



Alkanna tinctoria Derived Phytochemicals against Staphylococcus aureus Causing Eczema

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Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

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ABSTRACT

Alkanna tinctoria plant extract is traditionally used to heal eczema. It is caused by *Staphylococcus aureus*. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that 2-Hydroxy-3-Phenyl-1-4-naphthoquinone can effectively deactivate the shikimate dehydrogenase enzyme thereby interrupting the life cycle of the organism.

Keywords: *Phytochemical; Alkanna tinctoria; Staphylococcus aureus; eczema.*

1. INTRODUCTION

Mother nature is a great repository of medicines [1]. The presence of different phytochemical constituents gives the therapeutic nature to the plants. Phytochemicals can be derived from different parts of plants. Medicinal plant along with their phytochemical constituents shows

therapeutic properties [2]. These medicinal plants play a key role in human health care. Most of the people in the world believe in the traditional system of medication [3].

Alkanet is a plant of the Boraginaceae family. The phytochemicals present in Alkanet are utilised to heal the eczema. This

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work aims to recognise the phytochemical, which is able to inhibit the activity of the microorganism.

Alkanet contains "shikonin, acetylshikonin, anchusin, 1, 8-cineol, alpha-terpinyl acetate, 2-hydroxy-3-phenyl-1-4-naphthoquinone" etc. These phytochemicals might act against eczema. However, there is no such study available, which identifies the responsible phytochemicals of Alkanet for curing eczema disease.

This work aims to evaluate the phytochemicals of Alkanet which can cure eczema.

2. MATERIALS AND METHODS

2.1 Software Used

Discovery studio module of Biovia software (Dassault Systemes of France) was used for analysis. The software utilizes machine learning techniques to predict the level of molecular interaction.

The Discovery Studio module of Biovia is used for identifying molecular interaction and perform molecular docking of phytochemicals from plant extract that act as a ligand and form a strong covalent bond with bacterial protein to successfully inhibit microbe.

2.2 Methodology

2.2.1 List of phytochemicals

Phytochemicals are produced by plants as secondary metabolites to protect them from predators. The potential threats to plants include bacteria, viruses, fungi etc. When these plants or their parts are consumed by humans these phytochemicals fight off threats to health. Some phytochemicals have been used as poisons and others as traditional medicine. Published works showed that *Alkanna tinctoria* contains Shikonin, acetylshikonin, Anchusin, 1,8-Cineol, alpha-terpinyl acetate, 2-Hydroxy-3-Phenyl-1-4-naphthoquinone. It has already been established that *Alkanna tinctoria* plant belonging to Boraginaceae family has potential to help controlling eczema. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of eczema.

2.2.2 Enzyme found in *Staphylococcus*

It has been reported that eczema can cause as a result of *Staphylococcus aureus*. Various

metabolic cycles have been seen in the bacterial life cycle for its survival. These metabolic cycles are regulated by different enzymes. Brenda enzyme database was used to identify and list different enzymes found in *Staphylococcus aureus* bacteria. It has been found that Shikimate dehydrogenase enzyme (protein database code 1NYT) is involved in Phenylalanine, tyrosine, tryptophan biosynthesis (KEGG) and very crucial for the survival of the particular microbe.

2.2.3 Molecular docking

Molecular docking method has been used to identify the phytochemical from the plant extract, that act as a ligand and form a strong covalent bond with the bacterial protein to successfully inhibit the microbe. The Discovery studio module of Biovia software was used for identifying molecular interaction and perform molecular docking. In this process first, the sdf files for the phytochemicals found in the *Alkanna tinctoria* plant were downloaded from the website (<https://pubchem.ncbi.nlm.nih.gov>). The protein database code of the Shikimate dehydrogenase enzyme was identified from the website (www.rcsb.org). The active site of the enzyme was identified via "receptor cavity" protocol found under "receptor-ligand interaction" menu. Molecular docking was done using the CDOCKER protocol of Bioviasoftware under "receptor-ligand interaction". The enzyme molecule was treated as the receptor molecule and the phytochemical was treated as the ligand. The "-CDOCKER_ENERGY" and "-CDOCKER_INTERACTION_ENERGY" were used as an indicator for the quality of molecular docking. The high positive value of those indicators presented a good interaction between the ligand and the receptor. Thus, the interactions with high values might indicate the major phytochemical responsible for curing the disease.

