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SCREENING THROUGH COMPUTER AIDED APPROACH OF PHYTOCHEMICALS FROM *CINNAMOMUM CASSIA* TARGETING LUNG CANCER

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Abstract

Phytochemicals are plant based chemical constituents, that are found in grains, beans, fruits, vegetables, etc. These chemicals have gained interest as majority of them have potentials to protect the cells from damage that could lead to life threatening diseases like cancer. There are reports supporting the use of phytochemicals isolated from *Cinnamomum cassia* in the treatment of lung disorders. The phytochemicals present in it have the aptness to suppress the receptor such as, Tumor necrosis factor receptor (TNFR) that is associated with the enzyme Tumor necrosis factor alpha converting enzyme (TACE). In the present study, molecular docking of the phytochemicals screened from *Cinnamomum cassia* were measured against the enzyme by using BIOVIA Discovery Studio. The stability of the interaction was evaluated based on the scores of -CDocker energy and -CDocker interaction energy. High positive scores for both the variables indicated that out of the various phytochemicals present in *Cinnamomum cassia*, Proanthocya and Curcumin can effectively deactivate TACE.

Key words: Phytochemical, BIOVIA, Discovery studio, Cinnamomum cassia, Lung Cancer

Introduction

Cancer in today's date is considered to be one among the terminal illnesses that is associated with numerous health hazards in both advanced as well as developing nations. Among the treatments available for cancer, Radiation, surgery, medications have many auxiliary ill effects. In order to overcome the side effects linked with the treatments available for cancer, several adjuvant therapies that contemplate the treatment are looked as for rescue. These therapies include, herbal medications majorly stated in Ayurveda management system (Maller *et al*., 2006). A number of herbal and herb minerals amalgamations are being recorded for their anti-cancer activity (Vikas, 2014). Tumors are defined as *granthi* and *arbuda* in several of the ancient classical texts and are associated with prevalent neoplasms that can appear in any body tissue or organ. The term *Arbuda* is procured from the root *Arb* with suffix e*na* and along with *'nd'*. It destroys explicitly the *Mamsa Dhatu* (Muscles). Whereas, *Granthi* is a tiny swelling within the subcutaneous fat tissue, muscle, or blood vessels, or a slight neoplasm which is round, erect, and twisted in a localized area. According to the classical literature *arbuda* occurs due to the void *dosha's* and can be categorized on *dosha's aspect* as well as its occurrence position. When two *arbuda* appear concurrently, the condition is called *dvirarbuda*, which propounds to their pathology.

The various abnormal growths of pre-and post-cancer states belonging to, malignant or non-malignant phases are referred to as benign growths *(apaci),* cystic growths *(gulma),* lymphatic growths *(gandamala),* cystic tumors *(mutragranthi),* bone tumor *(asthila),* vaginal tumors *(yonikarnini),* and systemic tumors (*granthivisarpa* and *balmika*). These growths are associated with the morbid anatomy as neoplasm (Dutta and Chakraborty, 2018). Based on such diversity of benign and malignant growths, several herbal remediation was formulated in the ancient era (Wu *et al*., 2018; Chang *et al*., 2016).

Cinnamon is one of the traditional spices that is widely in use in the regular food preparations, in almost every household of tropical countries (Ling *et al*., 2015). It provides aroma and is also of nutritional benefit. One of the well-known utilities of cinnamon lies in the control of blood glucose levels in people with diabetes (He *et al*., 2005). Apart from it, recent research has found cinnamon to also have several other properties like anti-inflammatory and anti-oxidant activity. Such potentials can be beneficial for people suffering with lung cancer. Like turmeric, research needs to be driven towards finding out the supplements in cinnamon that can interact as medication for lung cancer patients.

