

Molecular Docking Studies for the Assessment of Wound Healing Activity of Phytoconstituents in *Heliotropium Indicum*

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Abstract:- One of the most crucial and complex processes is the skin's multi-stage process of healing after an injury. *Heliotropium indicum* is a potent antibiotic, anti-inflammatory, anti-neoplastic, anti-oxidant, and wound-healing agent. *Heliotropium indicum* Linn is the source of the chemical compound in question, which is abundant in sterols, ammines, volatile oils, and the pyrrolizidine alkaloids. Molecular docking studies were conducted on *Heliotropium indicum* using Argus lab 4.0.1 and Autodock 1.5.7. The proteins PDB ID:1YXO, 3V18, and 4G8R were selected because of their role in wound healing. The pieces work together with the protein responsible for mending wounds. The binding affinities of mupirocin and nitrofurazone are higher than those of the components stigmaterol, eugenol, borneol, and campesterol. In order to better customize *Heliotropium indicum* to our requirements, we now have a better knowledge of the components of the molecule that interact with their receptors in the wound healing process.


Keywords:- Docking, *Heliotropium Indicum*, Wound Healing, Software's.

I. INTRODUCTION

The skin is the body's first line of defense against bacteria and other potentially dangerous substances. Stress causes a wound by compromising the dermis (either physical or thermal). A wound is an alteration to an organism's regular form and function. A skin wound may range from being quite slight (just having a breach in the epithelium layer) to being extremely serious (affecting the deeper subcutaneous tissues and causing damage to the tendons, muscles, blood vessels, nerves, parenchymal organs, and even bone). Different factors influence the recovery of old vs new wounds. Direct contact with the skin may cause acute wounds, the severity of which varies [1-3]. Healing by itself and making progress via the healing process usually take between 5 and 10 days, and never more than 30 days. Instead, a combination of internal systems and a predisposing state led to chronic wounds. Common types of persistent wounds include leg ulcers, foot ulcers, and pressure sores. Some pathophysiological abnormalities, such poor blood flow to tissues (from blocked arteries or clogged veins) or an underlying metabolic problem, may lead to these types of wounds (such as diabetes mellitus). Wound repair involves a complex set of systems operating on cellular, humoral, and molecular scales.

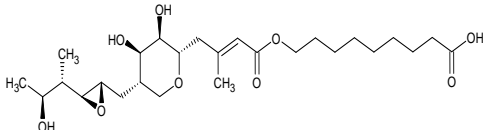
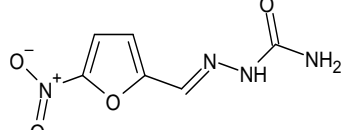
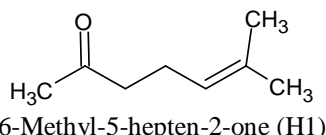
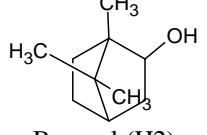
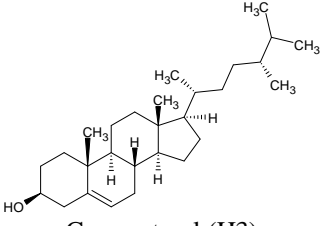
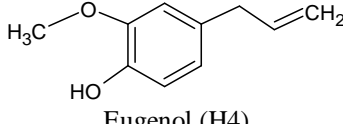
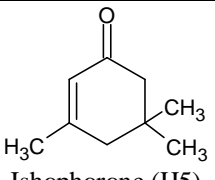
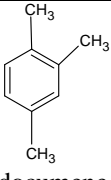
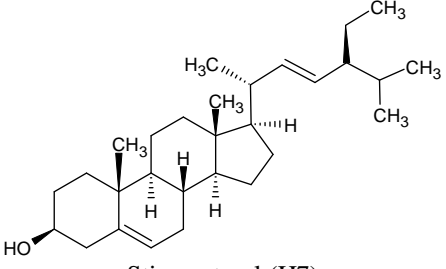
Common cutaneous wound healing stages include coagulation, inflammation, re-epithelialization, granulation tissue development, angiogenesis, connective tissue contraction, and remodeling. Wound healing is a complex process involving many different biological and immunological systems working together. Chronic wounds are more likely to get infected with germs due to poor nutrition and metabolic imbalances [4-8]. Prolonged inflammation, poor re epithelialization, and deficient matrix remodeling are hallmarks of nonhealing wounds, which are the result of a back-and-forth between the microorganisms in the wound and the patient. *Staphylococcus aureus*, *pseudomonas aeruginosa*, and -hemolytic streptococci are some of the bacteria that may be isolated from both infected and non-infected wounds. Since a computer tool, molecular docking is essential to structure-based drug design as it accurately predicts the binding configuration of protein and ligand. Before investing in expensive in vitro and in vivo studies, in silico research may provide useful insights. Researchers in this area are primarily interested in creating new synthetic compounds with improved therapeutic efficacy and lower toxicity [9-11]. Six chemical components of *Heliotropium indicum* (6-Methyl-5-hepten-2-one, Borneol, Campesterol, Eugenol, Ishophorone, Pseudocumene, Stigmaterol) and three distinct proteins were studied by docking using the Argus lab 4.0.1 and Autodock programs (1YXO, 3V18, 4G8R). 1.5.7. Local communities across the world rely on *Heliotropium indicum* (Tab. 1) as a primary treatment for a broad range of illnesses. Alkaloids, amines, sterols, triterpenes, and volatile oils are all components. Medicinally, this herb is exclusively used in age-old, time-honored customs. The medicinal uses for this plant are many. Research by G.k. Dash et al. on the wound-healing effects of this herb in rats is currently available. Here, we investigated the efficiency with which these molecules repair tissue after it has been damaged [12].

