

Cinnamon: Mystic powers of a minute ingredient

Pallavi Kawatra, Rathai Rajagopalan

Department of Pharmacology, M.S Ramaiah Medical College, Bengaluru, Karnataka, India

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ABSTRACT

Cinnamon, due to its exotic flavor and aroma, is a key ingredient in the kitchen of every household. From the beginning of its use in 2800 BC by our ancestors for various purposes such as anointment, embalming and various ailments, it has instigated the interest of many researchers. Recently many trials have explored the beneficial effects of cinnamon in Parkinsons, diabetes, blood, and brain. After extensive research on PubMed and Google scholar, data were collected regarding its antioxidant, anti-inflammatory, antilipemic, antidiabetic, antimicrobial, and anticancer effect. This systematic review underlines the surplus health benefits of this clandestine ingredient and the scope of further research in these clinical scenarios.

Key words: Blood, cinnamon, diabetes, parkinsons

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INTRODUCTION

Cinnamon an indigenous spice, belonging to the Lauracea family, is found in almost every household. Used mainly as a flavoring agent, it has been a major constituent of our food since a long time. For a long time, our ancestors have been using it as a remedy for respiratory and digestive ailments. However, less is known about its beneficial effect as an antioxidant, anti-inflammatory, antilipemic, antidiabetic, antimicrobial, and anticancer agent. This review highlights the diverse effects which can increase its use as an adjunct in complementary and alternative medicine.

Types of cinnamon

There are mainly four types of cinnamon:

- True cinnamon or Ceylon cinnamon or Mexican cinnamon (*Cinnamomum zeylanicum*)
- Indonesian cinnamon (*Cinnamomum burmanni*)
- Vietnamese cinnamon (*Cinnamomum loureiroi*)
- Cassia cinnamon or Chinese cinnamon (*Cinnamomum aromaticum*).

The following table depicts the main features of the different types of cinnamon [Table 1].

Address for correspondence:

Dr. Pallavi Kawatra, Department Of Pharmacology,
M.S Ramaiah Medical College, M.S.R.I.T Post,
Bengaluru - 560 054, Karnataka, India.
E-mail: dr.pallavikawatra@gmail.com

On the basis of the appearance of the quill, it is possible to differentiate Ceylon cinnamon from the others. It is softer and lighter in color and rolled in layers whereas the others are darker, hard, and hollow and rolled in only one layer. Even though very expensive, Ceylon cinnamon is preferred due to its ultra-low coumarin levels and the mild delicate taste. According to the European Food safe authority, cassia cinnamon has been the cause of exposure to coumarin which is highly hepatotoxic and carcinogenic.^[1] Another recently available low coumarin containing cinnamon substitute has been found which is obtained from the leaves of *Cinnamomum osmophlourum* from Taiwan.^[2]

BOTANY AND CHEMICAL COMPOSITION

Cinnamon is exported as cinnamon quills from four main countries: Indonesia, China, Vietnam and Sri Lanka. The quills are made by peeling the bark and then rolling it into pipes.

Different oils obtained from this interesting plant yield different constituents: Cinnamaldehyde (in the bark oil), eugenol (in the leaf oil), and camphor (in the root-bark oil).^[3] The fruits and flowers are a rich source of trans-cinnamyl acetate.^[4]

HISTORY OF CINNAMON

Use of cinnamon can be dated back to almost 2800 BC where it was initially referred to as “Kwai” in Chinese

Table 1: Types of cinnamon

	<i>Cinnamomum zeylanicum</i>	<i>Cinnamomum burmanni</i>	<i>Cinnamomum loureiroi</i>	<i>Cinnamomum aromaticum</i>
Country where it originates	Sri Lanka	Indonesia	Vietnam	China
Taste	Slightly sweet	Spicy	Spicy and sweet	Spicy but bitter
Color	Light to medium reddish brown	Dark reddish brown	Dark reddish brown	Dark reddish brown
Special features	Lowest coumarin content	Cheap, high coumarin, strong aroma	Strong aroma, spicy, high coumarin	High coumarin, very strong taste

