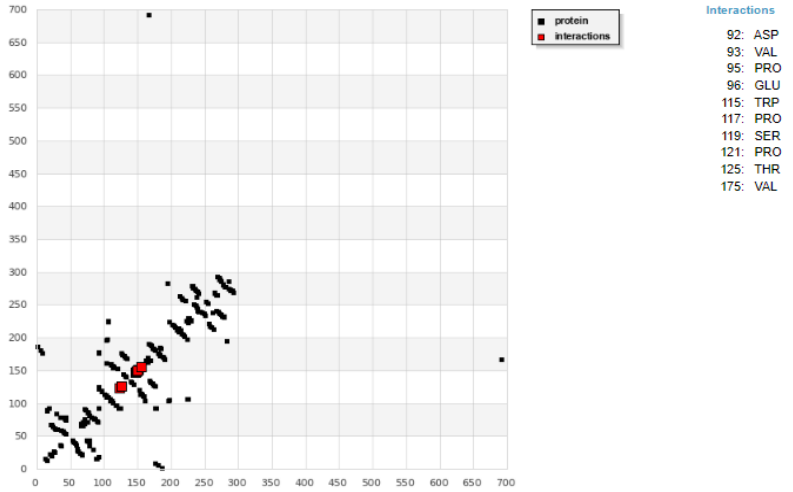
Non-ligand bond

Hydrogen bond and its length

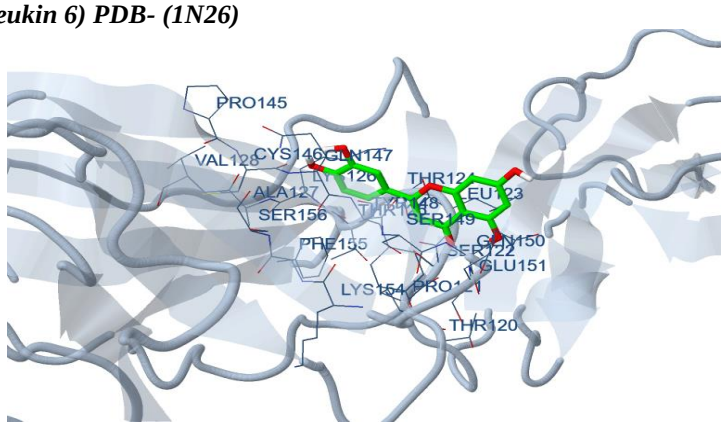
Non-ligand residues involved in other contact(s)

docking

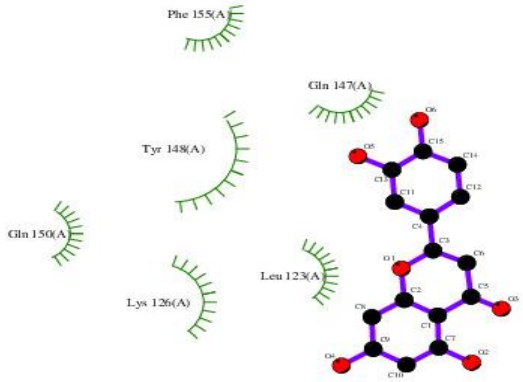
Hydrogen bond plotting with core amino acid Analysis



Luteolin with IL6 (Interleukin 6) PDB- (1N26)

