

***In silico* Analysis of Effects of Phytochemicals from *Michelia champaca* L. against Peptidase Do of *Bordetella pertussis* Causing Cough**

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ABSTRACT

Phytochemicals from *Michelia champaca* L. plant extract are traditionally used to cure cough. It is Cough can be caused by many reasons. Caugh can be caused by the infection of *Bordetella pertussis*. The objective of the study is to identify the phytochemical of *Michelia champaca* capable of curing cough. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDocker energy and -CDocker interaction energy" suggested that magnoflorine can effectively deactivate the peptidase Do enzyme which will interrupt the life cycle of the microorganism and inhibit the multiplication.

Keyword: Phytochemical; Michelia champaca; Bordetella pertussis; cough.

1. INTRODUCTION

Plants are used as medicine throughout the world and are the major resources of medicine [1]. Phytochemicals present in these plants responsible to treat various diseases. These plant-based chemical substances are derived from different parts of plants. The plant extracts show antimicrobial action against different microorganisms. [2]. These medicinal plants play a key role in human health care. Many people rely on the use of traditional medicine [3]. *Michelia champaca* belongs to family Magnoliaceae. *Michelia champaca* extract is used to cure diseases like cough. The objective of the study is to identify the phytochemical responsible to cure the disease. *Michelia champaca* flowers contain "β-sitosterol, germacranolide, lirioidenine, magnoflorine, parthenolide, ushinsunine" etc. These phytochemicals might act against cough. However, there is no such study available. The objective of the study is to identify the phytochemical of *Michelia champaca* capable of curing cough.

2. MATERIALS AND METHODS

2.1 Software Used

Discovery studio module of Biovia software (DassaultSystemesof 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 work shows that *Micheliachampaca* flowersβ-sitosterol, germacranolide, lirioidenine, magnoflorine, parthenolide, ushinsunine. It has already been established that *Micheliachampaca* plant belonging to family Magnoliaceae has the

potential to help controlling cough. This work is focused on the 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 cause 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 the peptidase Do enzyme (protein database code 3IVL).

Peptidase Do enzyme has a major role in metabolic pathway of *Bordetella pertussis* as lipoprotein biosynthesis (signal peptide cleavage) which is a part of protein modification.

It has another metabolic pathway known as peptidoglycan biosynthesis which is a part of cell wall biogenesis.

2.2.3 Molecular docking

Molecular docking method has been used to identify the phytochemical from the plant extract, that 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 perform molecular docking. In this process first, the sdf files for the phytochemicals found in the *Micheliachampacaplant* were downloaded from the website (<https://pubchem.ncbi.nlm.nih.gov/>). The protein database code of the peptidase Do enzyme was identified from the website

(<https://www.rcsb.org/structure/3IVL>). 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 peptidase Do-magnoflorine interaction has the highest positive value of -CDOCKER energy (6.50793) and minimum value of the difference (34.66487) between -CDOCKER interaction energy and -CDOCKER energy followed by parthenolide. Thus the results indicated that magnoflorinecan effectively deactivate the peptidase Do enzyme thereby interrupting the biological cycle of *Bordetella pertussis*.

Table 1. Results of CDocking of phytochemicals with peptidase Do (receptor)

SI no	Ligand	- C DOCKER energy	- C DOCKER interaction energy	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Magnoflorine	6.50793	41.1728	34.66487
2	Ushinsunine	-4.64953	31.4747	36.12423
3	Liriodenine	-14.3424	26.8966	41.236
4	Germacranolide	-18.5597	32.6054	51.1651
5	Parthenolide	-31.6875	30.6494	62.3369
6	β -sitosterol	-35.4176	41.1406	76.4936

4. CONCLUSION

It was previously known that *Micheliachampacaplant* has medicinal action against 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 phytochemical (Germacranolide, β -sitosterol, liriodenine, magnoflorine, parthenolide, ushinsunine), which can have significant interaction with the vital enzyme (peptidase Do) of the microbe. From the above study, it can be concluded that magnoflorine has successfully inhibited the metabolic cycle of the microbe. Ushinsunine is found to be less effective in deactivating the enzyme of the microbe. Liriodenine, Germacranolide, parthenolide, β -sitosterol can not interact with peptidase Do enzyme. Thus the key phytochemicals in preventing cough caused by *Bordetella pertussis* is magnoflorine.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. J Henrich, S Heine, A Norenzayan. The weirdest people in the world? Behavioral and Brain Sciences. 2010;33(2-3):61-83. DOI:10.1017/S0140525X0999152X
2. I. Hussain, R. Ullah, R. Ullah, M.Khurram, N. Ullah, A.Basee , F. Khan, M.Khattak, M. Zahoor, J. Khan, Dr. N. Khan. Phytochemical analysis of selected medicinal plant. African Journal of Biotechnology. 2011;10: 7487-7492.
3. P.Arulselvan, G.Karthivashan, S.Fakurazi, Journal of Chemical and Pharmaceutical Research 5 (7), 233-239, 2013
4. D. Das, S. Das, M. Pandey, D. Bhattacharyay. In silico Analysis of Phytochemicals from *Mucunapruriens* (L.) DC against *Mycobacterium tuberculosis* Causing Tuberculosis, European Journal of Medicinal Plants, 2020.
5. Brinda, O.P., Mathew, D., Shylaja, M.R., Davis, P.S., Cherian, K.A., &Valsala, P.A., (2019). Isovaleric acid and avicequinone-C are Chikungunya virus resistance principles in *Glycosmis pentaphylla* (Retz.) Correa. Journal of Vector Borne Diseases, 56(2), 111.