Table No. 1: Scientific classification of plant

Kingdom: Plantae	
Class: Dicotyledonae	
Order: Boraginales	
Family: Boraginaceae	
Species: <i>Heliotropium indicum</i>	
Scientific Name: <i>Heliotropium indicum</i> Linn	
Common Name: Indian Heliotrope	

II. MATERIALS AND METHODS

A. Structures

Structure of standard drug	
 <p>Mupirocin</p>	 <p>Nitrofurazone</p>
Structures of bioactive compound present in <i>Heliotropium indicum</i>	
 <p>6-Methyl-5-hepten-2-one (H1)</p>	 <p>Borneol (H2)</p>
 <p>Campesterol (H3)</p>	 <p>Eugenol (H4)</p>
 <p>Ishophorone (H5)</p>	 <p>Pseudocumene (H6)</p>
 <p>Stigmasterol (H7)</p>	

B. Wound healing proteins

- 1YXO (Crystal Structure of pyridoxal phosphate biosynthetic protein PdxA PA0593).
- 3V18 (Structure of the Phosphatidylinositol-specific phospholipase C from *Staphylococcus aureus*).
- 4G8R (Crystal Structure of a novel small molecule inactivator bound to plasminogen activator inhibitor-1).

C. Docking procedure:

Steps involved in docking by using Argus lab:

- Protein preparation
- Selection of active site
- Ligand preparation
- Docking procedure
- Visualization/ Interpretation of Docking

Steps involved in docking by using Autodock tools:

- Create a new folder
- Preparation of Protein and Ligand
- Configuration file
- Command prompt
- Analysis and Interpretation

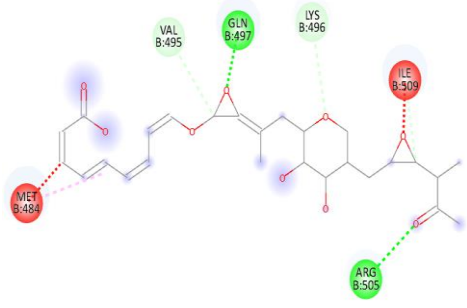
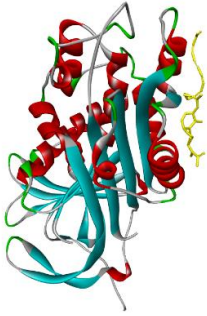
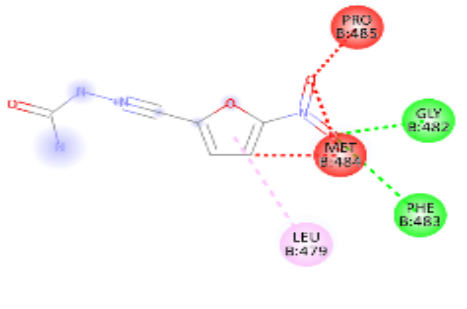
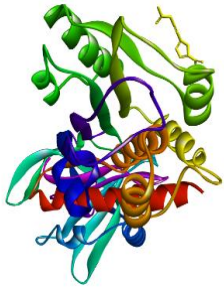
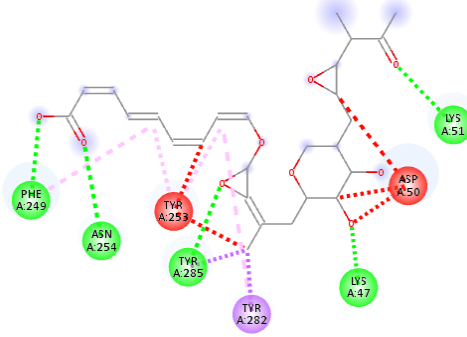
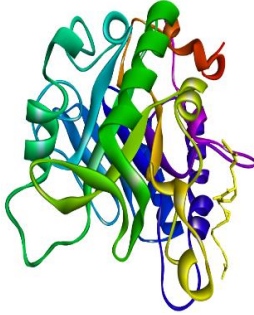
III. RESULT AND DISCUSSION

