ISSN 2349-7750

INDO AMERICAN JOURNAL OF

PHARMACEUTICAL SCIENCES

Available online at: http://www.iajps.com Review Article

CINNAMALDEHYDE CHEMICAL COMPOSITION AND ITS MULTI PHARMACEUTICAL USES

Ghulam Mohammad Jan

Govt. Degree College for Boys Anantnag Jammu & Kashmir (India).

Abstract:

The eternal tree of tropical medicine, belongs to the Lauraceae family. Cinnamon is one of the most important spices used daily by people all over the world. Cinnamon primarily contains vital oils and other derivatives, such as cinnamaldehyde, cinnamic acid, and cinnamate. In addition to being an antioxidant, anti-inflammatory, antidiabetic, antimicrobial, anticancer, lipid-lowering, and cardiovascular-disease-lowering compound, cinnamon has also been reported to have activities against neurological disorders, such as Parkinson's and Alzheimer's diseases. This review illustrates the pharmacological prospective of cinnamon and its use in daily life. The chemical constituents are mostly cinnamyl alcohol, coumarin, cinnamic acid, cinnamaldehyde, anthocynin, and essential oils together with constituents of sugar, protein, crude fats, pectin, and others. This review presents an overview of the current status and knowledge on the traditional usage, the pharmaceutical, biological activities, and phytochemical constituents reported for C. burmannii.

Address for Correspondence:
Ghulam Mohammad Jan,
Govt. Degree College for Boys,
Anantnag Jammu & Kashmir (India).
Corresponding author: gmjan64@gmail.com

INTRODUCTION:

Cinnamaldehyde is an organic compound with the formula $C_6H_5CH=CHCHO$. Occurring naturally as predominately the trans (E) isomer, it gives cinnamon its flavor and odor. It is a flavonoid that is naturally synthesized by the shikimate pathway. This pale yellow, viscous liquid occurs in the bark of cinnamon trees and other species of the genus Cinnamomum. The essential oil of cinnamon bark is about 50% cinnamaldehydeThe bark of various cinnamon species is one of the most important and popular spices used worldwide not only for cooking but also in traditional and modern medicines. Overall, approximately 250 species have been identified among the cinnamon genus, with trees being scattered all over the world [1, 2].Cinnamon is mainly used in the aroma and essence industries due to its fragrance, which can be incorporated into different varieties of foodstuffs, perfumes, and medicinal products [3]. The most important constituents of cinnamon are cinnamaldehyde and trans-cinnamaldehyde (Cin), which are present in the essential oil, thus contributing to the fragrance and to the various biological activities observed with cinnamon [4]. A study on Cinnamomum osmophloeum (C. osmophloeum) indicated that the essential oil from cinnamon leaves contains a high level of Cin. Consequently, C. osmophloeum is also used as an alternative spice for C. cassia [5]. One of the major constituents of essential oil extracted from C. zeylanicum named (E)-cinnamaldehyde has an antityrosinase activity [6], while cinnamaldehyde is the principal compound responsible for this activity [7].Cinnamon bark contains procyanidins and catechins [8] Table 1. The components of procyanidins include both procyanidin A-type and B-type linkages [9–11]. These procyanidins extracted from cinnamon and berries also possess antioxidant activities [10, 12].

Table 1 : Chemical composition of of cinnamaldehyde

Part of the plant	**Compound**
Leaves	Cinnamaldehyde: 1.00 to 5.00%
	Eugenol: 70.00 to 95.00%
Bark	Cinnamaldehyde: 65.00 to 80.00%
	Eugenol: 5.00 to 10.00%
Root bark	Camphor: 60.00%
Fruit	trans-Cinnamyl acetate (42.00 to 54.00%) and caryophyllene (9.00 to 14.00%)
C. zeylanicum buds	Terpene hydrocarbons: 78.00%
	alpha-Bergamotene: 27.38%
	alpha-Copaene: 23.05%
	Oxygenated terpenoids: 9.00%
C. zeylanicum flowers	(E)-Cinnamyl acetate: 41.98%
	trans-alpha-Bergamotene: 7.97%
	Caryophyllene oxide: 7.20%

