Cinnamon: an immune modulator food additive to coronavirus

Ravindra Verma\textsuperscript{a,b} and Prakash S. Bisen\textsuperscript{b}

\textsuperscript{a}School of Studies in Biotechnology, Jiwaji University, Gwalior 474001, India
\textsuperscript{b}Honorary Emeritus Professor, School of Studies in Biotechnology, Jiwaji University, Gwalior 474001, India

\textsuperscript{*}Corresponding author: Ravindra Verma, School of Studies in Biotechnology, Jiwaji University, Gwalior 474001, India. Tel: 91-11-7999212685; E-mail: vermaravindra917@gmail.com

DOI: 10.31665/JFB.20xx.000xx
Received: February 03, 2022; Revised received & accepted: March 08, 2022
Citation: Verma, R., and Bisen, P.S. (2022). Cinnamon: an immune modulator food additive to coronavirus. J. Food Bioact. 000: 000–000.

Abstract

This study explores the potential role of cinnamaldehyde from cinnamon to elicit immunity against the pathogens of COVID-19. In the culture of traditional and herbal treatments, it was more valuable than gold. It has been observed that coronavirus infects cells of an organism including innate and adaptive immune cells. Cinnamaldehyde, eugenol, and other secondary metabolism of cinnamon extract, have a potential role to interact with spike protein of coronavirus. Available literature supports the suitability of cinnamon for acute respiratory infectious diseases. It might be a promising source for the immune system to control viral infections like COVID-19. Preclinical and clinical trials are necessary for the safety and efficacy of the drug.

Keywords: Cinnamon; Coronavirus, COVID-19; Immunity; SARS-CoV-2.

1. Introduction

This communication is focused on the health benefits of the extracts of secondary metabolism of the compound found in cinnamon, a wonder herb for COVID-19 patients. Due to high mutation rates of SARS-CoV-2 spike protein may rise to variant of concern (VOC). Therefore, it can evade the vaccine-induced acquired immunity. Phytochemicals are considered as an effective alternative for treatment of COVID-19 infection (Chen, Wang, Wang and Wei, 2020; Jena et al., 2021; Nag et al., 2021). There are several significant risk factors for severe COVID-19 infection, such as diabetes mellitus, chronic lung disease, cardiovascular disease (CVD), obesity, and a range of other illnesses that make the patient immunocompromised (Zabetakis et al., 2020; Gasmii et al., 2021). An intimate relationship exists between the immune system and the metabolic response system. The metabolic and immune systems are essential to survival (Hotamisligil, 2006). Inflammation is a flow of information in response to infection. When tissue is injured, the basic challenge for the host is to detect whether infection is present. In the event of injury and infection, a quick response is required to stop the spread of infection, even at the cost of additional tissue damage. Repairing damaged tissue caused by inflammation or that inflammation damaged is necessary (Nathan, 2002).

Our objective is to explore the potential role of cinnamon to elicit an immune response in the pathogenesis of COVID-19. For the development of this literature, an extensive database search was carried out using scientific databases like MEDLINE, BIOSIS, PubMed, EMBASE, Mendeley database, TOXLINE, and Google Scholar, Google, Google Patent. After careful examination of the literature, we consider only those literatures that fit within the scope of our target.