The binding affinity of the standard drug with wound healing proteins by using Argus lab 4.0.1 (Table 2) and Autodock tools 1.5.7 (Table 4) and followed by the binding affinity of *Heliotropium indicum* with wound healing proteins by using above mentioned software's (Table 3 & 5). Using Autodock tools 1.5.7 and Argus lab 4.0.1. we analysed the binding impact of *Heliotropium indicum*'s phytoconstituents with many proteins (4G8R, 1YXO, 3V18) known to play a part in the wound-healing process. Using the RMSD and

binding affinity score, we were able to predict the most productive interactions between proteins and phytoconstituents. Inhibitor type I (4G8R) plasminogen activator protein is a zymogen of plasmin, the main enzyme responsible for degrading fibrin clots. In the process of healing wounds, plasminogen and its receptors control the inflammatory response. Staphylococcus aureus and Pseudomonas aeruginosa, respectively, are the sources of the

proteins 1YXO and 3V18. They raise levels of proinflammatory cytokines including IL-1 and TNF-, which contribute to wound chronicity. Overly aggressive inflammation slows the healing process. Suppressing these microbes will promote wound healing. The result obtained from Argus lab 4.0.1 (Table 6) and Autodock tools 1.5.7 (Table 7) in the respective wound healing proteins along with standard drug and Heliotropium indicum.

Table No. 2. Binding affinity of standard drug by Argus lab 4.0.1

S. No.	Standard drug	Capture		Final energy
		2D	3D	
4G8R				
1.	Mupirocin			-9.23565 kcal/mol
2.	Nitrofurazone			-6.91681 kcal/mol
3V18				
1.	Mupirocin			-10.3793 kcal/mol

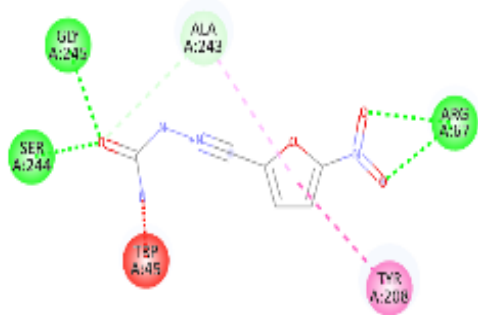
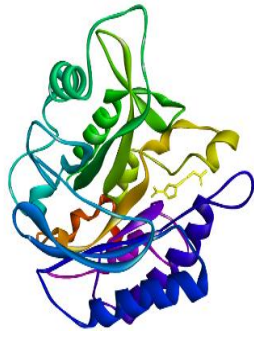
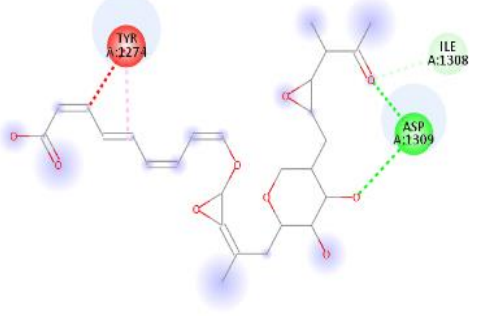

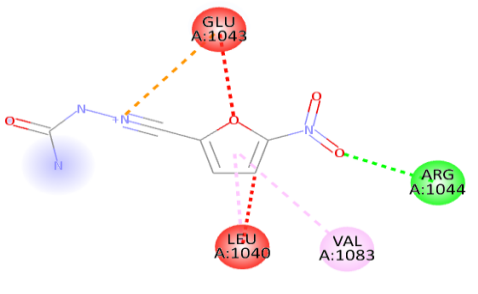
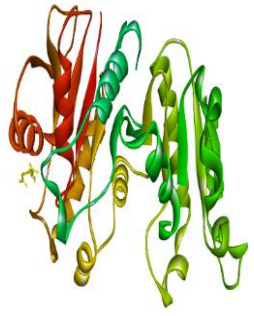
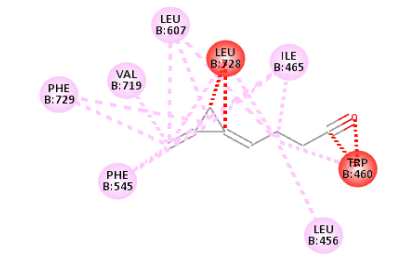

