European Journal of Medicinal Plants

31(6): 1-5, 2020; Article no.EJMP.55463
ISSN: 2231-0894, NLM ID: 101583475

In silico Analysis of Phytochemicals from Cocoa against Ribitol-5-Phosphate 2-Dehydrogenase of *Streptococcus pneumoniae* Causing Pneumonia

Sunanya Das[1], Suchismita Khatei[1], Saismita Sahoo[1], Sitaram Swain[1] and Dipankar Bhattacharyay[1*]

[1]Centurion University of Technology and Management, Odisha, India.

Authors' contributions

This work was carried out in collaboration among all authors. Author SD conceived and planned the study, performed the computational framework and analyzed the statistical data. Author S. Sahoo carried out the implementation. Author SD wrote the first draft of the manuscript. Authors S. Sahoo and SK managed the analyses of the study. Author SD took lead in the literature searches. Author S. Swain read and approved the final manuscript and provided assistance throughout the study. While author DB supervised and guided the whole study. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/EJMP/2020/v31i630240
Editor(s):
(1) Dr. Elena Maria Varoni, University of Milan, Italy.
(2) Prof. Marcello Iriti, University of Milan, Italy.
Reviewers:
(1) P. Rajakani, Manonmaniam Sundaranar University, India.
(2) Keith J. Stine, University of Missouri-St. Louis, USA.
Complete Peer review History: http://www.sdiarticle4.com/review-history/55463

Original Research Article

Received 10 January 2020
Accepted 16 March 2020
Published 20 March 2020

ABSTRACT

This analysis aims at evaluating the effects of Cocoa extract on Pneumonia. Pneumonia is caused by *Streptococcus pneumoniae*. Caffeine, Chorogenic acid, Ferulic acid, Iso- Orientin, luteolin, Naringenin and Vanillic acid of Cocoa were interacted with ribitol-5-phosphate 2-dehydrogenase which is involved in pentose and glucorunate interconversion pathways of *Streptococcus pneumoniae*. The enzyme was taken as receptor and phytochemicals were considered as ligands. All the interactions were done in Biovia discovery Studio 2020 and the process is known as molecular Docking. Molecular Docking provides us an opportunity to identify the potential phytochemical or component which can act as powerful tool against the pathogen. Out of all the

**Corresponding author: E-mail: dipankar.bhattacharyay@cutm.ac.in;*

phytochemicals, Luteolin of Cocoa inhibits or blocks the mechanism or action of ribitol-5-phosphate 2-dehydrogenase enzyme of *Streptococcus pneumoniae.* There is high possibility that these phytochemicals can potentially inhibit others enzymes involved in various metabolic pathways of *Streptococcus pneumoniae*.

Keywords: Phytochemical; biovia discovery studio 2020; cocoa; metabolic pathways; pneumonia; Streptococcus pneumonia.

1. INTRODUCTION

Plants are the precious gifts to Humans from Earth. They are like boon to us. They provide us a lot of things from Oxygen to food, from timber to firewood and medicines. Role of plants in our life isn't a new concept. We, the humans since the nomadic age have relied on plants for the various purposes. From the very beginning the trees were the soul providers on the earth. Our forefathers relied more on nature than western medicine for their ailments. Use of plants for curing diseases has been mentioned in various Vedas. Ayurveda is well known system of treating diseases with the help of substances taken from nature. In Ayurveda Plants play a major role as most of the constituents or ingredients are taken from plant. From roots to leaves, from stems to bark, from resins to secondary metabolites every part of the plant can be used in Ayurveda for treatment of diseases.

We belong to the 21st century. Life is never slow here. Speed excites us. We love it when our work is done in less span of time. With change in lifestyle our body also changes. When we suffer from any kind of disease we depend on chemical drug for fast relief from that disease. The chemical based drugs may provide the fast relief but we don't know about the cost our body is paying for the fast recovery using chemical drugs. The chemical drugs may pretend as a friend from outside but on inside they prove harmful to our systems. In the long run our systems will start failing as a side effect to chemical drugs.