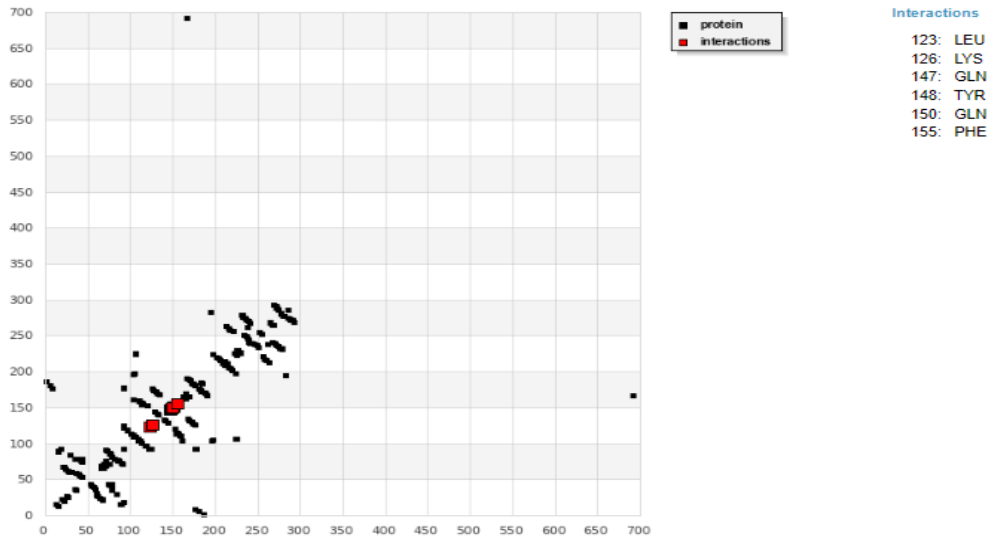


2D Interaction Plot Analysis

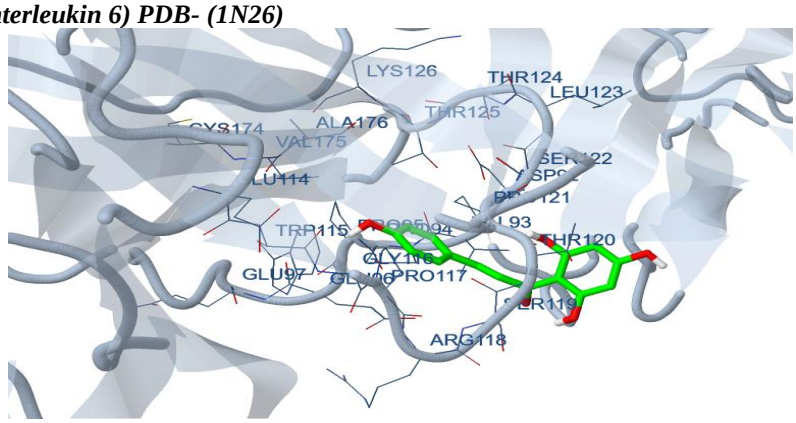


docking

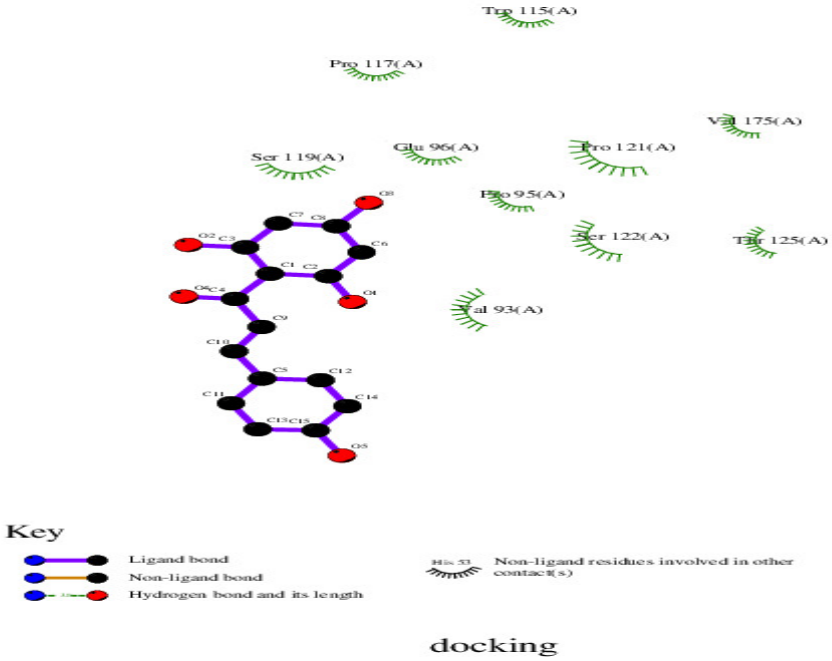
Hydrogen bond plotting with core amino acid Analysis



Apigenin with IL6 (Interleukin 6) PDB- (1N26)