Antibacterial activity

The extract of C. Burmannii was examined for antibacterial activity, minimum inhibitory concentration, and minimum bactericidal concentration using five common food-borne pathogenic bacteria such as Bacillus cereus, Listeria monocytogenes, Staphylococcus aureus, Escherichia coli, and Salmonella anatum. Additionally, scanning electron microscopy was used to observe the morphological changes of bacteria treated with the crude extract. The major constituents of the extract were identified by gas chromatography-Mass spectrum and Liquid chromatography-Mass spectrum, and (E)-cinnamaldehyde was found to be the most predominant volatile oil component, along with other polyphenols proanthocyanidins and (epi) catechins. The extract showed significant antibacterial activity, and both (E)-cinnamaldehyde and proanthocyanidins contributed significantly to the antibacterial activity.[13]

In another attempt, Shan et al. examined the extracts of 46 dietary spices and medicinal herbs including C. burmannii for antibacterial activities using agar well diffusion method. Five bacterial strains such as Bacillus cereus, Listeria monocytogenes, Staphylococcus aureus, Escherichia coli, and Salmonellaanatum were employed. They also assessed the total phenolic contents in the extracts. Interestingly, most of the extracts showed high levels of phenolics and good antibacterial activity, the inhibitory effects observed were higher for the Gram positive bacteria as compared to the Gram negative bacteria. Among the strains, the highest activity observed was against S. aureus and the least activity was observed against E. coli. Highly positive relationships (R^2 = 0.73–0.93) were observed between antibacterial activities and phenolic content of the tested extracts against each bacterium. On the basis of these results, the study suggested that the antibacterial activity of the tested extracts were closely associated with their phenolic constituents.[14]

Further, the effects of C. burmannii, Origanum vulgare, Eugenia caryophylata, Punica granatum and Vitis Vinifera on Listeria monocytogenes, Staphylococcus aureus, and Salmonella enteric in raw pork at ~20°C was assessed. The effect of these extracts on lipid oxidation in the meat and the pH, color parameters, and thiobarbituric acid-reactive substances values were also investigated. The authors observed that all the extracts of these natural herbs were found to be effective against the bacteria. Further, the color parameters of the extract-treated pork changed slightly and the extracts also increased the stability of raw pork against lipid oxidation.[15]

Anti-inflammatory, analgesic and anti-diabetic activity

Khatib et al. examined 20 different traditional Indonesian medicinal herbs including C. Burmannii for their anti-inflammatory activity using soybean lipoxygenase (SLO) and hyaluronidase (HAse). Among the extracts, C. burmannii indicates the highest anti-inflammatory activity. The ethyl acetate fraction derived from the methanol extract of the bark of C. burmannii showed the highest level of SLO inhibitory activity. The extract was subjected to preparative HPLC to yield two compounds namely coumarin and 2-hydroxy-cinnamaldehyde. Among these, 2-hydroxy-cinnamaldehyde exhibited good SLO inhibitory activity (IC_{50} = 60 μM). However, none of the compounds showed any significant HAse inhibitory activity.[16]

Wu and Chou reported a method for the preparation of an extract bearing anti-inflammatory and analgesic properties from a group of plants including C. burmannii. The plant materials are soaked in an organic solvent, heated, filtered, and concentrated under reduced pressure to yield an extract that possess anti-inflammatory and analgesic properties.[17]

In one attempt, Cao et al. examined the effects of aqueous extract of C. burmannii and HPLC-purified cinnamon polyphenols (CP) on the protein and mRNA levels of insulin receptor, glucose transporter 4 (GLUT4), and tristetraprolin (TTP/ZFP36) in mouse 3T3-L1 adipocytes. Immuno-blotting revealed that CP increased IRβ levels while both aqueous extract and CP increased GLUT4 and TTP levels in the adipocytes. Quantitative real-time PCR indicated that aqueous extract (100 μg/mL) rapidly increased TTP mRNA levels by nearly six-folds in the adipocytes. Indeed, aqueous extract at higher concentrations decreased IRβ protein and IR mRNA levels, and its effect on GLUT4 mRNA levels showed a biphasic pattern in the adipocytes. Thus, the study suggested that the plant possesses higher potential to enhance the levels of proteins involved in insulin signaling, glucose transport, and anti-inflammatory/anti-angiogenesis response.[18]

Preparation of herbal extracts from Lythraceae and Lauraceae family plants including C. burmannii was reported by Tjandrawinata et al. The extract was found to exhibit several activities and could be used as an insulin resistance reducer, syndrome X normalizer, pre-diabetes and type 2 diabetes treatments, particularly as activator in insulin signal pathway, as modulator in glucose transport system, as modulator in adiponectin secretion, and as suppressor in insulin resistance.[19]