Therefore the people are switching to plant based drugs. Plant based drugs on other hands is a safer alternative to chemical drugs. Plant based drugs are a wonderful combination of nature and science. With the help of science we identify the important component of the plant extract which have potential to inhibit the pathogenic activity of the microbe and try to deal with various component of plant extract. The plant based drugs will have the same efficacy as that of chemical drugs but without any adverse effect.

Cocoa (*Theobroma cacao*) is a plant which belongs to the family Malvaceae. Its origin is estimated to be in the deep tropical regions of Mesoamerica and Ayurveda have mentioned use of Cocoa in treatment of a number of disorders. [1]. Studies have revealed that Cocoa contains Phytochemical like caffeine, Chlorogenic Acid, Ferulic Acid, Iso- Orientin, Luteolin, Naringenin, Vanillic Acid and so on [2]. Cocoa is meant not only for confectioneries or bakeries but also known to cure diseases like anemia, tuberculosis, fever, gout, kidney stones, and pneumonia [3]. Cocoa has several health benefits such as improved Cardiac function, stimulation of the nervous system, improved digestion, and improved kidney and bowel function [4,3].

Pneumonia refers to the inflammation of the air sacs in the lungs (alveoli) and the tissue surrounding them. Pneumonia often leads to sudden high fever, uneasiness, cough and shortening of breath. Pneumonia is caused by *Streptococcus pneumoniae*. Pneumonia can prove fatal to babies and older people [5].

This study focuses on the identification of the phytochemical from *Cocoa* responsible to cure Pneumonia caused by *Streptococcus pneumoniae.*

2. MATERIALS AND METHODS

2.1 Software Used

All the operations were carried out in Discovery studio module of Biovia 2020 software (Dassault Systemes of France). Biovia 2020 discovery studio is one of the user-friendly software. Its user interface is quite easy to carry out the molecular docking. The software utilizes machine learning techniques to predict the level of molecular interaction between the receptor (enzyme) and Ligand (Phytochemicals).

2.2 Methodology

2.2.1 List of phytochemicals

Phytochemicals are the secondary metabolites produced by plants as a response to flight or fight mechanism against their predators. Phytochemicals are generally bio active compounds which can affect animal biochemistry and metabolism. Hence they are widely examined to prove their ability towards our health benefits. It becomes important for us to include them in our foods, as potential nutritionally active ingredients. Published works showed that Cocoa contains caffeine, Chlorogenic Acid, Ferulic Acid, Iso- Orientin, Luteolin, Naringenin, Vanillic Acid and so on. It has already been established that Cocoa plant belonging to Malvaceae family has potential to help controlling Pneumonia. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of Pneumonia [6].

2.2.2 Enzyme found in *Streptococcus pneumoniae*

From published books and papers we can say that Pneumonia is caused due to *Streptococcus pneumoniae* infestation [7]. the survival of pathogen inside its host is highly dependent on certain metabolic pathways. These metabolic pathways require certain enzymes as its co-factor to function properly. Brenda enzyme database helped us to identify and list different enzymes found in *Streptococcus pneumoniae*. It has been found that ribitol-5-phosphate 2-dehydrogenase (protein database code 2VSI) is involved in pentose and glucorunate inter conversion metabolism (KEGG) [8]. This metabolism proves to be very crucial for the pathogen thus blocking or inhibiting that pathway results in death of the particular microbe [9].

2.2.3 Molecular docking

Molecular docking method has been used to identify the phytochemical from the plant extract, which act as a ligand and forms a strong covalent bond with the bacterial protein to successfully inhibit the microbe. The Discovery studio module of Biovia2020 software was used for identifying molecular interaction and perform molecular docking. First of all a list of phytochemicals present in Cocoa from various research papers was made. Secondly the sdf files for the phytochemicals found in the Cocoa plant were downloaded from various websites like PubChem, MolInstincts etc. The protein database code of enzyme was identified from the RCSB-PDB 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 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

Fig. 1 shows the active site of ribitol-5-phosphate 2-dehydrogenase enzyme. It appears as light green color. CDOCK is a molecular dynamics (MD) simulated-annealing-based algorithm. It is a grid-based molecular docking method and optimized for accuracy. The ligand conformations were obtained by Molecular Dynamic methods.