3. RESULTS AND DISCUSSION

-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the nonbonded interaction that exists between the protein and the ligand. The criteria for best interaction was chosen based on a) high positive value of -CDOCKER energy and b) small difference between -CDOCKER energy and -CDOCKER interaction energy [4,5]. Table 1 shows that Shikimate dehydrogenase-2-Hydroxy-3-Phenyl-

Table 1. Results of C docking of phytochemicals with shikimate dehydrogenase (receptor)

Sl. no.	Ligand	-CDOCKER energy	-CDOCKER interaction energy	Difference between - C DOCKER interaction energy and -CDOCKER energy	Remarks
1	2-Hydroxy-3-phenyl-1-4-naphthoquinone	4.67599	19.6466	14.97061	Maximum inhibition of microbial enzyme
2	Alpha-terpinyl acetate	-9.16551	16.9887	26.15421	
3	1,8-Cineol	-13.3444	14.1596	27.504	
4	Shikonin	-9.43714	25.0992	34.53634	
5	Anchusin	-9.43714	25.0992	34.53634	
6	Acetyl shikonin	-97.8407	-18.4766	79.3641	

1-4-naphthoquinone interaction has the highest positive value of -CDOCKER energy (4.67599) and minimum value of the difference (14.97061) between - C DOCKER interaction energy and - C DOCKER energy. Thus the results indicated that 2-Hydroxy-3-Phynyl-1-4-naphthoquinone can effectively deactivate the Shikimate dehydrogenase enzyme thereby interrupting the biological cycle of *Staphylococcus aureus*. Higher positive values for 2-Hydroxy-3-Phynyl-1-4-naphthoquinone indicated that it was the most active ingredient against *Staphylococcus aureus*. On the other hand, alpha terpinyl acetate, 1,8-cineol, Shikonin and Anchusin can deactivate the enzyme upto a very small extent (negative -CDOCKER energy but positive -CDOCKER interaction energy). Thus, the key phytochemical preventing eczema caused by *Staphylococcus aureus* is 2-Hydroxy-3-Phynyl-1-4-naphthoquinone.

4. CONCLUSIONS

It was previously known that *Alkanna tinctoria* plant has medicinal action against eczema. Eczema is caused by *Staphylococcus aureus*. This study was carried out to provide the theoretical basis of this observation. Using Discovery studio module of Biovia software, molecular docking operation was performed to identify the phytochemical (2-Hydroxy-3-Phenyl-1-4-naphthoquinone, acetylshikonin, Anchusin, Shikonin, 1,8-Cineol, alpha-terpinyl acetate), which can have a significant interaction with the vital enzyme (Shikimate dehydrogenase) of the microbe. It was found that 2-Hydroxy-3-Phynyl-1-

4-naphthoquinone can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. 1,8-Cineol, alpha- terpinyl acetate, Anchusin, Shikonin found to be least effective in deactivating the enzyme of the microbe. Thus, this study could explain that the presence of 2-Hydroxy-3-Phynyl-1-4-naphthoquinone provided the medicinal values to *Alkanna tinctoria* against eczema caused by *Staphylococcus aureus*. Since the Shikimate dehydrogenase-2-Hydroxy-3-Phynyl-1-4-naphthoquinone interaction has been successful in inhibiting life cycle of *Staphylococcus aureus* by blocking its metabolic pathway like Phenylalanine, tyrosine and tryptophan biosynthesis hence it is proved that phytochemical 2-Hydroxy-3-Phynyl-1-4-naphthoquinone provide therapeutic values to Ratanjot plant against eczema diseases.

DISCLAIMER

The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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