



Budleja asiatica Derived Phytochemicals against Eye Disease

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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

The secondary metabolites in the plants are used for curing various diseases. The phytochemicals present in *Budleja asiatica* plant extract are traditionally used to cure Eye disease. It is caused by *Haemophilus influenza*, which is a facultatively anaerobic, gram-negative pathogenic bacteria. For analysis of ligand-protein interaction, the molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that lignoceric acid can effectively deactivate Aspararte semialdehyde dehydrogenase enzyme which is important macromolecule for the regulation of amino acid biosynthesis resulting in interrupting the life cycle of the microorganism.

Keywords: Phytochemical; lignoceric acid; *Haemophilus influenzae*.

1. INTRODUCTION

Manufactured medicine is not the only option for curing diseases, but natural remedies can be also used for curing both physical and mental health [1]. And these natural remedies are helpful as medicine only because of the presence of

phytochemicals in them. The different parts like root, seed, stem, leaves, fruits and flower can be taken for the phytochemicals extraction [2]. In this era, people rely on herbal medicine due to the various medicinal properties like anti-microbial, anti-diabetic, anti-cancer almost for all disease they believe in more in herbal medicine

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instead of using manufactured one. No doubt these herbal medicine practices will be safer and cost-effective [3].

Budleja asiatica is tender deciduous shrub belongs to the family Scrophulariaceae family, found in most part of India. This plant extract have various medicinal properties like anti-bacterial, anti-fungal, antihepatotoxic, antioxidant, hypotensive, anti-malaria, anti-inflammation. From literature, it was reported that this plant can be used as a potent medicine against eye disease. Lignoceric acid, B caryophyllene oxide, alpha amyryl, atigmasterol are major phytochemicals for their potency in herbal remedies. In the present study, the objective is to identify the most effective bioactive compound for the inhibition of the *Haemophilus influenza* curing eye disease. And to target the organism, a specific metabolic pathway has to be chosen to kill the bacteria. In this study, we focused on the Aspartate semialdehyde dehydrogenase and oxidoreductase which are known to regulate the biosynthesis of amino acid. It participate in the early branch point in the metabolic pathway forming lysine, methionine, leucine and isoleucine from aspartate and this pathway also produces diaminopimelate which plays a important role in bacterial cell wall formation.

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.

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 are harmful to humans and others used as traditional medicine. Published works showed that *Budleja asiatica* contains Apigenin, Lignoceric acid, B caryophyllene oxide, Alpha amyryl, Stigmasterol, etc. [3]. It has already been established that *Budleja asiatica* plant belonging to Scrophulariaceae family has the potential to help controlling Eye disease [4].

This work is focused on the identification of the particular phytochemical responsible for inhibiting and controlling of Eye disease.

2.2.2 Enzyme found in *Haemophilus influenzae*

It has been reported that Eye disease can cause as a result of *Haemophilus influenza* 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 *Haemophilus influenzae* bacteria. It has been found that Aspartate-Semialdehyde Dehydrogenase enzyme (protein database code 1NWC) is involved in Glycine, serine and threonine metabolism (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 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 *Budleja asiatica* plant were downloaded from the website (www.pubchem.ncbi.nlm.nih.gov). The protein database code of the Aspartate-Semialdehyde Dehydrogenase enzyme was identified from the website (<https://www.rcsb.org/pdb>). 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 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

Table 1. Results of C docking of phytochemicals with aspartate-semialdehyde dehydrogenase (receptor)

| Sl no | Ligand | -C DOCKER Energy | - CDOCKER Interaction Energy | Difference between - C DOCKER interaction energy and - C DOCKER energy | Remarks |
|-------|-----------------------|------------------|------------------------------|--|--|
| 1 | LIGNOCERIC ACID | 47.3416 | 46.9048 | 0.4368 | Maximum inhibition of microbial enzyme |
| 2 | APIGENIN | 30.422 | 35.8081 | 5.3861 | |
| 3 | B CARYOPHYLLENE OXIDE | -7.34646 | 22.901 | 30.24746 | |
| 4 | ALPHA AMYRIN | FAIL | FAIL | NA | |
| 5 | STIGMASTEROL | FAIL | FAIL | NA | |

interaction energy. Nonbonded interaction that exists between the protein and the ligand is given by CDOCKER interaction. The criteria for best interaction was chosen based on:

- High positive value of -CDOCKER energy and
- Small difference between -CDOCKER energy and -CDOCKER interaction energy [2].

Table 1 shows that Aspartate-Semialdehyde Dehydrogenase-Lignoceric acid interaction has the highest positive value of -CDOCKER energy (47.3416) and also has minimum value of the difference (0.4368) between - C DOCKER interaction energy [5] and - C DOCKER energy. Thus the results indicated that can effectively deactivate the Aspartate-Semialdehyde Dehydrogenase enzyme thereby interrupting the biological cycle of *Haemophilus influenzae*. Higher positive values for Lignoceric acid indicated that it was the most active ingredient against *Haemophilus influenza* and having a lower difference between -CDOCKER energy and -CDOCKER interaction energy is the most active ingredient. Apigenin and Bcaryophyllene oxide having some interaction can also slightly affect the enzyme. Whereas Alpha amyirin and Stigmasterol fails to interact with the enzyme and can't deactivate it.

4. CONCLUSIONS

It was previously known that *Budleja asiatica* plant has medicinal action against Eye disease. Eye disease is caused by *Haemophilus influenzae*. 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 (Apigenin, Lignoceric acid, B caryophyllene oxide, Alpha amyirin, Stigmasterol), which can have significant interaction with the vital enzyme (Aspartate-Semialdehyde Dehydrogenase) of the microbe. It was found that Lignoceric acid can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Apigenin and β -caryophyllene oxide were found to be less effective in deactivating the enzyme of the microbe. Alpha amyirin and stigmasterol cannot deactivate the enzyme as they fail to interact with the enzyme. Thus, this study could explain that the presence of Lignoceric acid provided the medicinal values to *Budleja asiatica* against Eye disease 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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