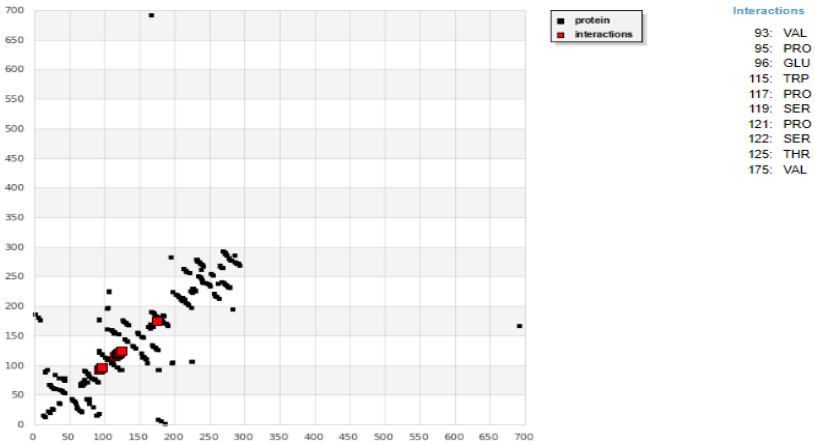


2D Interaction Plot Analysis

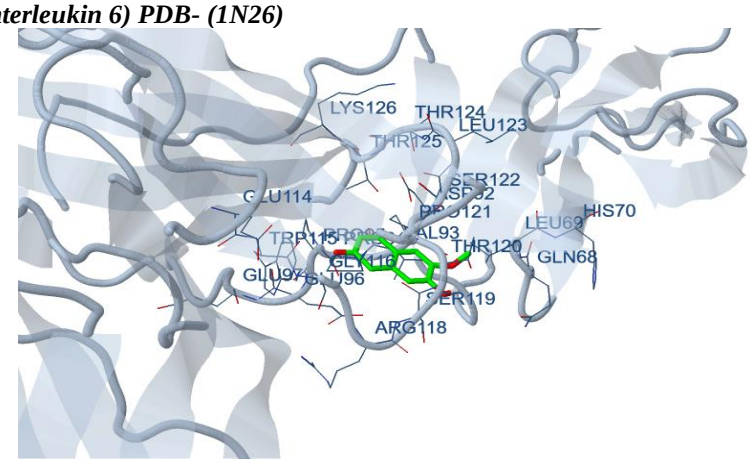


docking

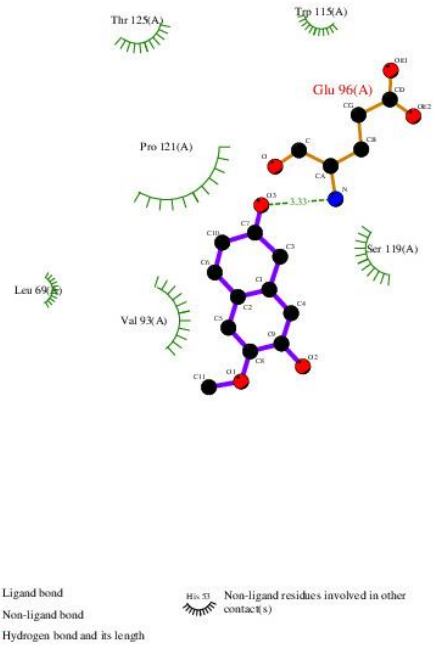
Hydrogen bond plotting with core amino acid Analysis



Scopoletin with IL6 (Interleukin 6) PDB- (1N26)

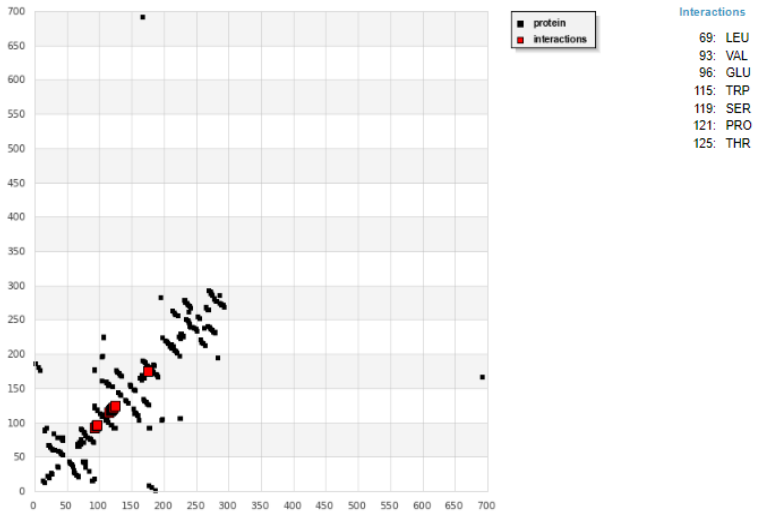


2D Interaction Plot Analysis



docking

Hydrogen bond plotting with core amino acid Analysis



DISCUSSION

Total of 4 bioactive lead compounds were retrieved from the herbs present in the siddha formulation. From reported data of the herb, the phytochemicals such as Lawsone, Apigenin and Scopoletin possess maximum of three to five interactions with the core active amino acid residues present on the target IL6 (Interleukin 6).

CONCLUSION

Based on the results of the computational analysis it was concluded that all the bio-active compound's like Lawsone, Apigenin and Scopoletin revels significant binding affinity against the target cytokine IL6 by interacting with active amino acid present on the active site thereby it was concluded that these compounds may exerts promising anti-inflammatory activity.

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