Gene expression and immune response activity

Cao et al. tested the cinnamon polyphenol extract (CPE) for regulating the immune function involving genes encoding tristetraprolin (TTP), proinflammatory cytokines, and glucose transporter (GLUT) families and the effects of CPE were compared with those of insulin and lipopolysaccharide (LPS) in mouse RAW264.7 macrophages. It was observed that CPE increased the TTP mRNA and protein levels, i.e., CPE (100 mg/L, 0.5–4 h) enhanced the TTP by two-folds and tumor necrosis factor (TNF) mRNA by six-folds when compared to controls. However, the base level of TTP was six-folds higher than that of TNF. Further, LPS (0.1 mg/L, 4 h) also increased the granulocyte-macrophage colony-stimulating factor, cyclooxgenase-2, interleukin 6 mRNA, TTP and TNF, levels by 39–1868 fold. In addition, the authors also observed that the CPE and LPS enhanced GLUT1 expression (the major GLUT form in macrophages) by three- and two-folds of that of the controls, respectively. Moreover, CPE increased TTP expression more rapidly than those of pro-inflammatory cytokines and the net increases of TTP mRNA levels were larger than those of pro-inflammatory cytokines. This study concluded that CPE can affect immune responses by regulating anti- and pro-inflammatory and GLUT gene expression.[20]

Cinnamon extracts are known to improve impaired glucose tolerance, a metabolic syndrome. Studies were carried out to assess the effects of aqueous extract of C. burmannii on gene expression in cultured mouse for the expression of genes coding for adipokines, glucose transporter (GLUT) family, and insulin-signaling components in mouse 3T3-L1 adipocytes, using quantitative PCR. The authors observed that the aqueous extract (100 µg/mL) of the plant increased GLUT1 mRNA levels by ~2, 4 and 7 folds compared to control after 2, 4, and 16 h of administration, respectively. Further, the extract also reduced the expression of further genes encoding insulin-signaling pathway proteins (GSK3B, IGF1R, IGF2R, and PIK3R1). Observations from this study signify that the C. burmannii extract can regulate the expression of multiple genes in adipocytes.[21]

Antioxidant activity

Methanolic extracts of 50 traditional Indonesian medicinal plants including C. burmannii were evaluated for their inhibitory effects on the nitric oxide production in lipo-polysaccharide stimulated RAW264.7 macrophages and for antioxidant activity through the evaluation of free radical scavenging effect and reducing power. Among these, the extracts of C. burmannii inhibited lipo-polysaccharide-induced nitric oxide release and showed antioxidant activity on RAW264.7 cell.[22]

Panickar et al. examined the protective effects of CPE, which is reported to bear anti-oxidant and insulin-potentiating effects on cell swelling and produce depolarization of the inner mitochondrial membrane potential ($\Delta\Psi_m$) in ischemic injury. The authors observed that CPE reduces oxygen-glucose deprivation-induced cell swelling and also influences the decline in the inner mitochondrial membrane potential ($\Delta\Psi_m$) in cultures. These protective effects observed may be due to the inhibition of mitochondrial permeability transition mPT.[23]

Huang et al. isolated a melanin-like pigment (0.34 g/100 g) from the berry of C. burmannii (CBM), which possess low solubility in water and most common organic solvents. However, it was found to be slightly soluble in DMSO while it is soluble in alkaline aqueous solution. The isolate was evaluated for its antioxidant and sun protection factor (SPF). It was observed that the antioxidant activity of CBM was superior to those of a well-known antioxidant, BHT. Further, it was also observed that the reducing power and the metal chelating activities of CBM was concentration dependent. The in vitro determination of melanin-bearing gel formulations indicated that the SPF value of every formulation increased with the amount of melanin, which suggested the presence of additional compounds with sunscreen activity in the melanin extract.[24]

From the fruit extract of C. burmannii, an anthocyanin was isolated using semi-preparative HPLC. The effects of temperature, light, and pH were examined for the radical scavenging activity of the anthocyanin. The IC_{50} of the anthocyanin was found to be 4.6 µg/mL, the antioxidant capacity found to reduce significantly after heating it at 100°C for 5 h or for 30 min at 130°C. The increase of pH did not have any effect on the DPPH radical scavenging activity, while the DPPH radical scavenging activity was reduced sharply by exposure to fluorescence radiation for 1 h, and the sunlight intensity also effected the DPPH radical scavenging activity of the anthocyanin.[25]