-CDOCKER energy was calculated based on the internal ligand strain energy and receptor-ligand interaction energy. -CDOCKER interaction signifies the energy of the non-bonded 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 [10].

Table 1 show that ribitol-5-phosphate 2-dehydrogenase-Luteolin interaction has the highest positive value of -CDOCKER energy (33.3811) and minimum value of the difference (4.5205) between - C DOCKER interaction energy and - C DOCKER energy followed by Chlorogenic Acid. Thus the results indicated that Caffeine and Chlorogenic Acid can effectively deactivate the ribitol-5-phosphate 2-dehydrogenase enzyme thereby interrupting the biological cycle of *Streptococcus pneumoniae*. Higher positive values for Luteolin indicated that it was the most active ingredient against *Streptococcus pneumoniae*. On the other hand, Iso- Orientin, Naringenin and Vanillic Acid can deactivate the enzyme to a small extent. Thus, the key phytochemicals preventing Pneumonia caused by *Streptococcus pneumonia* are Chlorogenic Acid and Luteolin.

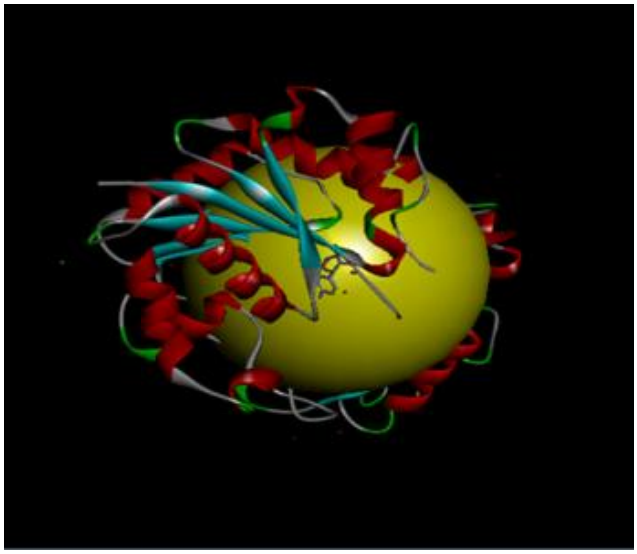

Fig. 1. Active site of ribitol-5-phosphate 2-dehydrogenase enzyme

Table 1. Results of CDocking of phytochemicals with ribitol-5-phosphate 2-dehydrogenase(receptor)

Sl. No	Ligand	-C DOCKER energy	-C DOCKER interaction energy	difference between - C DOCKER interaction energy and - C DOCKER energy
1	Caffeine	15.2824	23.4463	8.1639
2	Chlorogenic acid	34.4045	49.747	15.3425
3	Ferulic acid	23.974	27.6967	3.7227
4	Iso-orientin	26.5148	56.6787	30.1639
5	Luteolin	33.3811	37.9016	4.5205
6	Narigenin	26.3753	32.8289	6.4536
7	Vanillic acid	20.9174	23.6898	2.7724

