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Piper nigrum Derived Phytochemicals against Gonorrhoea

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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 *Piper nigrum* plant extract are traditionally used to cure Gonorrhoea. It is caused by *Neisseria gonnorrhoeae.* Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that p-cymenecan effectively deactivate the dihydrofolate reductase enzyme thereby interrupting the life cycle of the organism.

Keywords: Phytochemical; Piper nigrum; Neisseria gonorrhoeae.

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 plants play a key role in human health care. Many people rely on the use of traditional medicine [3,4].

Black pepper belongs to family Piperaceae. Black pepper extract is used to cure disease like

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Gonorrhoea. The objective of the study is to identify the phytochemical responsible to cure the disease.

Black pepper contains “beta-pinene, alpha-pinene, p-cymene, limonene, piperazine” etc. These phytochemicals mightact against Gonorrhoea. However, there is no such study available.

This objective of the study is to identify the phytochemical of *Piper nigrum* capable of curing Gonorrhea.

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 have been used as poisons and others as traditional medicine. Published works showed that *Piper nigrum* contains beta-pinene, alpha-pinene, p-cymene, Limonene, piperazine etc. It has already been established that *Piper nigrum* plant belonging to Piperaceae family has potential to help controlling Gonorrhoea. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of Gonorrhoea.

2.2.2 Enzyme found in mycobacterium

It has been reported that Gonorrhoea can cause as a result of *Neisseria gonorrhoeae* 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 *Neisseria gonorrhoeae* bacteria. It has been found that dihydrofolate reductase enzyme (protein database code 1RX2) has been purified from a trimethoprim resistance strain of *Neisseria gonorrhoeae*. The enzyme showed a single component on sodium dodecyl suphate-polycrylamide gel electrophoresis and on isoelectric focusing in amino acid sequence 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 bacterialotein 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 *Piper nigrum* plant were downloaded from the website. The protein database code of the dihydrofolate reductase enzyme was identified from the website. 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 softwere 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 [5,6,7]. Table 1 shows glycerol dehydrogenase-p-cymene interaction has the

Table 1. Results of C docking of phytochemicals with dihydrofolate reductase (receptor)

Sl. no.	Ligand	-CDOCKER energy	-CDOCKER interaction energy	Difference between -CDOCKER interaction energy and -CDOCKER energy	Remarks
1	P-cymene	14.2999	14.9983	0.6984	Maximum inhibition of microbial enzyme
2	Piperazine	1.99172	11.6549	9.66318	
3	Alpha-pinene	-13.7461	11.3739	25.4992	
4	Beta-pinene	-10.941	13.485	24.426	
5	Limonene	-26.5154	12.0783	38.5937	
6	Qurecitine	Failed	Failed	Failed	
7	Piperine	Failed	Failed	Failed	

highest positive value of -CDOCKER energy and minimum value of the difference between -CDOCKER interaction energy and -CDOCKER energy followed by piperazine [8,9]. Thus, the results indicated that p-cymene and piperazine can effectively deactivate the dihydrofolate reductase enzyme thereby interrupting the biological cycle of *Neisseria gonorrhoeae.* Higher positive values for indicated that it was the most active ingredient against *Neisseria gonorrhoeae.* On the other hand, Alpha-pinene, Beta-pinene, Limonene can deactivate the enzyme to a small extent (negative -CDocker energy but positive -CDocker interaction energy) Qurecitine & Piperine cannot interact with dihydrofolate reductase enzyme.

4. CONCLUSIONS

It was previously known that *Piper nigrum* plant has medicinal action against Gonorrhoea. Gonorrhoea is caused by *Neisseria gonorrhoeae.* 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 (beta-pinene, alpha-pinene, p-cymene, limonene, piperazine), which can have a significant interaction with the vital enzyme (dihydrofolate reductase) of the microbe. It was found that P-cymene and piperazine can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Alpha-pinene, Beta-pinene, Limonene were found to be not much effective in deactivating the enzyme of the microbe. Qurecitine & Piperine cannot deactivate the enzyme. Thus, this study could explain that the presence of P-cymene and Piperazine provided that the medicinal value to *Piper nigrum* against Gonorrhoeae caused by *Neisseria gonorrhoeae*.

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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