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Myristica fragrans Derived Phytochemicals against Shikimate Dehydrogenase of *E. coli* Causing Diarrhea

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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

Medicinal plants play a key role in human health care. Phytochemicals can be derived from different parts of plants. Different medicinal plants and their phytoextracts have shown anti-microbial action. Phytochemicals from *Myristica fragrans* plant extract are traditionally used to cure Diarrhea. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that Eugenol can effectively deactivate the shikimate dehydrogenase enzyme thereby interrupting the life cycle of the organism.

Keywords: Phytochemical; Myristica fragrans; diarrhea; enzyme.

1. INTRODUCTION

Nature is a major source of medicines [1]. The medicinal value of the plants is due to the phytochemicals present in it. Phytochemicals can be derived from different parts of plants. Different medicinal plants and their phytoextracts have shown anti-microbial action [2]. These medicinal

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plants play a key role in human health care. Many people rely on the use of traditional medicine [3]. *Myristica* extract is used to cure diseases like Diarrhea. The objective of the study is to identify the phytochemical responsible to cure the disease. *Myristica fragrans* contains "beta-pinene, alpha-pinene, p-cymene, limonene, piperazine" etc. These phytochemicals might act against jaundice. However, there is no such study available. This objective of the study is to identify the phytochemical of *Myristica fragrans* capable of curing Diarrhea.

2. MATERIALS AND METHODS

2.1 Software Used

The 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.

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 *Myristica fragrans* contains Eugenol, Citonelly acetate, Elemicin, Alpha-phellandrene, Beta- caryophyllene, Alpha terpinene, Limonene, Alpha- cubebene, Docosane, etc. It has already been established that *Myristica fragrans* plant belonging to Myristicaceae family has the potential to help controlling Diarrhea. This work is focused on the identification of the particular phytochemical responsible for inhibiting and controlling of Diarrhea.

2.2.2 Enzyme found in *Escherichia coli*

It has been reported that diarrhea can cause as a result of *Escherichia coli sp.* infestation. 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 *Escherichia coli* bacteria. It has been found that (Shikimate dehydrogenase) enzyme (protein database code 1NYT) is involved in (Chorismate Pathway) metabolism (KEGG) and is very crucial for the survival of the particular microbe.

2.2.3 Molecular docking

The molecular docking method has been used to identify the phytochemicals 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 performs molecular docking. In this process first, the sdf files for the phytochemicals found in the *Myristica fragrans* plant were downloaded from the website (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 the "receptor cavity" protocol found under the "receptor-ligand interaction" menu. Molecular docking was done using the -CDOCKER protocol of Biovia software 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 [4]. 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.

Table 1 shows that (Shikimate dehydrogenase) (Eugenol) interaction has the highest positive value of -CDOCKER energy (12.5266) and minimum value of the difference (13.2397) between - C DOCKER interaction energy and - C DOCKER energy followed by (Elemicin). Thus the results indicated that (Eugenol) can

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

Sl. no.	Ligand	-CDOCKER energy	-CDOCKER interaction energy	Difference between -CDOCKER interaction energy and -CDOCKER energy
1	Eugenol	12.5266	25.7663	
2	Citonelly acetate	-3.47589	28.4994	31.97529
3	Elemicin			
4	Alpha-phellandrene	-16.9702	14.8301	31.8003
5	Beta- caryophyllene	-19.0343	17.8391	36.8734
6	Alpha terpinene	-20.9061	13.1171	34.0232
7	Limonene	-25.5058	13.3869	
8	Alpha- cubebene	-41.5789	15.432	57.0109
9	Docosane	failed	failed	

effectively deactivate the (*Shikimate dehydrogenase*) enzyme thereby interrupting the biological cycle of *Escherichia coli.* Higher positive values for (Eugenol) indicated that it was the most active ingredient against *Escherichia coli.* On the other hand, (Elemicin) can deactivate the enzyme to a small extent (negative -CDOCKER energy but positive -CDOCKER interaction energy). (Docosane) cannot interact with (*Shikimate dehydrogenase*) enzyme. Thus, the key phytochemicals preventing diarrhea caused by *Escherichia coli* is Eugenol.

4. CONCLUSIONS

It was previously known that *Myristica fragrans* plant has medicinal action against Diarrhea. Diarrhea is caused by *Escherichia coli sp.* 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 Eugenol, Citonelly acetate, Elemicin, Alpha-phellandrene, Beta-caryophyllene, Alpha terpinene, Limonene, Alpha- cubebene, Docosane which can have a significant interaction with the vital enzyme (Shikimate dehydrogenase) of the microbe. It was found that (Eugenol) can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Alpha-phellandrene, Beta-caryophyllene, Alpha terpinene, Limonene, Alpha- cubebene, were found to be not much effective in deactivating the enzyme of the microbe. (Docosane) cannot deactivate the enzyme. Thus, this study could explain that the presence of (Eugenol) provided the medicinal values to *Myristica fragrans* against Diarrhea caused by *Escherichia coli.*

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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