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In silico Analysis of Phytochemicals from Coconut against Candidiasis

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Authors' contributions

This work was carried out in collaboration among all authors. Author SD conceived and planned the study, performed the computational framework, analyzed the statistical data and wrote the first draft of the manuscript. Author SSN took lead in the literature searches. Author SS 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.

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ABSTRACT

This *in sillico* analysis was carried out to evaluate the effect of Coconut extract on Candidiasis. Candidiasis is caused by *Candidia tropicalis*. The phytochemicals of Coconut were interacted with a 2-enoyl-CoA hydratase enzyme involved in Biosynthesis of Unsaturated Fatty Acid metabolic pathway of *Candidia tropicalis*. 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 phytochemicals, Folic Acid of Coconut inhibits or blocks the mechanism of action of 2-enoyl-CoA hydratase enzyme of *Candidia tropicalis*. There is high possibility that these phytochemicals can potentially inhibit others enzymes involved in various metabolic pathways of *Candidia tropicalis*.

Keywords: Phytochemical; biovia discovery studio 2020; coconut; metabolic pathways; candidiasis; Candidia tropicalis.

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1. INTRODUCTION

Candidiasis is one of the most common yeast infections which can occur in mouth, skin, genitals or sometimessite-specific invasive infection [1,2]. The fungus candida is a part of normal microbial flora of human body, which causes somewhat opportunistic infections targeting immune compromised persons. Babies, less than one month old, patients who are receiving cancer treatments, post organ transplant treatments, or are suffering from HIV/AIDS or diabetes, pregnant or breastfeeding women, people recovering from surgeries or admitted into an intensive care unit and other people with a weakened immune system have a great chances at developing a form of candidiasis [3,4]. A systemic candidiasis can result in 30-50% in mortality rate in case of people admitted in intensive care unit. It is estimated that, Mouth candidiasis occurs in about 6% of infants less than a month old, while 20% of those receiving chemotherapy for cancer and 20% of those with AIDS also develops the disease [5]. About three-quarters of women have at least one yeast infection at some time during their lives [6]. Nevertheless, candidal sepsis is rare but it can cause severe may be even fatal blood infection. Esophageal candidiasis is the most common esophageal infection in persons with AIDS. About two-thirds of people with AIDS and esophageal candidiasis also have oral candidiasis [7]. Seemingly insignificant yeast infection can cause hazardous outcome upon negligence.

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. Ayurveda is well known system of treating diseases with the help of substances taken from nature. 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. 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.

Cocos nucifera (coconut) belongs to the family Arecaceae. They are found in tropical regions but are most commonly found near sandy shorelines. The plant is propagated by both natural and man-made ways. After germination the plant is eligible to bear fruits only after 6-10 years. It continues to fruit until it reaches the age of 80 years. The seed of coconut is roughly ovoid and is composed of a thick, fibrous husk. There is a thin, white, fleshy layer known as the "meat". When the coconut is immature, the meat is soft and jelly-like but at maturity it becomes firm. The nut is filled with watery liquid called "coconut milk". The amount of coconut milk is more in unripe fruits but it is absorbed during ripening. We can observe that when they are unripe they are green in color but when they rip or become mature they turn brown. Coconut is important commercially and nutritionally. From copra of the coconut, coconut oil is produced. The coconut oil used for making margarine, soap and cooking oils. The seed kernel is consumed as local food [8]. Coconut contains certain phytochemicals which are known to cure Candidiasis.

The genus Candida contains over 200 heterogeneous species but only a few can induce Candidiasis in humans. Candida infections can be invasive or superficial depending on the species. Superficial infection affects the mucous membranes or the skin and can be treated with antifungal drugs. Candidiasis is caused by *Candida tropicalis* infestation [9].

This study focuses on the identification of the phytochemical from *Coconut* responsible to cure Candidiasis caused by *Candidia tropicalis.*

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 Coconut contains Biotin, Catechins, Folic acid, Riboflavin, Nicotinic acid etc. [10]. It has already been established that Coconut plant belonging to Malvaceae family has potential to help controlling Candidiasis. This work is focused on identification of the particular phytochemical responsible for inhibiting and controlling of Candidiasis.