Anti-tumor and anti-thrombotic effects

A preparation possessing anti-tumor effects was prepared from Humulus lupulus, Pimenta officinalis, Salvia officinalis, Syzygium aromatica, Piper nigrum, and Cinnamomum plants including C. burmani, and Myristica fragrans, by pulverizing the plants and extracting them with water and organic solvent, followed by column chromatographic separations to isolate the active ingredient. The preparations possess inhibitory effects against Epstein Barr virus and nasopharyngeal carcinoma.[26] Hwang et al.

prepared an extract from Woodfordia floribunda, C. burmannii, Areca catechu, Cinnamomum sintok, Parameria laevigata, and Homalomena javanica by pulverizing the plants and then extracting them with 75% or 100% methanol at room temperature for 48 h, followed by filtering, concentration, and freeze drying. The extract was found to exhibit anti-thrombotic effects.

CONCLUSION:

C. burmanni, a traditional medicinal plant has long been used as a spice, food preservative, and food flavoring. The pharmacological studies have shown anti-bacterial, anti-fungal, antioxidant, anti-thrombotic, anti-inflammatory, anti-tumor, dental plaque formation and periodontal disease inhibitory, glycosylation inhibitory, and radical scavenging activities. C. burmanni. Cinnamon has been used as a spice in daily life without any side effects. Several reports have dealt with the numerous properties of cinnamon in the forms of bark, essential oils, bark powder, phenolic compounds, flavonoids, and isolated components. Each of these properties plays a key role in the advancement of human health. The antioxidant and antimicrobial activities may occur through the direct action on oxidants or microbes, whereas the anti-inflammatory, anticancer, and antidiabetic activities occur indirectly via receptor-mediated mechanisms

REFERENCES:

1.A. Sangal, "Role of cinnamon as beneficial antidiabetic food adjunct: a review," Advances in Applied Science Research, vol. 2, no. 4, pp. 440–450, 2011.

2.M. Vangalapati, N. Sree Satya, D. Surya Prakash, and S. Avanigadda, "A review on pharmacological activities and clinical effects of cinnamon species," Research Journal of Pharmaceutical, Biological and Chemical Sciences, vol. 3, no. 1, pp. 653–663, 2012.

3.T.-C. Huang, H.-Y. Fu, C.-T. Ho, D. Tan, Y.-T. Huang, and M.-H. Pan, "Induction of apoptosis by cinnamaldehyde from indigenous cinnamon Cinnamomum osmophloeum Kaneh through reactive oxygen species production, glutathione depletion, and caspase activation in human leukemia K562 cells," Food Chemistry, vol. 103, no. 2, pp. 434–443, 2007.

4.H.-F. Yeh, C.-Y. Luo, C.-Y. Lin, S.-S. Cheng, Y.-R. Hsu, and S.-T. Chang, "Methods for thermal stability enhancement of leaf essential oils and their main Constituents from Indigenous Cinnamon (Cinnamomum osmophloeum)," Journal of Agricultural and Food Chemistry, vol. 61, no. 26, pp. 6293–6298, 2013.

5.C.-W. Chang, W.-L. Chang, S.-T. Chang, and S.-S. Cheng, "Antibacterial activities of plant essential oils against Legionella pneumophila," Water Research, vol. 42, no. 1-2, pp. 278–286, 2008.

6.B. Marongiu, A. Piras, S. Porcedda et al., "Supercritical CO_2 extract of Cinnamomum zeylanicum: chemical characterization and antityrosinase activity," Journal of Agricultural and Food Chemistry, vol. 55, no. 24, pp. 10022–10027, 2007. (b) S.-T. Chou, W.-L. Chang, C.-T. Chang, S.-L. Hsu, Y.-C. Lin, and Y. Shih, "Cinnamomum cassia Essential Oil inhibits α-MSH-induced melanin production and oxidative stress in murine B16 melanoma cells," International Journal of Molecular Sciences, vol. 14, no. 9, pp. 19186–19201, 2013.

7.G.-I. Nonaka, S. Morimoto, and I. Nishioka, "Tannins and related compounds. Part 13. Isolation and structures of trimeric, tetrameric, and pentameric proanthicyanidins from cinnamon," Journal of the Chemical Society, Perkin Transactions 1, pp. 2139–2145, 1983.

