Review Article

Medicinal and pharmacological role of traditional Asian Food condiment: *Cinnamomum zeylanicum* Blume

Mohd Fahad¹, Mohd Muazzam khan², Mohd Tahir¹, Mohammad Jameel³, Md Afroz Ahmad²
Mohammad Khushtar²*.

¹Department of Pharmacology), Faculty of Pharmacy, Integral University, U.P., INDIA.
²Faculty of Pharmacy, Integral University U.P., INDIA.
³Regional Research Institute of Unani Medicine, CCRUM, Ministry of AYUSH, Govt. of India, Aligarh-202001, U.P., INDIA.

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**ABSTRACT**

Darchini (*Cinnamomum zeylanicum* Blume) is an aromatic crop of Sri Lanka and Malabar coasts of India, the integral condiment of the kitchen in Asian traditional dishes and medicine in different cultures and systems. It is used as a flavoring agent, carminative, astringent, germicidal, respiratory, digestive, diabetes, hypertension, cancer and gynecological problems. Volatile oils from different parts of cinnamon species viz leaves, bark, fruits, root bark, flowers, and buds have been proven to exhibit antioxidant, antimicrobial, antifungal, anti-inflammatory, lipid-lowering, and immunomodulatory activities. Cinnamon has also been reported to have activities against neurological disorders, such as Parkinson’s and Alzheimer’s diseases. Cinnamaldehyde is majorly constituted in its volatile content responsible for several therapeutic and medicinal applications. This review illustrates the pharmacological prospective of cinnamon and its use in daily life.

*AUTHOR FOR CORRESPONDENCE*
E-mail address: mohdkhushtar@gmail.com

**INTRODUCTION**

*Cinnamomum zeylanicum* Blume, (family: Lauraceae) (CZ) is commonly known as Qirfa (Arabic), Dalchini (Hindi), Darchini (Persian) and Cinnamon (English) (Anonymous, 2007). It consists of the dried inner bark of the shoots coppiced the tree of various cinnamon species being scattered all over the world, around 250 species utilized worldwide not only for cooking but also in traditional and modern medicines. This evergreen tree is grown in the humid area, well-thought-out to be native of Sri Lanka and Malabar Coast of India also found in Jamaica, Brazil, and China. Sri Lanka is the prime supplier of it and most of the world requirements are met by it as True Cinnamon (Sangal et al., 2011; Vangalapati et al., 2011).

**Vernacular Names:**

<table>
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<tr>
<th>Arabic</th>
<th>Darsini, Qirfa</th>
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<tr>
<td>Persian</td>
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<td>Assamese</td>
<td>Dalcheni</td>
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<td>Bengali</td>
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<td>English</td>
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<td>Gujarati</td>
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<td>Malayalam</td>
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<td>Marathi</td>
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<td>Punjabi</td>
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<td>Urdu</td>
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Cultivation and collection

The trees are commonly grown from seeds in nurseries and planted out on well-drained sandy or clayey soil at altitudes up to 500 meters. Rainfall, soil, temperature, and drainage have an influence on the quality of the bark. When the shoot of the seedling is a few centimeters high, the tip is cut off to encourage the formation of lateral branches. These are allowed to cultivate for two years, or until the bark initiates to turn brown with the development of a corky layer. The shoots are then 2-3 meters high, and 3-5 cm in diameter. In May, the buds are usually cut down after the monsoons, but smaller gathering in November. Bigger knives are used for shedding and rubbing, as steel causes staining. Side branches and leaves are cut down, the bark is rubbed with the handle of the knife. The parts are then piled collected and enclosed to preserve moisture and heat, and therefore encourage small fermentation (Mohammed Ali., 1998).

Macroscopical characters

Outer surface dull yellowish-brown, while the inner surface is dark yellowish-brown in color, the fragrance is pleasant with compound squill sized up to 1 m in length and 1 cm in diameter. The breadth of the bark is about 0.5 mm, perfumed and sweet followed by deep sensation.

