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

Itishree Pattnaik¹, Preeti Pallavi², Manisha Tripathy³, Soumya Jal⁴

¹²³⁴ Centurion University of Technology and Management, Odisha, India

Corresponding Author:

Dr. Soumya Jal
Associate Professor, Centurion University of Technology and Management, Odisha, India
E-mail: soumya.jal@cutm.ac.in

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, Proanthocyanin 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 ena and along with ‘nda’. 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 were 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>
<thead>
<tr>
<th>SL No</th>
<th>Ligand</th>
<th>CDocking energy</th>
<th>CDocking energy interaction</th>
<th>Difference between CDocking energy-CDocking energy interaction</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Gossypetin</td>
<td>36.9828</td>
<td>40.4964</td>
<td>3.5136</td>
</tr>
<tr>
<td>2</td>
<td>Quercetin</td>
<td>33.7357</td>
<td>36.9221</td>
<td>3.1864</td>
</tr>
<tr>
<td>3</td>
<td>Vanillin</td>
<td>18.9165</td>
<td>24.8016</td>
<td>5.8851</td>
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</table>
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


