

IN SILICO ANALYSIS OF PHYTOCHEMICALS FROM *Cinnamomum zeylanicum* (Cinnamon) Against Aspartate Semialdehyde Dehydrogenase of *Aspergillus fumigatus* Causing Aspergillosis

ABSTRACT:

Cinnamomum zeylanicum is an ethno-medicinal plant which has very essential activity against bacteria and fungi. It has been reported that this plant extract used to cure Aspergillosis. Multiple Research work emphasize the therapeutic importance of bioactive principles of *Cinnamomum zeylanicum* in the treatment of aspergillosis. This plant extracts contains different phytochemicals which prevents the activity of *Aspergillus fumigatus* that is the causative agent of aspergillosis. One of the important enzyme of *Aspergillus fumigatus* is aspartate semialdehyde dehydrogenase involved in its amino acid pathway. The molecular docking of the phytochemicals with the enzyme was studied using BIOVIA Discovery studio. The strength of the interaction was calculated based on-CDOCKER energy and -CODOCKER interaction energy. High positive values for the both the parameters indicated that out of different phytochemicals **Cinnamic acid** and **vallinin** can effectively deactivate the aspartate semialdehyde dehydrogenase by which life cycle of *Aspergillus fumigatus* interrupted.

KEYWORDS:

Phytochemicals , BIOVIA, Discovery studios, *Cinnamomum zeylanicum*, *Aspergillus fumigatus*

INTRODUCTION:

The faster and developed lifestyles put effects on the health and behavior of an individual. In recent decades, the lifestyles an important factor of health is more interested by researchers. According to WHO 60% of health factors directly related to the way of living. Millions of peoples follow an unhealthy lifestyle like unhealthy diet, smoking, alcohol consuming, drug abuse, stress and so on. Hence, they are encountered illness, disability and problems like joint pain, cardiovascular disease, hypertension, overweight, skin lesions, low vision and low hearing problems in early age is very common in now –a – days world. . A little care and some basic changes in the way of living can prevent these diseases from annexing our society.

From Vedic period, the nature is the best doctor of all individual. According to the great scholar Charaka, the every plants has its own medicinal properties. The main component of the plants which are used in therapeutic purpose is called phytochemicals. These phytochemicals produce a definite physiological actions in the human body. The presence of phytochemicals has revealed the presence of numerous chemicals including Alkaloids, tannin, flavonoids, saponins etc. these are secondary metabolites of plants. serves as defense mechanism against bacteria, insects and many microorganism (Cowan, 1999).Based on current research it seems to be medicinal plants will play an important role health condition of society (Hoareau and Dasilva,1999).The use of traditional medicinal plants in most of the developing countries, as a normative basis for the maintenance of good health, has been widely observed (UNISCO, 1996). In order to a comprehensive compilation of medicinal plants that can be used in disease prevention. is obtained, collation of the original data from the traditional knowledge is essential (Tan et al. 2010). For knowing ethno-botanical values of medicinal plants survey should be conducted (Biswas et al. 2011). Various phyto extracts has numerous properties like anti cancer, antioxidant, anti-inflammatory, anti microbial, anti diabetic etc. .(Ullah N. et.al, 2011). The

popularity of the medicinal plants are due to their safety, efficacy and their cost effectiveness. For preparing a drug from botanical origin it can be any part of the plants like roots, stem, seeds, fruits etc. For example, the anticancer property of Neem leaves (*Azadirachata indica*) has phytochemicals like terpenoids and steroids. This plant is very preventive, protective, immune modulatory and apoptotic effects against various types of cancer (Paul et al. 2011). *Allium sativum* (Garlic) constituents allicin, disulfide, diallyl trisulfide have a chemo preventive agent for lung and breast cancer (Chu et. al.2012;Li et al. 2012).Research should be emphasized in the field of medicinal plants. which will be beneficial for both economical side and therapeutic purpose.