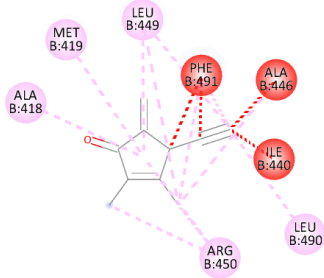
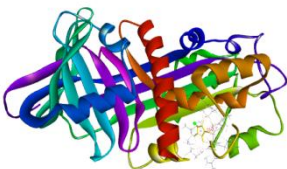
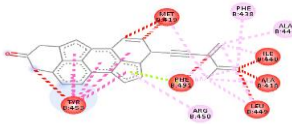
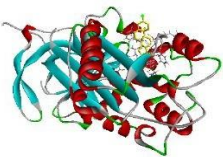
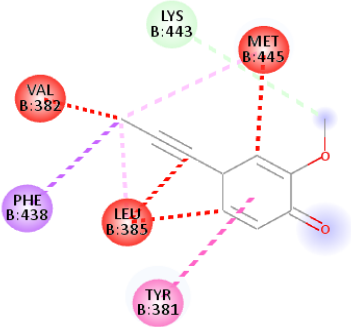
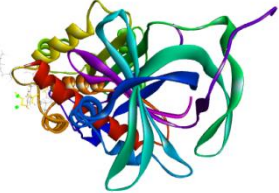
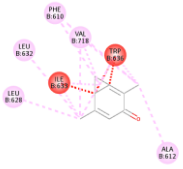
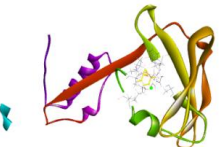
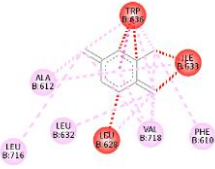
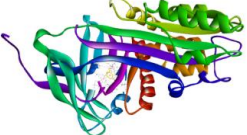
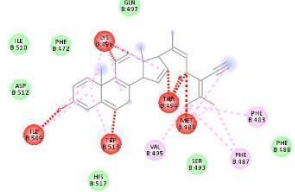
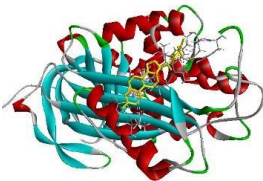
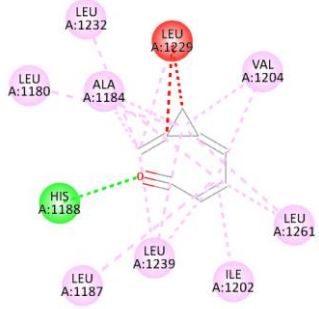

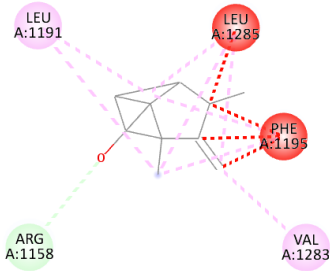

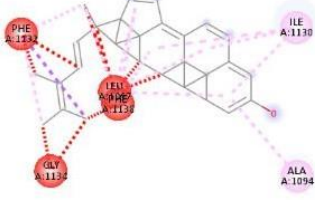
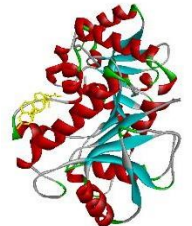
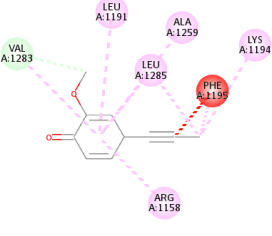

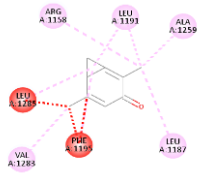
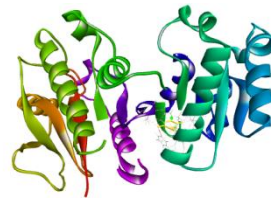
2.	Nitrofurazone			-7.01352 kcal/mol
1YXO				
1.	Mupirocin			-9.85249 kcal/mol
2.	Nitrofurazone			-6.57333 kcal/mol

