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Nigella sativa Derived Phytochemicals against Cough

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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

Nigella sativa plant extract is traditionally used to cure cough. It is caused by *Bordetella pertussis.* Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that p-cymene can effectively deactivate the adenylate cyclase thereby interrupting the life cycle of the organism.

Keywords: Phytochemicals; Nigella sativa; Bordetella pertussis; cough.

1. INTRODUCTION

Mother nature held a good source of medicine in her [1]. Presence of phytochemicals or secondary metabolite in the plant holds the key for different medicinal property. Secondary metabolites are present in various amounts in different parts [2]. A major role is played by the medicinal plant in the health care system. Majority of the population depend upon the traditional healing process [3].

Nigella Sativa is an annual plant of the Ranunculaceae family. Phytochemical extracts from black cumin can prevent cough. The study aims to evaluate secondary metabolite responsible for inhibiting the enzyme.

Black cumin contains "p-cymene, carvacrol, carvone, thymol, thymoquinone, alpha-pinene and limonene" etc. The above said secondary metabolite may inhibit the growth of bacteria which is very much indicated in the indigenous

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medicine. However there is no published data to authenticate.

The study was carried out to identify the secondary metabolite in controlling the cough.

2. MATERIALS AND METHODS

2.1 Software Used

Discovery studio module of Biovia software (Dassault Systems 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. 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 *Nigella sativa* contains etc. It has already been established that *Nigella sativa* plant belonging to Ranunculaceae family has potential to help controlling cough. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of cough.

2.2.2 Enzyme found in *Bordetella pertussis*

It has been reported that cough can be caused as a result of *Bordetella pertussis* 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 *Bordetella pertussis* bacteria. It has been found that adenylate cyclase enzyme (protein database code 5CXL) is involved pyrimidine metabolism (KEGG) and very crucial for 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 *Nigella sativa*plant were downloaded from the website (www.molinstinct.com/www.pubchem.org). The protein database code of the adenylate cyclase 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 adenylate cyclase and thymoquinone interaction has the highest positive value of -CDOCKER energy (1.86885) and P-cymene has minimum value of the difference (0.412) between -CDOCKER interaction energy and -CDOCKER energy followed by carvacrol and thymol. Thus, the results indicated that p-cymene, carvacrol and thymol effectively deactivate the adenylate cyclase enzyme thereby interrupting the biological cycle of *Bordetella pertussis*. Higher positive values for p-cymene indicated that it was the most active ingredient against *Bordetella pertussis*. On the other hand, thymoquinone, alpha-pinene, carvone and limonene can deactivate the enzyme to a small extent (only alpha-pinene has negative -CDOCKER energy but positive -CDOCKER interaction energy). Thus, the key phytochemicals preventing cough caused by *Bordetella pertussis* are p-cymene, carvacrol and thymol.

Table 1. Results of C docking of phytochemicals with adenylate cyclase (receptor)

Sl. no.	Ligand	-CDOCKER energy	-CDOCKER interaction energy	Difference between - C DOCKER interaction energy and -CDOCKER energy	Remarks
1	P-cymene	16.1206	16.5326	0.412	Maximum inhibition of microbial enzyme
2	Carvacrol	18.9098	19.9551	1.0453	
3	Thymol	16.4732	18.1083	1.636	
4	Thymoquinone	1.86885	17.0157	15.14685	
5	Alpha-pinene	-13.7825	11.0652	24.8477	
6	Carvone	14.8632	16.8942	31.7574	
7	Limonene	23.0784	15.6033	38.6817	

4. CONCLUSIONS

It was previously known that *Nigella sativa* plant has medicinal action against cough. Cough is caused by *Bordetella pertussis*. 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 (alpha pinene, carvone, p-cymene, carvacrol, limonene, thymoquinone and thymol), which can have a significant interaction with the vital enzyme (adenylate cyclase) of the microbe. It was found that p-cymene, carvacrol and thymol can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Alpha-pinene, thymoquinone, carvone and limonene were found to be not much effective in deactivating the enzyme of the microbe. Thus, this study could explain that the presence of all the phytochemicals provided the medicinal values to *Nigella sativa* against cough caused by *Bordetella pertussis*, but p-cymene, carvacrol and thymol are more effective to cure cough.

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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