2. Cinnamon may be immunity booster agent for Covid-19 patients

Cinnamon, a tree of the Lauraceae family, grows up to the height of 10–15 meters. In our traditional culture of herbal treatment, it was more valuable than gold, commonly used in kitchens. There is suitable evidence that confirmed that cinnamon was used in the treatment of influenza and several related diseases (Ross 1906). Phytochemical study of cinnamon identified 2- propenal, 3-phenyl (trans-cinnamaldehyde-87.013%), and Eugenol (9.317%), as major compounds. While other important phytochemicals are identified as Tricyclo [3.3.1.0 (2,8)] nona-3,6-dien-9-on (0.137%), O-Methoxy cinnamic aldehyde (0.236%), α-muurolene (0.133%),...
Cinnamaldehyde (TCA), a principal constituent in cinnamon, has the potential to reduce the maturation of influenza A/PR/8 virus in bronchoalveolar lavage fluid. These findings support the suitability of the empirical indication of Cinnamomum cortex-containing herbal formulations for acute respiratory infections (Hayashi et al., 2007). Phenolic compounds of Cinnamomum zeylanicum like caffeic acid (IC50 = 84%) and cinnamic acid (IC50 = 53%) had the most enzyme inhibition potential. Angiotensin-converting enzyme (ACE2) and type 2 transmembrane serine protease (TMPRSS2) are the target cell contributors in SARS-CoV-2 infection (Shahwar et al., 2012; Amawi et al., 2020; Prasanth et al., 2020). The water extract of cinnamon (CWE) substantially reduced the secretion of TNF-α and IL-6 and induced macrophages, and a substantial decrease in its mRNA expression was observed (Kunnumakkara et al., 2021). Another study confirms the moderate effects of butanol fraction (containing procyanidin A2 and procyanidin B1) on Cinnamomum Cortex (CC/Fr. 2) on antiviral activity against HIV/SARS-CoV S pseudovirus infections (Zhuang et al., 2009). Researchers have noted that procyanidin type A compound (IND02) derived from cinnamon has the potential to inhibit SARS-CoV-2 at the early phase of viral infection, because of its propensity toward ACE2 receptor and binding glycans on the spike protein of SARS-CoV2 (Ghosh, 2020). Free radical induced immunosuppression contributes to the pathogenesis of viral infection and expansion of viral pathogens. Cinnamaldehyde possesses anti-inflammatory properties. It is perceived that cinnamaldehyde suppressed NF-κB activation and inhibits the TNF-α-induced inflammation. It also suppresses hyper-expression of Toll-like receptors (TLRs) and cytosolic sensor NOD-like receptors (NLRs), PYD domain-containing protein 3 (NLRP3) inflammasome signalling pathways (Liao et al., 2008; Lee et al., 2018). Cinnamaldehyde modulates the production of prostaglandins (PGEs) by reducing IL-1β-induced COX-2 activity (Gao et al., 2006). Scientific evidence confirms that cinnamon is a potential anti-inflammatory, antioxidant functional food and could be useful in mitigation of SARS-CoV-2 induced hyper inflammation. There is an increasing demand among covid-19 patients towards the consumption of cinnamon powder as preventive functional food against SARS-CoV-2 infection (Tallei et al., 2020).
HSV was strong (Tragoolpua and Jatisatienr, 2007). Combination of eugenol and acyclovir supported the inhibited herpes virus replication in vitro. It has been studied that eugenol delays the growth of herpes virus induced keratitis (Benencia and Courreges, 2000). Recent study observed that eugenol interlinked with spike (S1) protein of SARS-CoV-2 and strongly suppressed the entry of pseudo-type SARS-CoV-2 into human ACE2-expressing HEK293 cells. They also noticed that eugenol modulates NF-kB, IL-6, IL-1β and TNFα in human A549 lung cells (Paidi et al., 2021). Inhibiting the main 3-chymotrypsin-like protease (3CLpro), also called Nsp5 (non-structural protein 5) is the fundamental strategy for coronavirus. (Rizzuti et al., 2021), reported that eugenol inhibits the enzymatic activity of 3CLpro.

Camphor has an excellent bond against protease of SARS-CoV-2 and ACE2 receptors (Omar et al., 2020). Camphor is a solid bicyclic organic compound derived from the cinnamon tree. Camphor improves catalase and Nrf-2 activities, and reduces NO, TNF-α, TLR4 serum levels in the covid-19 infections (Salama et al., 2021).