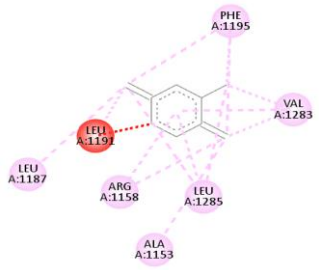
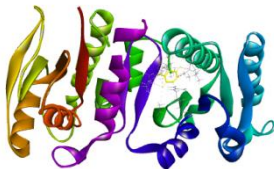
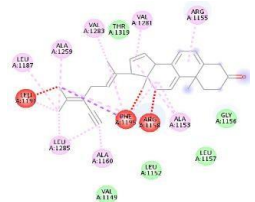
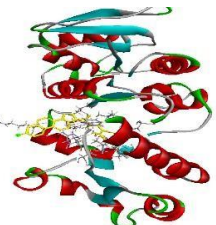
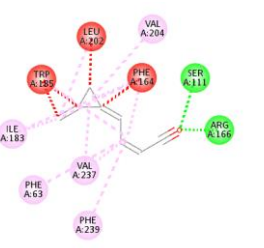
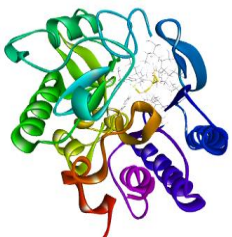
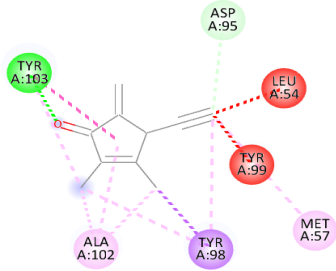

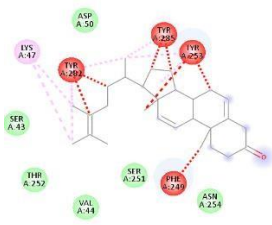
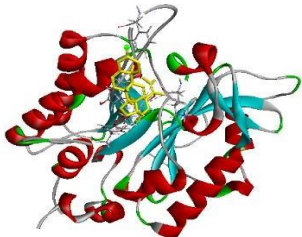
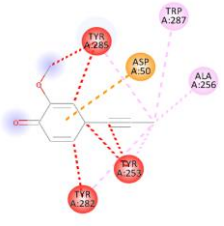

Table No. 3. Binding affinity of Heliotropium indicum by Argus lab 4.0.1

S. No.	Chemical constituent	Capture		Final energy
		2D	3D	
4G8R				
1.	H-1			-10.5348 Kcal/mol

2.	H-2			-9.97975 Kcal/mol
3.	H-3			-16.0316 kcal/mol
4.	H-4			-8.4735 Kcal/mol
5.	H-5			-10.2765 Kcal/mol
6.	H-6			-10.6224 kcal/mol
7.	H-7			-14.3211 kcal/mol

1YXO

8.	H-1			-9.65797 kcal/mol
9.	H-2			-10.3689 Kcal/mol
10.	H-3			-13.436 Kcal/mol
11.	H-4			-8.86885 Kcal/mol
12.	H-5			-7.5779 Kcal/mol

13.	H-6			-10.1213 Kcal/mol
14.	H-7			-13.8273 Kcal/mol
3V18				
15.	H-1			-11.2388 Kcal/mol
16.	H-2			-9.954504 Kcal/mol
17.	H-3			-13.2849 Kcal/mol
18.	H-4			-9.10107 Kcal/mol