8.R. A. Anderson, C. L. Broadhurst, M. M. Polansky et al., "Isolation and characterization of polyphenol type-A polymers from cinnamon with insulin-like biological activity," Journal of Agricultural and Food Chemistry, vol. 52, no. 1, pp. 65–70, 2004. (b) X. Peng, K.-W. Cheng, J. Ma et al.,

9."Cinnamon bark proanthocyanidins as reactive carbonyl scavengers to prevent the formation of advanced glycation endproducts," Journal of Agricultural and Food Chemistry, vol. 56, no. 6, pp. 1907–1911, 2008.

10.T. Tanaka, Y. Matsuo, Y. Yamada, and I. Kouno, "Structure of polymeric polyphenols of cinnamon bark deduced from condensation products of cinnamaldehyde with catechin and procyanidins," Journal of Agricultural and Food Chemistry, vol. 56, no. 14, pp. 5864–5870, 2008.

11.K. R. Määttä-Riihinen, M. P. Kähkönen, A. R. Törrönen, and I. M. Heinonen, "Catechins and procyanidins in berries of vaccinium species and their antioxidant activity," Journal of Agricultural and Food Chemistry, vol. 53, no. 22, pp. 8485–8491, 2005.

12.Shan B, Cai YZ, Brooks JD, Corke H. Antibacterial properties and major bioactive components of cinnamon stick (Cinnamomum burmannii): Activity against foodborne pathogenic bacteria. J Agric Food Chem. 2007;55:5484–90

13.Shan B, Cai YZ, Brooks JD, Corke H. The in vitro antibacterial activity of dietary spice and medicinal herb extracts. Int J Food Microbiol. 2007;117:112–9.

14.Shan B, Cai YZ, Brooks JD, Corke HJ. Antibacterial and antioxidant effects of five spice and

herb extracts as natural preservatives of raw pork. J Sci Food Agric. 2009;89:1879–85.
15.Khatib A, Kim MY, Chung SK. Anti-inflammatory activities of Cinanamomum burmanni Bl. Food Sci Biotechnol. 2005;14:223–7.
16.Wu TS, Chou TT. Chinese medicinal compositions containing Bletilla and Cinnamomum and others used as anti-inflammatory and analgesic agents. Patent number WO 011026267. 2011
17.Cao H, Polansky MM, Anderson RA. Cinnamon extract and polyphenols affect the expression of tristetraprolin, insulin receptor, and glucose transporter 4 in mouse 3T3-L1 adipocytes. Arch Biochem Biophys. 2007;459:214
18.Tjandrawinata RR, Sinambela JM, Mayasari O, Dwi DD, Puspasari M. Herbal extract as sensitivity enhancer toward insulin and antidiabetes. US patent number 2011/0177177. 2011
19.Cao H, Urban JF, Anderson RA. Cinnamon polyphenol extract affects immune responses by regulating anti- and proinflammatory and glucose transporter gene expression in mouse Macrophages. J Nutr. 2008;138:833–40.
20.Cao H, Graves DJ, Anderson RA. Cinnamon extract regulates glucose transporter and insulin-signaling gene expression in mouse adipocytes. Phytomedicine. 2010;17:1027–32.
21.Choi EM, Hwang JK. Screening of Indonesian medicinal plants for inhibitor activity on nitric oxide production of RAW264.7 cells and antioxidant activity. Fitoterapia. 2005;76:194–203.
22.Panickar KS, Polansky MM, Anderson RA. Cinnamon polyphenols attenuate cell swelling and mitochondrial dysfunction following oxygen-glucose deprivation in glial cells. Exp Neurol. 2009;216:420–7
23.Huang S, Pan Y, Gan D, Ouyang X, Tang S, Ekunwe SIN, et al. Antioxidant activities and UV-protective properties of melanin from the berry of Cinnamomum burmannii and Osmanthus fragrans. Med Chem Res. 2011;20:475–81.
24.Zhang J, Wen S, Fulin L, Huang S, Diao S, Zhu Y, et al. Effects of temperature, light and pH on DPPH radical scavenging activity of anthocyanin extracted from fruit of Cinnamomum burmannii. J Food Sci. 2009;30:120–3.
25.Matsumoto A, Matsumoto T, Tokuda H. A Chinese medicinal preparation for preventing nasopharyngeal carcinoma caused by Epstein Barr (EB) virus and its preparation method. Patent number JP 199033522. 1991.