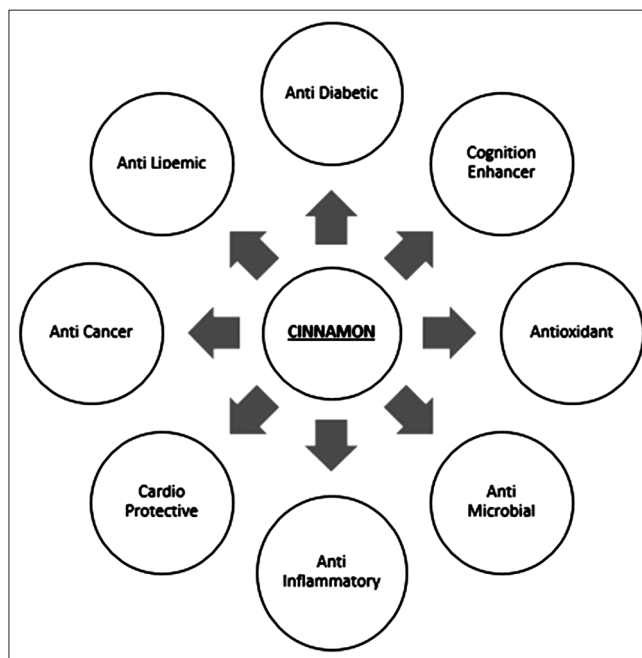
language. It was a component of the anointing oil used by Moses for the purpose of anointment (to make a person holy) as mentioned in the Bible. The Romans used it for its medicinal properties for ailment of the digestive and respiratory tract. It was also used in Roman funerals in order to fend off the odor of dead bodies. It was used in Egypt for embalming of mummies as well as for its fragrance and flavoring properties.

However being very expensive and highly treasured, the quest for cinnamon led to a world exploration in the 15th century. It was the motivation behind Christopher Columbus's voyage which led to the discovery of the new world and for Vasco da Gama's exploration of South India and Sri Lanka. The native of true cinnamon or Ceylon cinnamon was then found to be in Sri Lanka (also known as Ceylon). Thus it became evident, that any country which could hold that area captive, had a control over the world trade of cinnamon and would ultimately reap immense profits. Thus over years, initially the Portuguese ruled, who were later overpowered by the Dutch, followed by the British in 1815. Now it's cultivated in Sri Lanka along the coastal belt from Negombo to Matara.

Following picture illustrates the many pleiotropic effects of this wonderful spice [Figure 1].

CINNAMON IN DIABETES

Management of the glycemic index in a diabetic is one of the foremost challenges confronted by the physicians in daily practice. Various known studies have demonstrated that a meticulous control with intensified insulin treatment and sulphonylureas (UK Prospective Diabetes Study Trial) can result in a decrease in microvascular complications as well as the hospitalization costs.^[5-7] Furthermore, a precise control of not only the blood glucose levels, but also the lipid profile and blood pressure (BP) play an eminent role in preventing complications in a diabetic.^[8] Along with that, the lack of compliance due to various patient centered factors^[9] such as decrease effect of medicine over time^[10] and development of dependence^[11] with the allopathic medications due to the fear of a lifelong intake further adds on to the existing problem.

**Figure 1:** Pleiotropic effects of cinnamon

At this point, introduction of cinnamon, as a natural product has revived the interest of many scientists due to its abundant pleiotropic effects. Role of cinnamon in regulating the glucose levels in the body has been implied in numerous small randomized control trials. However, the results have either been conflicting or not significant enough. A meta-analysis by Allen *et al.* done for 10 randomized controlled trials including 543 patients has established that cinnamon, when taken in a dose of 120 mg/day to 6 g/day for approximately 4 months leads to a statistical decrease in levels of fasting plasma glucose along with an improvement in the lipid profile.^[12]

Various hypothesis regarding its mechanism of action in diabetes have been put forth. Cinnamon has been said to have an insulin mimetic and insulin sensitizing action.^[13] *Cinnamon cassia* plays a significant role in phosphorylation of signaling proteins and enhancement of expression of insulin sensitive glucose transporters which results in mitigation of the insulin resistance.^[14] It has been demonstrated that following the exposure to cinnamon water extracts, there is an increase expression of peroxisome proliferator activated

receptor (PPAR) α and γ which can contribute to its role in insulin resistance.^[15] Its effect on PPAR γ is analogous with that of the thiazolidinediones in type 2 diabetes.^[16]