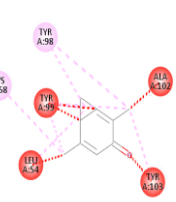
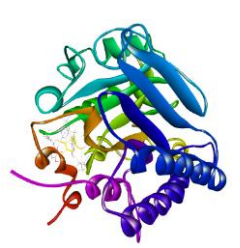
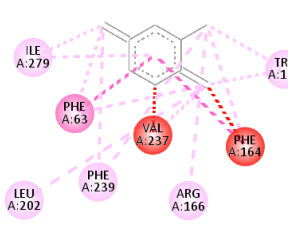
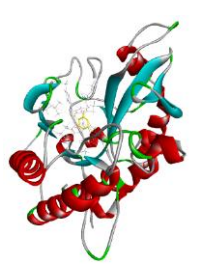
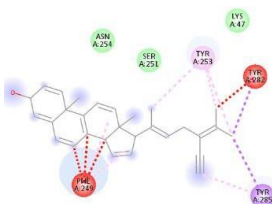
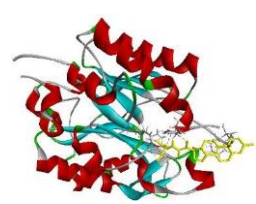
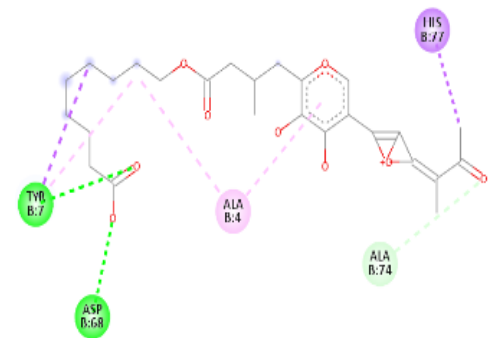
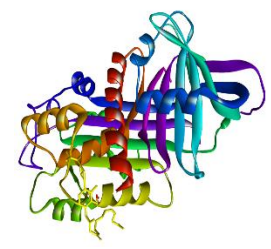
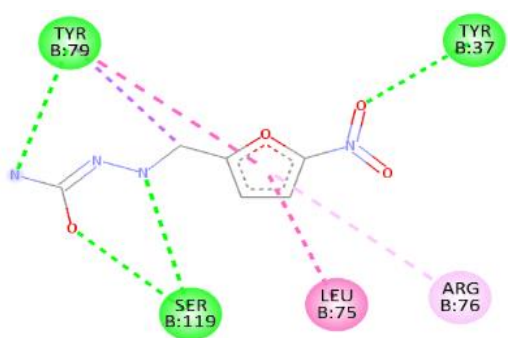
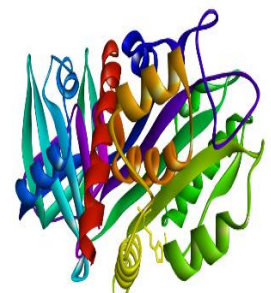
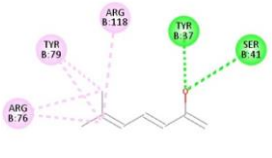

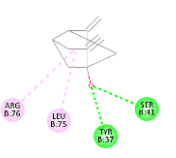

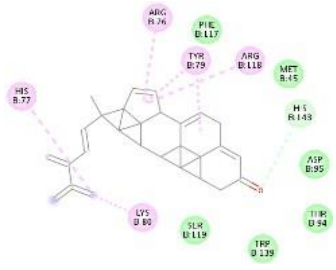
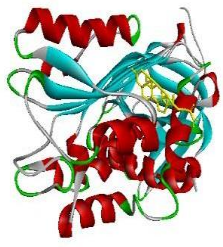
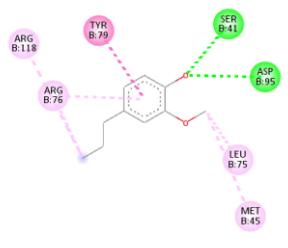
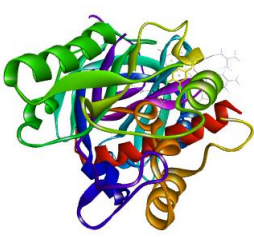
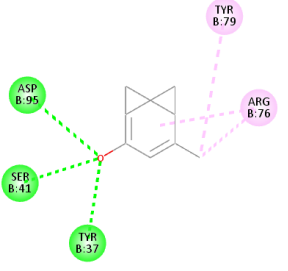
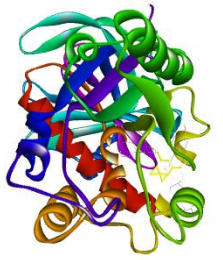

19.	H-5			-9.10107 Kcal/mol
20.	H-6			-11.9344 Kcal/mol
21.	H-7			-13.2245 Kcal/mol

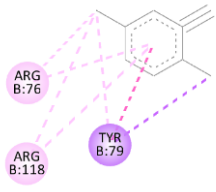
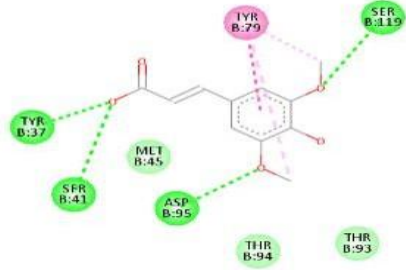
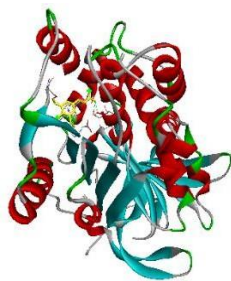
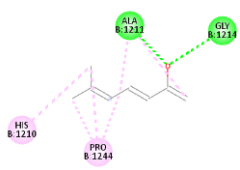