In recent years, natural bioactive components draw a major attention for their potent anticarcinogenic activity. Cinnamon is being exploited to study for its efficacy to combat cancer, as certain active components present in several herbs exhibit significant antineoplastic activity against several types of cancer (Rao and Gan, 2014). The anticarcinogenic potential of the phytochemicals present in cinnamon could vary with the type of cancer and also with respect to the administered active compound individually or in combination. Some of its active components may also exert chemosensitization of some anticancer drugs. These properties immersed in spices necessitates their investigation for pharmaceuticals and nutraceuticals possibilities for formulation of novel drugs (Lin *et al*., 2014). Although its medicinal application is quoted in ayurveda, but lately its potency is extensively investigated (Lu *et al*., 2013; Chhotaray *et al*., Das *et al*., 2020; Dash *et al*., 2020; 2020; Sahoo *et al*., 2020; Tripathy *et al*., 2020). However, its role in cancer treatment is not yet fully explored at the molecular level. The present study offers compilation of information to reflect on the profound anticarcinogenic activity of cinnamon. Active compounds in cinnamon ware evaluated for their effectiveness to hinder the process of cancer development. This work envisages further possibility to utilize age-old spice or their active components in pharmaceutical formulations. This might initiate further analytical investigations to exploit cinnamon for designing novel anticancer drug (Yang *et al*., 2013).

Materials & methods

Software used

Dassault Systemes BIOVIA Discovery studio program was utilized for analyzing the present study. The software utilizes CDOCKER, a CHARMm-based docking engine to accurately predict the ligand binding energy by using new free energy perturbation (FEP) method.

List of phytochemicals

Phytochemicals are plant based secondary metabolites that can protect them from the attack by predators. When consumed by humans it can provide protection to them by warding off several diseases. In the present study, *Cinnamomum cassia* was screened for the presence of phytochemicals in it. It was found that *Cinnamomum cassia* contains phytochemicals such as, curcumin, linolic acid, vanillin, gossypetin, proanthocya, etc. These phytochemicals were screened for their potential for inhibiting and controlling lung cancer.

Molecular docking

Molecular docking technique can be used to identify the phytochemicals from plant, which could act as ligand by forming covalent association to inhibit the metabolic pathway associated with the disease. The Dassault Systemes BIOVIA Discovery studio program was used for identification of efficiency of molecular interaction and for performing molecular docking (Bhaskar *et al*., 2019). At first, the sdf files for the screened phytochemicals that are present in *Cinnamomum cassia* plant were downloaded. The protein database code for Tumor necrosis factor alpha converting enzyme was identified from RCSB. The active site of the enzyme was identified via “receptor cavity” protocol found under "receptor-ligand interaction" menu. Molecular docking was performed using the CDocker option in Dassault Systemes BIOVIA Discovery studio program, which is available under “receptor-ligand interaction” menu. The enzyme molecule was regarded as the receptor molecule, while the phytochemical was regarded as the ligand molecule. The “-CDOCKER_ENERGY” and “-

CDOCKER_INTERACTION_ENERGY" were used as benchmark for accessing the quality of molecular docking. The high positive score during the analysis, designated a good and stable interaction between the ligand and the receptor. Thus, the interactions with high values are indicators of major phytochemicals that are responsible for curing the disease.

Results and Discussion

Figure 1 shows the active site of Tumor necrosis factor alpha converting enzyme, that appears light green in color. CDOCK is a molecular dynamics (MD) algorithm. It is a grid-based molecular docking method that is developed with accuracy for simulation techniques. The ligand- receptor conformations were obtained by Molecular Dynamic methods.