2.2.2 Enzyme found in *Candidia tropicalis*

From published books and papers, we can say that Candidiasis is caused due to *Candidia tropicalis* infestation [11]. 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 *Candidia tropicalis*. It has been found that 2-enoyl-CoA hydratase (protein database code 1PNG) is involved in Biosynthesis of unsaturated fatty Acid metabolism (KEGG). This metabolism proves to be very crucial for the pathogen thus blocking or inhibiting that pathway results in death of the particular microbe.

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 Biovia 2020 software was used for identifying molecular interaction and perform molecular docking. First of all a list of phytochemicals present in Coconut from various research papers was made. Secondly the sdf files for the phytochemicals found in the Coconut plant were downloaded from various websites like PubChem, MolInstincts etc. The protein database code of 2-enoyl-CoA hydratase 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 2-enoyl-CoA hydratase 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 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 [12].

Table 1 shows that (2-enoyl-CoA hydratase - Folic Acid) interaction has the highest positive value of -CDOCKER energy (31.7969) and minimum value of the difference (12.9674) between - C DOCKER interaction energy and - C DOCKER energy followed by Catechins. Thus, the results indicated that Folic Acid and Catechins can effectively deactivate the 2-enoyl-CoA hydratase enzyme thereby interrupting the biological cycle of *Candidia tropicalis*. Higher positive values for Folic Acid indicated that it was the most active ingredient against *Candidia tropicalis*. On the other hand, Nicotonic Acid and

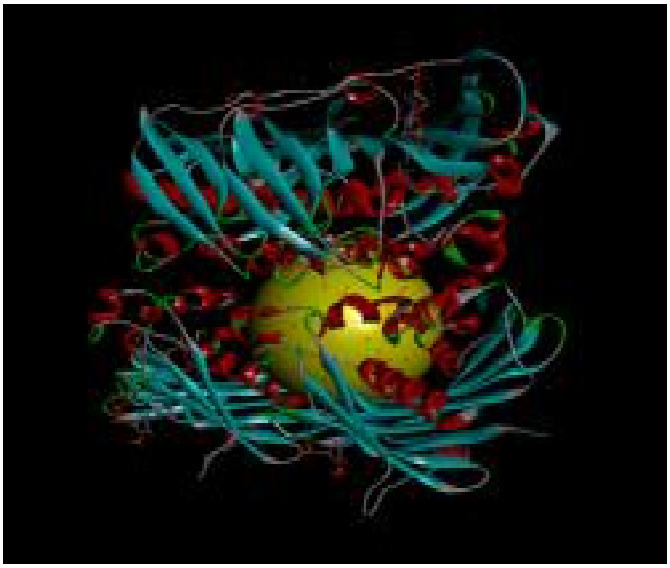

Fig. 1. Active site of 2-enoyl-CoA hydratase enzyme

Table 1. Results of CDocking of phytochemicals with 2-enoyl-CoA hydratase (receptor)

Sl No	Ligand	- C DOCKER energy	- C DOCKER interaction energy	Difference between - C DOCKER interaction energy and - C DOCKER energy
1	Biotin	21.4026	29.257	7.8508
2	Catechins	24.9815	31.4966	6.5151
3	Folic acid	31.7969	44.7643	12.9674
4	Riboflavin	18.8844	38.6206	19.7362
5	Nicotinic acid	12.0148	14.197	2.1822
6	Leucoanthocyanidin	Failed		

Riboflavin can deactivate the enzyme to a small extent. Leucoantho Cyanidins cannot interact with 2-enoyl-CoA hydratase. Thus, the key phytochemicals preventing Candidiasis caused by *Candidia tropicalis* are Folic Acid and Catechins.

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 Coconut. Coconut is a well-known for its use in making soaps, perfumes and used in other cosmetic products. But coconut water has many medicinal properties like antifungal, antidermatophytic, antiviral, anti-parasitic, antibacterial, anti-oxidant, hypoglycemic, hepatoprotective and immunostimulant [13]. It was previously known that Coconut plant has medicinal action against Candidiasis. Candidiasis is caused by *Candidia tropicalis*. 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 which can have a significant interaction with the vital enzyme 2-enoyl-CoA hydratase of the microbe. It was found that Folic Acid and Catechins can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Leucoantho Cyanidins cannot deactivate the enzyme. Thus, this study could explain that the presence of Folic Acid and Catechins provided the medicinal values to Coconut against Candidiasis caused by *Candidia tropicalis*. But we can also conclude that other phytochemicals may or may not inhibit other enzymes present in other biological cycles of *Candidia tropicalis*.

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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