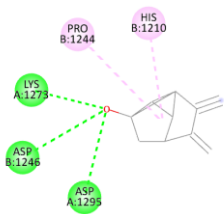

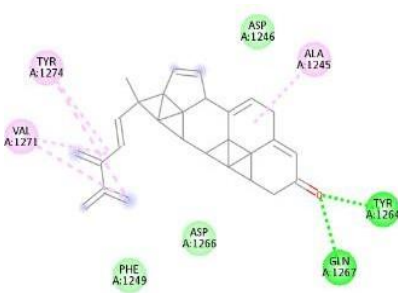
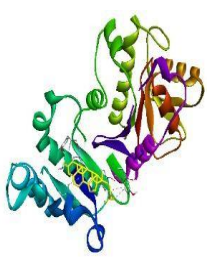
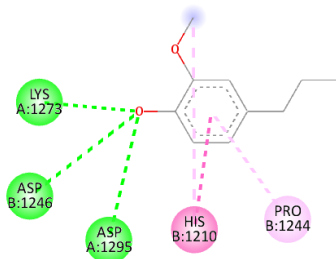

Table No. 4. Binding affinity of standard drug by Autodock tools 1.5.7

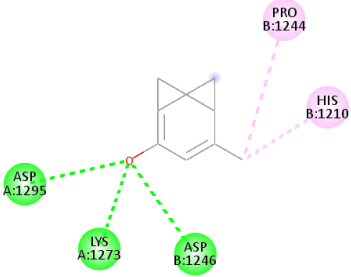

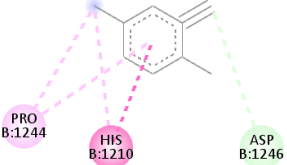

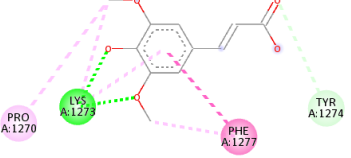
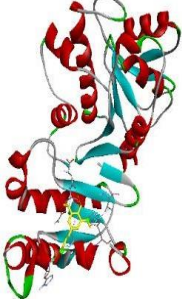
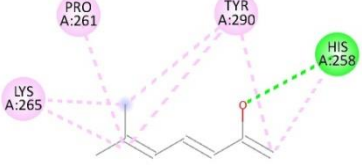

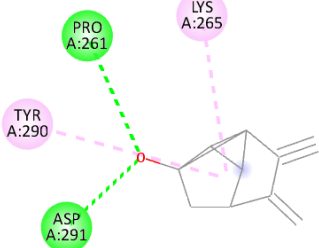
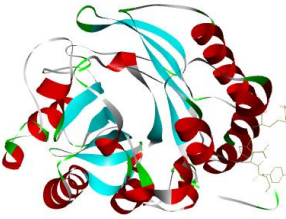
S. No	Standard drug	Capture		Final energy
		2D	3D	
4G8R				
1.	Mupirocin			-4.3 kcal/mol
2.	Nitrofurazone			-5.9 kcal/mol

3V18				
1.	Mupirocin			-6.0 kcal/mol
2.	Nitrofurazone			-4.8 kcal/mol
1YXO				
1.	Mupirocin			-6.6 kcal/mol
2.	Nitrofurazone			-6.0 kcal/mol

Table No. 5. Binding affinity of Heliotropium indicum by Autodock tool 1.5.7

S. No.	Chemical constituent	Capture		Final energy
		2D	3D	
4G8R				
1.	H-1			-5.3 kcal/mol
2..	H-2			-7.3 kcal/mol
3.	H-3			-10 kcal/mol
4.	H-4			-5.9 kcal/mol
5.	H-5			-6.3 kcal/mol
6.	H-6			-5.8 kcal/mol

				
7.	H-7			-6.7 kcal/mol
1YXO				
8.	H-1			-3.2 kcal/mol
9.	H-2			-4.9 kcal/mol
10.	H-3			-8.9 kcal/mol
11.	H-4			-4.4 kcal/mol

12.	H-5			-3.9 kcal/mol
13.	H-6			-3.9 kcal/mol
14.	H-7			-4.8 kcal/mol
3V18				
15.	H-1			-4.3 kcal/mol
16.	H-2			-5.5 kcal/mol

