



Coffea arabica L. Derived Phytochemicals against *Haemophilus influenza* Causing Conjunctivitis

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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

Phytochemicals from *Coffea arabica* plant extract are traditionally used to cure conjunctivitis. It is caused by *Haemophilus influenza*. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that caffeine and chlorogenic acid can efficiently deactivate the shikimate dehydrogenase enzyme which will result in interruption of the life cycle of the microorganism.

Keywords: *Phytochemical; Coffea arabica L.; Haemophilus influenza.*

1. INTRODUCTION

Plants are the valuable resources of new drugs [1]. Herbal derived remedies need a powerful and deep assessment of their pharmacological

efficacy. Different types of phytochemicals are responsible for the medicinal properties. Plant extracts derived from different parts show antimicrobial activity against different microorganisms [2]. Herbs are natural products and

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play a major role in human health care. Therefore, traditional medicines are given importance to treat different diseases [3]. *Coffea arabica* L belongs to family Rubiaceae. *Coffea arabica* L extract is used to cure diseases like conjunctivitis. The objective of the study is to identify the phytochemical responsible to cure the disease. *Coffea arabica* L contains “cafestol, caffeine, chlorogenic acid and triglycerides” etc. These phytochemicals might act against conjunctivitis. However, there is no such study available. This objective of the study is to identify the phytochemical of *Coffea arabica* L capable of curing conjunctivitis.

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 strong covalent bond with bacterial protein to successfully inhibit microbe.

2.2 METHODOLOGY

2.2.1 List of phytochemicals

Plants secrete phytochemicals as secondary metabolites to protect them from predators that may 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 *Coffea arabica* contains cafestol, caffeine, chlorogenic acid and triglycerides. It has already been established that *Coffea arabica* plant belonging to Rubiaceae family has the potential to help controlling conjunctivitis. This work is focused on the identification of the particular phytochemical responsible for inhibiting and controlling of conjunctivitis.

2.2.2 Enzyme found in *Haemophilus influenzae*

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 *Haemophilus influenzae*. It has been found that shikimate dehydrogenase enzyme (EC 1.1.1.25 and protein database code 1NPY) is involved in phenylalanine, tyrosine, and tryptophan biosynthesis (KEGG) and is very crucial for survival of this particular microbe.

2.2.3 Molecular docking

Molecular docking method has been used to identify the phytochemicals from the plant extract, which acts as a ligand and forms 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 *Coffea arabica* 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 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 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 - caffeine interaction has the highest positive value

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	Caffeine	14.444	22.5148	8.0708
2	Chlorogenic acid	31.8327	49.9994	18.1667
3	Cafestol	-40.0542	25.8173	65.8715
4	Triglycerides	Failed	Failed	Failed

of -CDOCKER energy (14.444) and minimum value of the difference (8.0708) between - C DOCKER interaction energy and - C DOCKER energy followed by chlorogenic acid. Thus the results indicated that caffeine and chlorogenic acid can effectively deactivate the shikimate dehydrogenase enzyme thereby interrupting the biological cycle of *H. influenzae*. Higher positive values for caffeine indicated that it was the most active ingredient against *H. influenzae*. On the other hand, cafestol can deactivate the enzyme to a small extent (negative -CDOCKER energy but positive -CDOCKER interaction energy). Triglycerides cannot interact with shikimate dehydrogenase enzyme. Thus, the key phytochemicals preventing conjunctivitis caused by *H. influenzae* are caffeine and chlorogenic acid.

4. CONCLUSIONS

It is reported that *Coffea arabica* plant has medicinal action against conjunctivitis. *Haemophilus influenza* is known to cause conjunctivitis. 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 phytochemicals (cafestol, caffeine, chlorogenic acid, triglycerides), which can have significant interaction with the vital enzyme i.e. shikimate dehydrogenase of the microbe. It was found that caffeine and chlorogenic acid can form a strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Cafestol was found to be not much effective in deactivating the enzyme of the microbe. On the other hand, triglycerides cannot deactivate the enzyme. Thus, this study could explain that the presence of caffeine and chlorogenic acid provide therapeutically values to *Coffea arabica* plant against conjunctivitis caused by *Haemophilus influenzae*.

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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