It has the splintery fracture. The external surface of the bark is clear by wavy longitudinal markings with small holes of scratches left by the divisions. The internal surface also shows the longitudinal markings. The bark is free of cork tissue (Khandelwal et al., 2008).

Microscopical characters

The outer most layer consists of a well-developed continuous band of characteristics stone cells (sclereids). Sclereids are more or less rectangular and pitted with thickened inner and radial walls. The outer side of the sclerenchymatous band a few groups of small pericyclic fibers are seen. Some of the parenchymatous cells have minute acicular rapids and abundant starch. Secondary phloem, which forms the bulk, consists of characteristics phloem fibers, phloem parenchyma and 2-3 layers of medullary rays. Phloem fibers, lignified tangentially elongated, mostly isolated, rarely in groups of 2-3, scattered in phloem parenchyma with the secretory cell containing oil cell, another characteristic of this bark large cells containing mucilage as shown in figure 1 (Gupta et al., 2003).

Chemical constituents

The chemical constituents cinnamon bark contains up to 4% of essential oil consisting primarily of cinnamaldehyde (60-75%), cinnamyl acetate (1-5%), eugenol (1-10%), β-caryophyllene (1-4%), Linalool (1-3%) and 1.8-cineole (1-2%) and pinene (Calapai et al., 2014, Lincoln et al., 1984), verbenone, pinene oxide, verbenol and verbetyl hydroperoxide (Köse et al., 2010, Couturier et al., 2010). Pinene has been used as the anti-cancer agent in Traditional Chinese medicine along with anti-inflammatory, antiseptic, expectorant and bronchodilator properties (Wade et al., 2006). It also contains a sweet substance Mannitol. Fresh volatile oil is light yellow in color and changed to red after storage (Kokate et al., 2012).

Chemical test

Ferric chloride solution to a drop of volatile oil, a pale green color is produced. With ferric chloride, cinnamaldehyde gives brown color and eugenol gives a blue color, resulting in the formation of pale green color (Sweety., 2013; Kokate et al., 2012).

Substituents and adulterants

Jungle cinnamon: the bark is obtained from wild growing trees, dark color, less aromatic than the cultivated trees, and a little bitter.

Cinnamon chips: these are the parts of untrimmed bark. They can be illustrrious from the unaffected drug by the occurrence of rich cork cell.

Saigon cinnamon: the bark is obtained from the trees of Cinnamomum loureirii (Lauraceae). The bark is the greenish brown color with light patches and sweet taste.

Java cinnamon: it is consisting from Cinnamomum burmanii (Lauraceae). The bark is less aromatic, peeled and found in the form of double quills (Kokate et al., 2012).
Authentication Parameter

TLC and HPLC analysis

The isolated compound (cinnamaldehyde) is obtained from *Cinnamomum zeylanicum* bark oil was dissolved in suitable solvent and then applied to silica gel plates, Merck (Germany) 20 cm × 20 cm, 0.25 mm in width, and well-known using a solvent system containing benzene–MeOH (8:2, v/v). The separated cinnamaldehyde zone was imaged under a UV lamp. Standard cinnamaldehyde aided the positive control. HPLC analysis was using a Shimadzu LC 2010 HPLC system (Japan), equipped with a Shimadzu LC 2010 UV–VIS detector with a thermostated flow cell and two selected wavelengths of 190–370 nm or 371–600 nm. The detector signal was recorded on a Shimadzu LC 2010 integrator. The column used was a C18 block heating-type Shim-pack VP-ODS (4.6 mm i.d.×150 mm long) with a particle size of 5 μm. Cinnamaldehyde was separated with a mobile phase of water–MeOH (40:60 v/v) at a flow rate of 1.0 mL/min, column temperature 35°C. Injection volume was 20 μl and detection was carried out at 260 nm (Sadek et al., 2002).