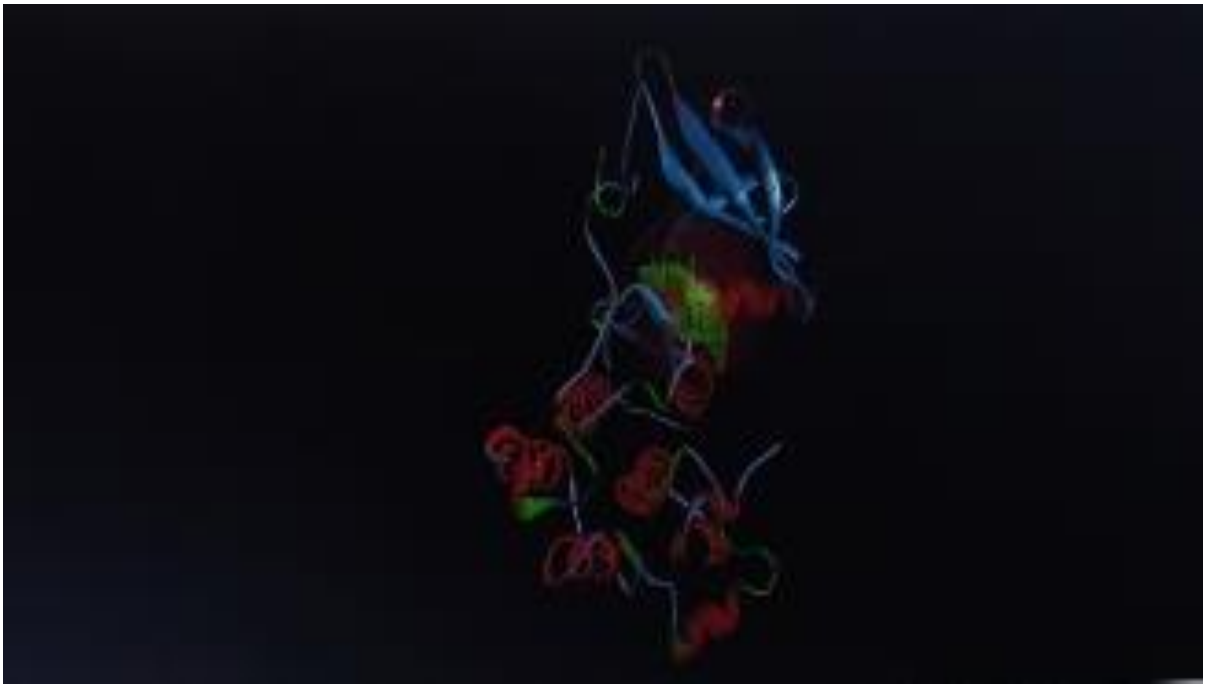

Fig.1 Active site of Tumor necrosis factor alpha converting enzyme

The internal ligand strain energy along with the receptor-ligand interaction energy were used for calculating the -CDOCKER energy. -CDOCKER interaction signifies the level of interaction existing between the protein and the phytochemical molecule. The criterion for evaluating the best interaction of phytochemical with the protein was selected based on a) greater positive score of -CDOCKER energy and lesser difference between -CDOCKER energy and -CDOCKER interaction energy. Table 1 shows the interaction of TACE with all the selected phytochemicals. The highest positive score of -CDOCKER energy (33.7357), with a difference of (3.1864) between - C DOCKER interaction energy and - C DOCKER energy, was observed in case of the phytochemical Quercetin, followed by Gossypetin with -C Docker energy of (36.9828) and with a difference of (3.5136) between - C DOCKER interaction energy and - C DOCKER energy . Thus, the results indicate that Quercetin and Gossypetin can effectively deactivate the Tumor necrosis factor alpha converting enzyme.

Table 1. Results of CDocking of phytochemicals with TNFR (receptor)

SL No	Ligand	CDocking energy	CDocking energy interaction	Defference between CDocking energy-CDocking energy interaction
1	Gossypetin	36.9828	40.4964	3.5136
2	Quercetin	33.7357	36.9221	3.1864
3	Vanillin	18.9165	24.8016	5.8851

4	Linoleic acid	1.8516	33.9072	32.0556

Conclusion

It was previously known that *Cinnamomum cassia* plant has medicinal action against lung cancer. The current study was carried out for providing theoretical evidence for this observation. Using BIOVIA Discovery studio software, molecular docking operation was carried out to identify the phytochemicals having significant interaction with the vital enzyme (TACE). It was found that Quercetin and Gossypetin can form strong bond with the enzyme.