4. CONCLUSION

Our dependence on chemical drugs has put an adverse effect on our body. Thus we need to incorporate more plant based drugs in our life. One of the important plants that can be used for plant based drugs is Cocoa. Cocoa is a well-known for its use in confectioneries and bakeries. But it also have health benefits like stimulation of nervous systems, improved digestion, improved kidneys and bowels etc. [11]. It was previously known that Cocoa plant has medicinal action against Pneumonia [12]. Pneumonia is caused by *Streptococcus pneumoniae*. This study was carried out to provide the theoretical basis of this observation. Using Discovery studio module of Biovia 2020 software, molecular docking operation was performed to identify the phytochemical (caffeine, Chlorogenic Acid, Ferulic Acid, Iso- Orientin, Luteolin, Naringenin and Vanillic Acid) which can have a significant interaction with the vital enzymeribitol-5-phosphate 2-dehydrogenase of the microbe. It was found that Luteolin, Ferulic Acid and Chlorogenic Acid can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Thus, this study could explain that the presence of Luteolin, Chlorogenic Acid and Ferulic Acid provided the medicinal values to Cocoa against Pneumonia caused by *Streptococcus pneumoniae*. But we can also conclude that other phytochemicals may or may not inhibit other enzymes present in other biological cycles of *Streptococcus pneumoniae*.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Lee KW, Kim YJ, Lee HJ, Lee CY. Cocoa has more phenolic phytochemicals and a higher antioxidant capacity than teas and red wine. Journal of Agricultural and Food Chemistry. 2003;51(25):7292-7295.
2. Subhashini R, Rao UM, Sumathi P, Gunalan G. A comparative phytochemical analysis of cocoa and green tea. Indian Journal of Science and Technology. 2010; 3(2):188-192.
3. Shahanas E, Seeja T, Panjikkaran ER, Aneena CL, Sharon, Remya PR. Health benefits of bioactive compounds from cocoa (*Theobroma cacao*). Agricultural Reviews. 2019;40(2):143-149.
4. Kim J, Lee KW, Lee HJ. Cocoa (*Theobroma cacao*) seeds and phyto-chemicals in human health. In Nuts and seeds in health and disease prevention. Academic Press. 2011;351-360.
5. InformedHealth.org [Internet]. Cologne, Germany: Institute for Quality and Efficiency in Health Care (IQWiG); 2006-. Pneumonia: Overview. 2018;9. Available:https://www.ncbi.nlm.nih.gov/books/NBK525774/
6. Lateef Agbaje, Musibau A. Azeez, Tesleem B. Asafa, Taofeek A. Yekeen, Akeem Akinboro, Iyabo C. Oladipo, Luqmon Azeez, Sunday A. Ojo, Evariste B. Gueguim-Kana, Lorika S. Beukes. Cocoa pod husk extract-mediated biosynthesis of silver nanoparticles: Its antimicrobial, antioxidant and larvicidal activities. Journal of Nanostructure in Chemistry. 2016;6(2): 159-169.
7. Chawla K, Gurung B, Mukhopadhyay C, Bairy I. Reporting emerging resistance of *Streptococcus pneumoniae* from India. Journal of Global Infectious Diseases. 2010;2(1):10.
8. Baur Stefanie, Jon Marles-Wright, Stephan Buckenmaier, Richard J. Lewis, Waldemar Vollmer. Synthesis of CDP-activated ribitol for teichoic acid precursors in *Streptococcus pneumoniae*. Journal of Bacteriology. 2009;191(4):1200-1210.
9. Nayak Subhalaxmi, Dibyabhaba Pradhan, Harpreet Singh, Sudhakara Reddy M. Computational screening of potential drug targets for pathogens causing bacterial pneumonia. Microbial pathogenesis. 2019; 130:271-282.
10. Brinda OP, Deepu Mathew, Shylaja MR, Sangeetha Davis P, Anita Cherian K, Valsala PA. isovaleric acid and avicequinone-C are chikungunya virus resistance principles in Glycosmispenta-phylla (Retz.) Correa. 2019;56(2):111-121.
11. Scapagnini G, Davinelli S, Di Renzo L, De Lorenzo A, Olarte HH, Micali G, Gonzalez S. Cocoa bioactive compounds: Signifi-cance and potential for the maintenance of skin health. Nutrients. 2014;6(8):3202-3213.
12. Moorhead ES. The treatment of pneumonia. Canadian Medical Association Journal. 1930;22(5):669.

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sdiarticle4.com/review-history/55463