Traditional uses

Cinnamon is traditionally used as a flavoring agent, astringent, germicide (Mukherjee et al., 2007). Cinnamon is considered a remedy for respiratory, digestive, and gynecological ailments (Ranasinghe et al., 2012). In Ayurveda its bark is bitter, pungent, with a flavor; aphrodisiac, anthelmintic, tonic; useful in the parched mouth, bronchitis, diarrhea, itching, heart and urinary problems. The oil is styptic, carminative; useful in loss of appetite, flatulence, eructations, vomiting, and toothache. In the Unani system, its bark is used as tonic, alexiteric, carminative, aphrodisiac, expectorant, causes salivation, useful in hydrocele, flatulence, headache, hiccough, piles, scorpion-sting; strengthens the liver. The oil is carminative, emmenagogue, tonic to the liver; useful in inflammation, abdominal pains, cold in the head, bronchitis (Kirtikar et al., 2010). In Homeopathic CZ preparations used as carminative, aphrodisiac,
Cinnamaldehyde showed significantly decreased plasma glucose level in streptozotocin (STZ) induced diabetic rat’s model as compared to the control groups. The administration of cinnamaldehyde at a dose of 20 mg/kg body weight significantly decreased glycosylated hemoglobin (HbA1C), serum total cholesterol, triglyceride levels and at the same time significantly increased plasma insulin, hepatic glycogen and high-density lipoprotein–cholesterol levels (Babu et al., 2007). Antidiabetic effect of Cinnamomum cassia extract (CCE) and CZ extract (CZE) in vivo and in vitro. The CCE was superior to the CZE, slightly more efficacious than the equivalent amount of Cassia bark. The elevation in plasma insulin was direct since a stimulatory in vitro effect of insulin release from INS-1 cells (an insulin-secreting cell line) was observed. Hence the cassia extract was showed direct antidiabetic potency (Verspohl et al., 2005). CZE polyphenol content administration in STZ induced diabetic rats at a dose of 200 mg/kg, body weight for 30 days lower blood glucose levels and ameliorates oxidative stress (Krishna Kumar et al., 2014). The administration of CZE to the mice, total LDL cholesterol levels were lower on day 30th in both healthy and diabetes-induced animals. The difference in food consumption was shown only in diabetes-induced rats. Similarly, the significant difference following cinnamon-extracts in fasting blood glucose (FBG) and 2-hour postprandial blood glucose from day 0 to 30th day was shown only in diabetes-induced rats (Ranasinghe et al., 2012). Aqueous extract of CZ bark for STZ induced type-1 diabetes mellitus (T1DM) in rats showed the anti-diabetic, and hypolipidemic activities in diabetic rats and significantly decreased levels of total cholesterol (TC), triglyceride (TG), LDL-cholesterol (LDL) and VLDL-cholesterol (VLDL) were found in the diabetic animals as compared to initiative animal. The extract increased HDL-cholesterol (HDL) and tissue glycogen levels in diabetic rats (Hassan et al., 2012). CZ using STZ induced diabetic rats (type-1 diabetic rats) and cultured adipocyte showed the insulin-independent effect as the oral administered with an aqueous CZ extract for 22 days and the dose of more than 30 mg/kg/day it exhibited its anti-diabetic effect independently from insulin (Shen et al., 2010). CZE increases insulin action in the brain and lowers liver fat in obesity mouse model. The insulin-stimulated locomotor activity, fasting blood glucose level and glucose tolerance was significantly enhanced in mice along lower triglyceride level, enhanced liver glycogen content and enhanced insulin action in liver tissues was found (Sartorius et al., 2014).