**Table 1. Important phytocompounds of cinnamon and their interaction with coronavirus and immune system**

<table>
<thead>
<tr>
<th>Phytocompounds</th>
<th>Chemical Formula</th>
<th>Molecular weight</th>
<th>Chemical Structure</th>
<th>Interaction with Coronavirus</th>
<th>Immune response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cinnamaldehyde</td>
<td>C9H8O</td>
<td>132.16</td>
<td><img src="image1.png" alt="Image" /></td>
<td>Spike Protein</td>
<td>TLR2 and TLR4 activation, NRF2 inducer, detoxify ROS/RNS, mitigate PI3K/Akt pathway</td>
</tr>
<tr>
<td>Eugenol</td>
<td>C10H12O2</td>
<td>164.20</td>
<td><img src="image2.png" alt="Image" /></td>
<td>Spike protein</td>
<td>Modulates NF-kB, IL-6, IL-1β and TNFα</td>
</tr>
<tr>
<td>Camphor</td>
<td>C10H16O</td>
<td>152.23</td>
<td><img src="image3.png" alt="Image" /></td>
<td>Mpro of COVID-19 (Omar et al., 2020)</td>
<td>modulation of Nrf-2 and TLR4 (Salama et al., 2021)</td>
</tr>
<tr>
<td>Trans-cinnamyl acetate</td>
<td>C11H12O2</td>
<td>176.21</td>
<td><img src="image4.png" alt="Image" /></td>
<td>Binding with GLU471, ARG454, SER46 (Kulkarni et al., 2020)</td>
<td>inhibits the activity of NF-κB and the production of tumor necrosis factor alpha (TNFα) induced interleukin-8 (IL-8) (Cabello et al., 2009)</td>
</tr>
<tr>
<td>Caryophyllene</td>
<td>C15H24</td>
<td>204.35</td>
<td><img src="image5.png" alt="Image" /></td>
<td>interactions with PHE 294, 3CLpro, NSP3, NSP9, and RDRP (Narkhede et al., 2020)</td>
<td>B cells, T cells, CD8+ lymphocytes, CD4+ lymphocytes, NK cells, neutrophils, macrophages, basophils, eosinophils, platelets, mast cells, dendritic cells, microglia, and astrocytes (Howlett and Abood, 2017; Jha et al., 2021)</td>
</tr>
</tbody>
</table>
et al., 2021). In the traditional system of medicine, camphor was applied to the neck and chest skin for cough problems. It is also used as steam inhalation in the form of aerosol to prevent coughing (Pappas and Hendley, 2011; Eccles, 1994). Reddy et al., 2004, demonstrated the inhibition of NFkB by the cinnamon ingredients in human macrophages. A study examining the cinnamon acetate suppression of NFkB inflammatory signaling in endothelial cells has confirmed the suppression of TNFα-induced p65 translocation (Liao et al., 2008). Another study concluded that dietary administration of cinnamyl acetate inhibited NF-κB activation through the ERK and p38 MAPK pathways in the mouse (Kim et al., 2007). Papain-Like cysteine protease (PLpro, NSP3) is required for coronavirus replication and a promising agent for antiviral drugs (Rut et al., 2020). These phytochemicals substantially act on viral main protease of SARS-CoV-2. On the basis of available literature, cinnamon inhibits the main protease of covid-19 and can be a potential drug candidate as an immunity booster.

3. Conclusion

Plenty of scientific literature confirms the antiviral and immunomodulatory potential of cinnamon extracts for influenza. Cinnamon aldehyde and eugenol are effective antiviral agents and interact with spike protein of coronavirus. Cinnamon might be a promising source for the immune system to control viral infections like SARS-CoV-2. Functional food and food additives have the potential to elicit immunity against covid-19 infection and post-covid-19 care. Further preclinical and clinical trials are necessary to evaluate the efficacy level of major constituents of cinnamon extract as antiviral drugs.

Acknowledgments

None.

Conflict of interest

The authors confirm that this article’s content has no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Reference

Cinnamon: an immune modulator food additive to coronavirus

Verma et al.