Cinnamomum zeylanicum is known as True Cinnamon or Ceylon Cinnamon. It belongs to family lauracea. Members of this family are ever green plants up to 10-17m high, that found in south-eastern asia, Australia and America(Cheng, 1983).This is a common spice and flavoring agent in most of the Asian countries . The Cinnamon is a remedies for aspergillosis , respiratory tract infection, skin diseases, gynecological fatality. Almost Especially its bark contains essential oils. This oil has antifungal property and inhibit the growth of mycelia of *Aspergillus sp.*, *Candidas albicans* etc.(Singh, 1995;Lima ,1993). It also lowers the triglycerides of plasma (Kim , 2006). It also plays an important role in prevention of food oxidation by beta carotene (Mancini-Filho et.al) and anti - inflammatory activity . The most essential phytochemicals are present in *Cinnamomum zeylanicum* are Procyanidin A2, eugenol 3D, catechin, cinnamic acid, curcumin,nicotin, ,quercetin,vanillin (PUBMED). There is a high chance that these phytochemicals can cure asperogilosis.

A group of fungus belonging to genus *Aspergillus* generally causes aspergillosis. They are vesicle shape of a circle, with filamentous extensions growing out of it and belonging to

Ascomycota phylum .*Aspergillus fumigatus* infection (aspergillosis) is a common fungal disease that affects the respiratory tract skin, heart, brain, kidneys. This pathogens leads to high mortality in AIDS and organ transplant patients (Denning et.al 1991;Kwon-chung and Sugai 2013). This study focuses on the investigation of the phytochemical of responsible to cure aspergillosis caused by *Aspergillus fumigatus*.

MATERIALS AND METHODS

Software Used:

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

Methodology:

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. Published works showed that *Cinnamomum zeylanicum* contains Procyanidin, A2,eugenol 3D, catechin, cinnamic acid curcumin,nicotine, quercetin,vanillin.It has already been established that plant *Cinnamomum zeylanicum* belonging to lauraceae family has potential to help controlling aspergillosis. This work is focused on identification of the particular phytochemical responsible for inhibiting and decreasing the effect of aspergillosis.

Enzyme Found In *Cinnamomum zeylanicum*:

It has been reported that aspergillosis can cause as a result of *Aspergillus fumigatus* infestation. Various metabolic cycles have been seen in the fungi life cycle for its survival. These metabolic cycles are regulated by different enzymes. Brenda enzyme database was used to find the list of different enzymes found in *Aspergillus fumigatus* fungi. It has been found that aspartate semialdehyde dehydrogenase enzyme (protein base code 5JW6) is involved in amino acid metabolism (mainly synthesis of the amino acids like glycine, serine, threonine, cysteine, methionine, lysine) [KEGG] and very crucial for survival of the particular microbe.

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 *Cinnamomum zeylanicum* plant were downloaded from the website (PUBCHEM). The protein database code of the aspartate semialdehyde dehydrogenase enzyme was found from the website (RCBS PDB). The active site of the enzyme was identified via “receptor cavity” protocol found under “receptor-ligand interaction” menu. Molecular docking was done with the help of 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 indicators 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 controlling the disease.

RESULTS AND DISCUSSION

Fig. 1 shows the active site of the shikimate dehydrogenase. 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.