### Pharmacological activity

#### Anti-diabetic activity

CZ showed good anti-inflammatory activity. Its water extract (CWE) in vivo and in vitro Lipopolysaccharide (LPS) induced model showed significantly decreased the serum levels of TNF-α and IL-6 in mice. CWE treatment in vitro decreased the mRNA expression of TNF-α. CWE blocked the LPS-induced degradation of IκBα as well as the activation of JNK, p38, and ERK1/2 (Hong et al., 2012). Cinnamon bark extract (CBE) in carrageenan-induced albino rats model with a dose of 400mg/kg showed a significant decrease in the volume of inflammation (Maridass et al., 2008). Pro-inflammatory cytokine TNF-α using flow cytometry by CZ ethanolic extract showed suppression of intracellular release of TNF-α in murine neutrophils as well as leukocytes in pleural fluid. The extract was found to inhibit TNF-α gene expression in LPS stimulated human PBMCs at 20 μg/ml concentration. A potent anti-inflammatory activity of cinnamon extract is suggestive of its anti-arthritic activity (Joshi et al., 2010). CZBE in the rat’s in vitro, carrageenan-induced rat paw edema (CPE) and adjuvant-induced arthritis showed a significant anti-inflammatory effect at the dose of 4, 8 and 25 mg/kg, p.o. The dose of 8 mg/kg, p.o. was selected for the evaluation of anti-arthritic activity in the model and showed disease-modifying potential in animal models of inflammation and arthritis in rats (Vetal et al., 2013). Ameliorative effects of the bark of CZ polyphenolic (CPP) fraction in animal models of inflammation and arthritis at a dose of 200 mg/kg, p.o. for 10 days showed a significant decrease in elevated serum TNF-α concentration without causing gastric ulcerogenicity in the AIA model in rats. CPP also demonstrated mild analgesic effects during acute treatment as evidenced by the reduction in the writhing and paw withdrawal threshold of the inflamed rat paw during the acetic acid-induced writhing model and Randall-Selitto test. CPP was found to inhibit cytokine (IL-2, IL-4, and IFN-γ) release from stimulated lymphocytes in vitro (Rathi et al., 2013).

#### Anticancer activity

Cinnamon essential oil showed anticancer potential against head and neck squamous cell carcinoma (HNSCC) via decreasing epidermal growth factor receptor-tyrosine kinase. The mechanism underlying its anticancer action was attributed to the suppression of EGFR-TK. It also significantly suppressed the tumor regression in the Hep2 xenograft model (Yang et al., 2015). CZ bark extracts (CZBE) against the antimicrobial and anticancer activity, in vitro by MTT assay on Hep G2 cell line in the presence of methanolic CZBE showed
an IC50 value of 150 μg/ml. This study proved that CZB is a reliable and safer herbal drug that can be used in pharmaceutical preparations for infectious and malignant diseases (Varalakshmi et al., 2014).

2'-Hydroxycinnamaldehyde from CZ showed antitumor activity against oral cancer in vitro and in vivo in a rat tumor model. Cell histological analysis showed that it decreased tumor cell proliferation and induced apoptosis in a rat tumor model (Kim et al., 2010).

**Antioxidant activity**

CZ bark extracts showed antioxidant activity through various in vitro models with reference to antioxidant compounds like butylated hydroxy anisole (BHA), ascorbic acid (AA). It is potent free radical scavenging activity especially against 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals and 2,2'-azinobis 3-ethylbenzothiazoline-6-sulfonic acid (ABTS) radicals. The hydroxyl and superoxide radicals were also scavenged by the tested compounds along with metal chelating activity (Mathew et al., 2006). CZ fruit extracts (CZFE) showed antioxidant and strong antimutagenic activities of in vivo and in vitro models due to the presence of phenolics (Jayaprakasha et al., 2007). CZ and Syzygium cumini used in traditional system of medicines for oxidative stress and insulin resistance in STZ induced diabetic rats. Both plants possessed antioxidant activity by functioning to normalize the level of insulin, hyperglycemia, hyperlipidemia, oxidative stress, and kidney and liver dysfunctions (Sharafeldin et al., 2015). CZ bark with greater cardamom (Amomum subulatum) seeds in rats fed with high-fat diet showed significantly increased antioxidant enzymes whereas glutathione content was markedly restored in rats fed a fat diet with spices. These spices partially counteracted the increase in lipid conjugated dienes and hydroperoxides, the primary products of lipid peroxidation (Dhuley et al., 1999).

