



Moringa oleifera Derived Phytochemicals against 2-hydroxy-3-oxopropionate Reductase of *Salmonella typhi* Causing Typhoid

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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 *Moringa oleifera* plant extract can cure Typhoid. It is caused by *Salmonella typhi*. Molecular docking method applied using "Biovia Discovery Studio". "High positive values of -CDOCKER energy and -CDOCKER interaction energy" suggested that 4,8,12,16-tetramethylheptadecan-4-olide can effectively deactivate the 2-hydroxy-3-oxopropionate reductase enzyme thereby interrupting the life cycle of the organism.

Keywords: Phytochemical; *Moringa oleifera*; *Salmonella typhi*; typhoid.

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

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

Moringa oleifera belongs to family moringaceae. *Moringa oleifera* extract is used to cure disease like Typhoid. The objective of the study is to identify the phytochemical responsible to cure the disease.

Moringa oleifera contains “3, 7, 11, 15-trimethyl-2-hexadecan-1-ol, 3-ethyl-2, 4-dimethylpentane, 4, 8, 12, 16-tetramethylheptadecan-4-olide, 4-hydroxyl-4-methyl-2-pentanone, 4-hydroxyphenyl tanamide-alpha-L-rhamnopyranoside, 9-octadecenoic acid” etc. These phytochemicals might act against Typhoid. However, there is no such study available.

The objective of the study is to identify the phytochemical of *Moringa oleifera* capable of curing Typhoid.

2. MATERIALS AND METHODS

2.1 Software Used

For analysis Discovery studio module of Biovia software (Dassault Systemes of France) was used. The software utilizes machine learning techniques to predict the level of molecular interaction.

2.2 Methodology

2.2.1 List of phytochemicals

Phytochemicals as secondary metabolites are produced from plant to protect them from predators and having important medicinal properties. Bacteria, viruses, fungi etc. are potential threats to plants. When human consume these plants or their parts these phytochemicals having medicinal properties fight off threats to health. Some phytochemicals have been used as poisons and others as therapeutically medicine. Published works showed that *Moringa oleifera* contains phytochemicals like 3,7,11,15-trimethyl-2-hexadecan-1-ol,3-ethyl-2,4-dimethylpentane,4,8,12,16-tetramethylheptadecan-4-olide,4-hydroxyl-4-methyl-2-pentanone,4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside,9-octadecenoic acid etc. It has already been established that *Moringa oleifera* plant is one of the species of

Moringaceae family has potential to help cure typhoid. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of typhoid.

2.2.2 Enzyme in *Salmonella*

It has been reported that typhoid can be caused by *Salmonella sp. bacteria*. For survival, bacteria requires various metabolic pathway. Different enzymes regulate these metabolic cycles. Brenda enzyme database was used to identify and list different enzymes found in *Salmonella sp. bacteria*. It has been found that 2-hydroxy-3-oxopropionate reductase enzyme (protein database code 4DLL) is involved in glyoxylate and dicarboxylate 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 *Moringa oleifera* plant were downloaded from the website [4]. The protein database code of the enzyme was identified from the website [5]. 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.

Table 1. Results of C Docking of phytochemicals with 2-hydroxy-3-oxopropionate reductase (receptor)

Sl. no.	Ligand	-CDOCKER energy	-CDOCKER interaction energy	Difference between -CDOCKER interaction energy and - CDOCKER energy	Remarks
1	3,7,11,15-Tetramethyl-2-Hexadecent-1-ol	15.7857	47.0737	31.2867	
2	3-ethyl-2,4-dimethylpentane	13.5053	21.3761	7.8708	
3	4,8,12,16-tetramethylheptadecan-4-olide	33.9622	48.1479	14.1857	Maximum inhibition of microbial enzyme
4	4-hydroxyl-4-methyl-2-pentanone	26.6276	28.639	2.0114	
5	4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside	25.292	27.8167	2.5247	
6	9 - octadecenoic acid	30.0714	43.551	13.4796	

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 2-hydroxy-3-oxopropionate reductase 4-hydroxyl-4-methyl-2-pentanone interaction has the highest value of CDOCKER energy (28.639) and minimum value of the difference (2.0114) between CDOCKER interaction energy and CDOCKER energy followed by 4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside. Thus the results indicated that 4-hydroxyl-4-methyl-2-pentanone and 4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside can effectively deactivate the 2-hydroxy-3-oxopropionate reductase enzyme thereby interrupting the biological cycle of *salmonella typhi*. Higher positive values for phytochemical 4-hydroxyl-4-methyl-2-pentanone and 4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside indicated that it was the most active ingredient against *Salmonella sp.* On the other hand 3,7,11,15-trimethyl-2-hexadecent-1-ol and 4,8,12,16-tetramethylheptadecan-4-olide can deactivate the enzyme to a small extent (negative-CDOCKER energy but positive-CDOCKER interaction energy).

Thus, the key phytochemicals preventing typhoid caused by *salmonella sp.* are 4-hydroxyl-4-methyl-2-pentanone and 4-

hydroxyphenyltanamide-alpha-L-rhamnopyranoside.

4. CONCLUSIONS

It was previously known that *Moringa oleifera* plant has therapeutically action against typhoid. *Salmonella typhi* is the causative agent of typhoid. 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 (3,7,11,15-trimethyl-2-hexadecent-1-ol, 3-ethyl-2,4-dimethylpentane, 4,8,12,16-tetramethylheptadecan-4-olide, 4-hydroxyl-4-methyl-2-pentanone, 4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside, 9-octadecenoic acid etc.), which can have a significant interaction with the vital enzyme (2-hydroxy-3-oxopropionate reductase) of the microbe. It was found that phytochemicals 4-hydroxyl-4-methyl-2-pentanone and 4-hydroxyphenyltanamide-alpha-L-rhamnopyranoside can form strong bond with the enzyme successfully inhibiting the metabolic cycle of microbes. 3,7,11,15-trimethyl-2-hexadecent-1-ol and 4,8,12,16-tetramethylheptadecan-4-olide were found to be not much effective in deactivating the enzyme of the microbe. This study could explain that the presence of phytochemicals 4-hydroxyl-4-methyl-

2-pentanone and 4-hydroxyphenyltanamide- α -L-rhamnopyranoside provided the medicinal values to *Moringa oleifera* against typhoid caused by *Salmonella typhi*.

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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