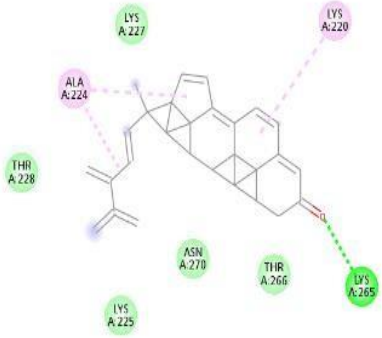
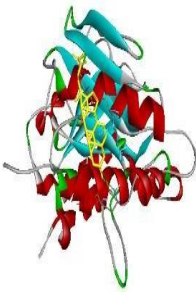
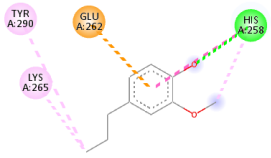
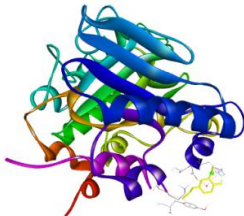
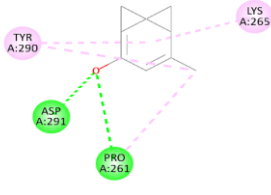

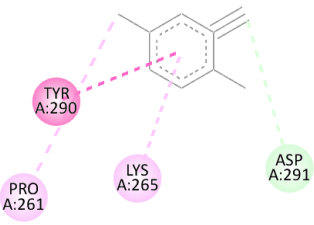

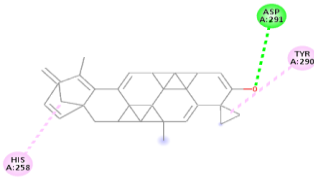
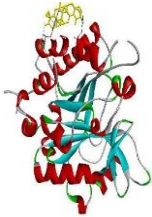
<p>17.</p>	<p>H-3</p>			<p>-7.2 kcal/mol</p>
<p>18.</p>	<p>H-4</p>			<p>-4.4 kcal/mol</p>
<p>19.</p>	<p>H-5</p>			<p>-4.4 kcal/mol</p>
<p>20.</p>	<p>H-6</p>			<p>-4.5 kcal/mol</p>
<p>21</p>	<p>H-7</p>			<p>-8.5 kcal/mol</p>

Table No. 6. The results obtained from Argus lab 4.0.1

Plant name	Protein name	Standard	Phyto constituents having best affinity compared with standard drug		
<i>Heliotropium indicum</i>	4G8R	Mupirocin	6-methyl-5-hepten-2-one Campesterol Pseudocumene Stigmasterol Ishophorone	Borneol	Eugenol
		Nitrofurazone	Campesterol Stigmasterol	-	-
	3V18	Mupirocin	6-methyl-5-hepten-2-one Campesterol Pseudocumene Stigmasterol	Borneol Eugenol Ishophorone	-
		Nitrofurazone	Campesterol Stigmasterol	-	-
	1YXO	Mupirocin	Borneol Campesterol Pseudocumene Stigmasterol	6-methyl-5-hepten-2-one	Eugenol Ishophorone
		Nitrofurazone	Campesterol Stigmasterol	-	-

Table No. 7. The results obtained from Autodock tools 1.5.7

Plant name	Protein name	Standard	Phyto constituents having best affinity compared with standard drug		
<i>Heliotropium indicum</i>	4G8R	Mupirocin	Borneol Campesterol Ishophorone Stigmasterol	-	-
		Nitrofurazone	Borneol Campesterol Stigmasterol	6-methyl-5-hepten-2-one Eugenol Pseudocumene	-
	3V18	Mupirocin	Campesterol Stigmasterol	-	6-methyl-5-hepten-2-one Borneol Eugenol Ishophorone Pseudocumene
		Nitrofurazone	Borneol Campesterol Stigmasterol	6-methyl-5-hepten-2-one Eugenol Ishophorone Pseudocumene	-
	1YXO	Mupirocin	Campesterol	-	6-methyl-5-hepten-2-one Borneol Eugenol Ishophorone Pseudocumene Stigmasterol
		Nitrofurazone	Campesterol	-	Borneol Eugenol Stigmasterol

IV. CONCLUSION

Protein-ligand interactions are critical in understanding the structural basis of therapeutic action. The docking affinities of plant proteins for three different wound-healing proteins were evaluated using Autodock and Argus lab, and the findings were compared to those obtained using a common topical anti-bacterial medication (mupirocin or nitrofurazone) (1YXO, 3V18, 4G8R). Heliotropium indicum (6-Methyl-5-heptene-2-one, Borneol, Campesterol, Eugenol, Ishophorone, Pseudocumene, Stigmasterol) has chemical components with wound healing function, according to the present study. According to the findings, Heliotropium indicum contains antibacterial, antifungal, and anti-inflammatory activities, indicating it may be effective in the treatment of wounds.

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