Essential oil of CZ and eugenol showed very powerful antioxidant activity (Chericoni et al., 2005). CZ extract on scopolamine-induced cognitive impairment and oxidative stress in rats showed significantly impaired acquisition and retention of memory. Pre-treatment with CZ extract 200 and 400 mg/kg/oral for 21 days significantly reversed SCOP-induced amnesia as evidenced by increased step-down latency in passive avoidance and decreased latency in Morris water maze test compared to the SCOP treated group. SCOP administration also caused the increase of MDA and reduction of GSH levels. Pretreatment with CZ extract 200 and 400 mg/kg/oral resulted in a significant decrease in MDA levels and increase in GSH levels as compared to the SCOP-treated animals (Jain et al., 2015).

**Antihypertensive activity**

Methanolic extract of CZ stem bark was effective against acute and chronic antihypertensive activity in L-nitroarginine methyl ester-induced hypertensive rats. Acute intravenous administration of different doses of induced hypertensive rats provoked a long-lasting decrease in blood pressure. Mean arterial blood pressure decreased. In chronic administration, extract and captopril significantly prevented the increase in blood pressure and organs weight. It also significantly lowers the plasma level of triglycerides, total cholesterol, and LDL cholesterol with increasing of HDL-cholesterol with a significant low atherogenic index (Nyadjeu et al., 2013). Ethanolic extract of CZ i.v. administration resulted in a biphasic dose-related hypotensive activity in rats at different dose levels. The results showed a vasorelaxant effect on the rat thoracic aortic ring segments with (+E) or without (-E) endothelium precontracted with KCl (60 mM), suggesting that, it might be inhibiting extracellular Ca²⁺ through L-type voltage-sensitive channels. (Wansi et al., 2007). Aqueous extract of stem bark of CZ showed antihypertensive and vasorelaxant effects in rats by decreasing in mean arterial blood pressure in anesthetized normotensive Wistar rats, salt-loaded hypertensive, L-nitrogenine amino methyl ester hypertensive and spontaneously hypertensive rats. Pre-treatment of rats with either propranolol or atropine significantly inhibited the hypotensive effects of the plant extracts. Also, pre-treatment of rats with L-nitrogenine amino methyl ester inhibited the sustained plant antihypertensive effects, suggesting a possible active vasodilatation. The vasorelaxation effects may be involved in the antihypertensive mechanism, partially by increasing the endothelial nitric oxide and by activating the potassium adenosine triphosphate channels in vascular smooth muscle (Nyadjeu et al., 2011).

**Alzheimer’s disease**

Cognitive effects of aqueous bark extract of CZ on the monosodium glutamate-induced non-transgenic rat model have been studied. The results were showed that improved the insulin sensitivity, increased phosphorylated glycogen synthase kinase-3β (pGSK3β), inhibited the cholinesterase activity, and improved the learning ability (Madhavadas et al., 2017). Cinnamomum extract on the amyloid formation of hen egg-white lysozyme and study of its possible role in Alzheimer’s disease. The result showed that it has no any effect on protein stabilization and thus directly interact with amyloid structure and inhibit the formation of these structures (Ramshini et al., 2015). Anticholinesterase inhibitory activity of crude methanol extract of CZ leaves and cinnamon oil was
evaluated by 96 well microtiter plate assay and thin layer chromatography bioassay detection methods showed that cinnamon oil has better anticholinesterase activity than its methanol extract in the symptomatic treatment of Alzheimer’s disease (Dalai et al., 2014).

Wound healing activity
CZ bark extracts significantly enhanced the wound breaking strength in the case of incision wound, the rate of wound contraction and the period of epithelization in the case of excision wound. The granulation tissue weight, its breaking strength, and its hydroxyproline content was also increased by the extract in the dead space wound (Kamath et al., 2003).

Immunomodulator activity
Cinnamon extract in collagen-induced arthritic mice showed good ameliorative effects after the second day of treatment. A greater therapeutic role was observed for the 4 mg/kg/oral of body weight dosage of the methanolic extract. Swelling of the spleen was greatly reduced along with the generation of free radicals by lymphocytes, post-treatment (Qadir et al., 2018).