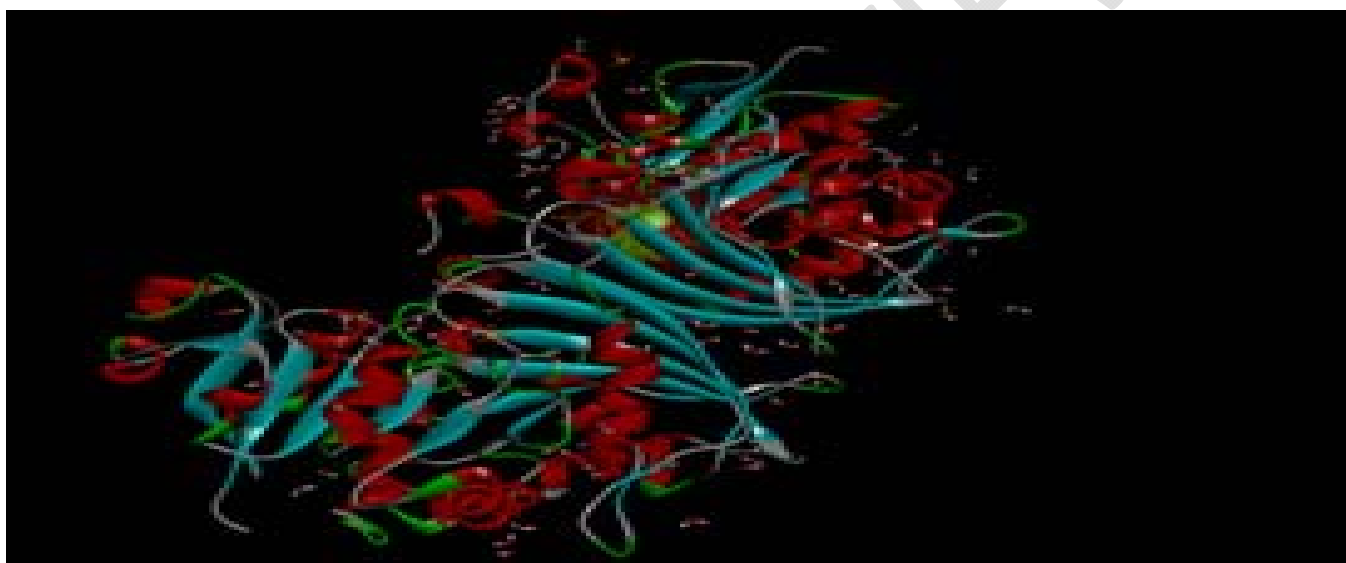


Figure 1. Active site of Aspartate semialdehyde dehydrogenase enzyme

-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 [6]. Table 1 shows that aspartate semialdehyde dehydrogenase cinnamic acid interaction has the highest positive value of - CDOCKER energy (21.7962) and minimum value of the difference (2.7916) between - CDOCKER interaction energy and - C DOCKER energy followed by vallinin Thus the results indicated that cinnamic acid and vallinin can effectively deactivate the aspartate semialdehyde dehydrogenase enzyme thereby interrupting the biological cycle of *Aspergillus fumigatus*. Higher positive values for cinnamic acid indicated that it was the most active component against *Aspergillus fumigatus*. On the other hand, quercetin, catechin, eugenol 3D, curcumin, nicotin can deactivate the enzyme to a small extent. Procyanidin A2 cannot interact with aspartate semialdehyde dehydrogenase enzyme. Thus, the key phytochemicals preventing aspergillosis caused by *Aspergillus fumigatus* are **cinnamic acid** and **vallinin**.

Table 1: Results of Cdocking of Phytochemicals With Shikimate Dehydrogenase (Receptor)

| | | | | |
|----|---------------|---------|----------|----------|
| 1 | Cinnamic acid | 21.7962 | 24.5878 | 2.7916 |
| 2 | Vallinin | 16.6475 | 23.0593 | 6.4118 |
| 3 | Quercetin | 31.8607 | 39.0157 | 7.1550 |
| 4 | Catechin | 32.2154 | 40.6862 | 8.4708 |
| 5. | Eugenol 3D | 14.6182 | 24.7064 | 10.0882 |
| 6 | Curcumin | 32.6891 | 50.252 | 17.5629 |
| 7 | Nicotin | 3.12172 | 23.62840 | 20.50668 |
| 8 | Procyanidin | Failed | NA | |

CONCLUSION

It was previously known that that *Cinnamon zeylancium* plant has medicinal action against aspergillosis. Aspergillosis is caused by *Aspergillus fumigatus*. This study was carried out to provide the theoretical knowledge of this observation. Using Discovery studio module of BIOVIA software, molecular docking operation was performed to identify the phytochemical (cinnamic acid,vallinin,quercetin, catechin , eugenol 3D, curcumin, nicotin,procyanidin A2), which can have a significant interaction with the vital enzyme (aspartate semialdehyde dehydrogenase) of the microbe .It was found can form strong bond with the enzyme successfully inhibiting the metabolic cycle of the microbe. Curcumin and nicotin werefound to be not much effective in deactivating the enzyme of the microbe. Procyanidin A2 cannot deactivate the enzyme.Thus, this study could explain that the presence of cinnamic acid and vallinin provided the medicinal values to Cinnamomum zeylanicum against aspergillosis caused by *Aspergillus fumigatus*

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