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References

1. Bhaskar, V., K. Namboori,and L.K. Pappachen. 2019. *In Silico* Discovery of Novel Ligands for AntiTubercular Targets using Computer Aided Drug Design. Research Journal of Pharmacy and Technology. 12: 5646-5650.
2. Chang, W. L., F.C. Cheng, S.P. Wang, S.T. Chou, and Shih, Y. 2016. *Cinnamomum cassia* essential oil and its major constituent cinnamaldehyde induced cell cycle arrest and apoptosis in human oral squamous cell carcinoma HSC-3 cells. Environmental Toxicology. 32: 456-468.
3. Chhotaray, S., P. Pallavi, K.V.D. Prakash, S.K. Jha and S. Jal. 2020. Evaluation of Phytochemical Compounds from *Curcuma longa* (Turmeric) as a Potential Drug against Sinusitis: An *In-silico* approach. Indian Journal of Natural Sciences. 10: 18949-18953.
4. Das, S., D. Das, P. Panda, S. Jal, and D. Bhattacharyay. 2020. In silico Molecular Docking Studies of Phytochemicals Screened from Ocimum tenuiflorum against Enoyl-Acyl Carrier Protein Reductase of Streptococcus pneumoniae Causing Sinusitis. Indian Journal of Natural Sciences. 10: 18959-18963.
5. Dash, S.K., S. Ray, S.R. Behera, S. **Jal**, and D. Bhattacharyay. 2020. *Michelia champaca* L. Derived Phytochemicals against Peptidase Do of *Bordetella pertussis* Causing Cough. Journal of Pharmaceutical Research International. 32: 133-135.
6. Dutta, A., and A. Chakraborty. 2018. Cinnamon in Anticancer Armamentarium: A Molecular Approach. Journal of Toxicology. 8978731.
7. He, Z. D., C.F. Qiao, Q.B. Han, C.L. Cheng, H.X. Xu, R.W. Jiang, P.P. But, and P.C. Shaw. 2005. Authentication and quantitative analysis on the chemical profile of cassia bark (cortex cinnamomi) by high-pressure liquid chromatography. Journal of Agricultural and Food Chemistry. 53: 2424–2428.
8. Lin, C. Y., P.N. Chen, Y.S. Hsieh, and S.C. Chu. 2014. *Koelreuteria formosana* extract impedes *in vitro* human LDL and prevents oxidised LDL-induced apoptosis in human umbilical vein endothelial cells. Food Chemistry. 146: 299-307.
9. Ling, F., C. Jiang, G. Liu, M. Li, and G. Wang. 2015. Anthelmintic efficacy of cinnamaldehyde and cinnamic acid from cortex cinnamon essential oil against *Dactylogyrus intermedius*. Parasitology. 142: 1744–1750.
10. Lu, K. H., H.W. Yang, C.W. Su, K.H. Lue, S.F. Yang and Y.S. Hsieh. 2013. *Phyllanthus urinaria* suppresses human osteosarcoma cell invasion and migration by transcriptionally inhibiting u-PA via ERK and Akt signaling pathways. Food and Chemical Toxicology. 52: 193-199.
11. Maller, C., M. Townsend, A. Pryor, P. Brown, and L. Leger. 2006. Healthy nature healthy people: 'contact with nature' as an upstream health promotion intervention for populations. Health Promotion International. 21: 45-54.
12. Rao, P.V., and S.H. Gan. 2014. Cinnamon: A Multifaceted Medicinal Plant. Evidence Based Complementary and Alternative Medicine, 642942.

13. Sahoo, P., S. Chhotaray, K.V.D. Prakash, S.K. Jha, and S. Jal. 2020. In-silico Molecular Docking Studies and Anti-Microbial Activity of Phytochemicals from *Jasminum sambac* against Gingivitis. Indian Journal of Natural Sciences. 10: 18969-18973.
14. Tripathy, B., E. Sahoo, S. Ray, S. Jal and D. Bhattacharyay. 2020. *Trigonella foenum-graecum* Derived Phytochemicals against Tuberculosis. Journal of Pharmaceutical Research International. 32: 121-124.
15. Vikas, S. 2014. Manuscripts in Indian System of Medicine- A Review. International Journal of Ayurveda and Pharma Research. 2: 11-16.
16. Wu, H. C., C.T. Horng, Y.L. Lee, P.N. Chen, C.Y. Lin, C. Y. Liao, Y.S. Hsieh and S.C. Chu. 2018. *Cinnamomum cassia* extracts suppress human lung cancer cells invasion by reducing u-PA/MMP expression through the FAK to ERK pathways. International Journal of Medical Sciences. 15: 115–23.
17. Yang, J. S., C.W. Lin, Y.S. Hsieh, H.L. Cheng, K.H. Lue, S.F. Yang, and K.H. Lu. 2013. *Selaginella tamariscina* (Beauv.) possesses antimetastatic effects on human osteosarcoma cells by decreasing MMP-2 and MMP-9 secretions via p38 and Akt signaling pathways. Food and Chemical Toxicology. 59: 801-807.