Antimicrobial activity
Syzygium aromaticum (SA), Ocimum sanctum (OS) and CZ plant extracts exhibited antimicrobial efficacy against Enterococcus faecalis (EF). Complete bacterial inhibition in planktonic form after exposure of 15, 30, 35 and 1 min, respectively. NaOCl was associated with complete bacterial inhibition after contact of 2 min, whereas 10% CZ, 10% S. aromaticum and 40% O. sanctum showed the cessation of growth after 12 and 24 h, respectively (Gupta et al., 2013). The essential oil of CZ showed strong antimicrobial activity against all microorganisms tested and indicating the possibilities of its potential use in the formula of natural remedies for the topical treatment of infections and neoplasms (Unlu et al., 2010). CZ showed in vitro activity against fluconazole-resistant and susceptible Candida isolates. The MICs of the bark of CZ were slightly better than commercially available cinnamon powder (Quale et al., 1996).

Anti-asthmatic activity
Cinnamon bark showed anti-asthmatic effects in hyper-responsiveness laboratory animals. It exhibited the significant decrease in breathing rate and peak inspiratory flow whereas the peak expiratory flow and forced vital capacity expired in one second was significantly increased as compared to airway hyperresponsiveness control rats (Kandhare et al., 2013).
Hepatoprotective activity

Studied that hepatoprotective activity of cinnamon ethanolic extract against CCl4-induced liver injury in rats. Administration with cinnamon extracts (0.01, 0.05 and 0.1 g/kg) for 28 days significantly reduced the impact of CCl4 toxicity on the serum markers of liver damage, aspartate aminotransferase, alanine aminotransferase and alkaline phosphatase. In addition, treatment of cinnamon extract resulted in markedly increased the levels of superoxide dismutase and catalase enzymes in rats suggested that cinnamon extract acts as a potent hepatoprotective agent against CCl4 induced hepatotoxicity in rats (Eidi et al., 2012).

Memory enhancing activity

Standardized lyophilized CZ bark extract showed attenuating effect against streptozotocin-induced experimental dementia of Alzheimer’s type. In the Morris water maze test, it significantly decreased the transfer latency and increased the time spent by the animals in target quadrant. Similarly, in the object recognition test, the extract-treated animals exhibited an improved discrimination between a familiar object and a novel object, indicating the reversal of STZ-induced memory impairment. It also restored STZ-induced alteration in AChE activity and oxidative stress parameters in both brain parts (Malik et al., 2015).

Anti-convulsant activity

Pharmacological screening of herbal extract of Piper nigrum and CZ for anticonvulsant activity by maximal electroshock (MES) and pentylentetrazol (PTZ) induced seizures in Wistar albino rats. In the PTZ model, the anticonvulsant property of Piper nigrum and CZ was assessed by its ability to delay the onset of myoclonic spasm and clonic convulsions produced by intraperitoneal administration of PTZ. In the MES model, Piper nigrum and CZ reduced all the phases of convulsion (Belemkar et al., 2013).

Anti-hyperlipidemic activity

Alcoholic cinnamon extract on cholesterol-induced hyperlipidemia and alloxan induced diabetic rats and estimation of hematological, biochemical and immunological parameters exhibited that extract is effective in controlling blood glucose level, serum lipids among hyperlipidemic and diabetic rats (Mhammad et al., 2015).

CONCLUSION

Cinnamon has been used as a spice and medicine in daily life evidenced with several reports. It has numerous traditional, medicinal and pharmacological properties in the forms of bark, essential oils, phenolic compounds, flavonoid, and other 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. The significant health benefits of numerous types of cinnamon have been explored. Further investigations are necessary to provide additional clinical evidence for the traditional uses of this spice against cancer, inflammation, cardioprotective and neurological disorders. No work has been done such as cardiac heart failure, myocardial infarction, antidepressant activity, constipation, diarrhea, schizophrenia, global cerebral ischemia, focal cerebral ischemia.

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