CINNAMON AS A COGNITION ENHANCER

A novel study evaluated the effect of lyophilized extract of CZ bark (LCZE) on streptozocin-induced dementia in rodents. It was concluded that LCZE treated group performed better in the Morris water maze model and had improved discrimination between a familiar and a new object in case of Object recognition test.^[17] Cinnamon contains phytochemicals which boost the brain's ability to utilize glucose. This has even been illustrated by the decrease in markers of oxidative stress like malondialdehyde (MDA) in rats pretreated with extract of CZ in Scopolamine treated rats.^[18] Its ability to improve insulin resistance also constitutes an important mechanism, whereby it limits the Alzheimer induced changes in the brain as well as modulates the brain insulin signaling.^[19]

ANTI-MICROBIAL ACTION

The cinnamaldehyde component of cinnamon is responsible for its anti-microbial activity. It can inhibit the growth of *Listeria* and *Escherichia coli* in food products thereby potentiating their shelf life.^[20] In one of the studies, the effect of cinnamon was studied against various organisms like bacteria such as *Staphylococcus aureus*, fungus like (*Aspergillus flavus*, *Mucor plumbeus* and yeast species such as (*Candida lipolytica*). Its combination along with clove oil has been effective against *A. flavus*.^[21] The cinnamon oil possesses antimicrobial action in the range 10-150 $\mu\text{g/ml}$ – 1.^[22] One of the studies investigated the antimicrobial activity of *C. zeylanicum* against fluconazole resistant *Candida*. They went ahead and experimented the effect of commercially available preparations in five HIV patients suffering from oral candidiasis. It was concluded that there was improvement in these patients, highlighting the need of further research on this aspect.^[23]

Another interesting fact about cinnamon is its role in altering the expression of a gene *icaA* which plays a role in the formation of biofilms.^[24] *Staphylococcus epidermidis* is one of the leading causes of biofilms which is why it has emerged as a notorious nosocomial pathogen.^[25] The literature on the effect of cinnamon on viruses is limited. However, it is said to inhibit protein synthesis which is responsible for its ability to improve survival in mice following infection with influenza A/PR/8 virus.^[26]

ANTIOXIDANT PROPERTY

Lipid oxidation is a major challenge during the food processing in the food industry. A natural antioxidant is hereby the need of the hour. The methanol extract is said to have maximum anti-oxidant property as compared to the ethanolic and water extract.^[27] The antioxidant property is due to the eugenol component which inhibited peroxynitrite-induced nitration and lipid peroxidation in *in vitro* models.^[28] The oil is said to form a phosphomolybdenum complex which is responsible for its antioxidant activity.^[29]

This anti-oxidant effect has been recently extended to its application in liver disorders. The ethanolic extract has demonstrated to decrease the carbon tetrachloride induced lipid peroxidation resulting in a fall in markers of oxidative stress such as MDA.^[30]

ANTI-INFLAMMATORY EFFECT

The multifaceted nature of cinnamon has incited researchers to look further into its likely uses. Cinnamon water extract possesses anti-inflammatory effect *in vitro* ascribed to fall in levels of tumor necrosis factor α and Interleukin 6.^[31] Twigs of *C. osmophloeum* contain compounds such as trans-cinnamaldehyde, caryophyllene oxide, eugenol, L-borneol which possess anti-inflammatory activity.^[32]

CINNAMON AND HEART DISEASES

An animal study on Sprague Dawley rats evaluated the effect of *C. cassia* on Ischemic Heart Disease. The active components cinnamaldehyde and cinnamic acid are said to be cardio protective due to their ability to produce nitric oxide as well as the associated anti-inflammatory property.^[33] Its vasorelaxation effect has also been attributed to the cinnamaldehyde component which inhibits the L type calcium channels.^[34]

CINNAMON AND LIPID PROFILE

Cinnamon is also known to have a lipid lowering effect. An *in vitro* study proved *C. zeylanicum* extract (0.75 g/kg bark powder) to be as effective as simvastatin (0.6 mg/kg body weight).^[35] However, whether this effect is significant or not in humans remains to be elucidated. According to another study, the effect of cinnamon on cholesterol level becomes insignificant in rats even after increasing the intake to up to 5 times the normal.^[36] One of the studies which studied the effect of cinnamon on gastric emptying as well as postprandial glycemic and lipemic responses did not find any change in the nine individuals enrolled in the study.^[37]

CINNAMON AND CANCER

The pathogenesis of cancers have been multimodal and various treatment medications aim at various steps in order to inhibit the process. One of the main etiologies of gastric carcinoma is the gram-negative bacilli *Helicobacter pylori* (*H. pylori*). It is also known to be responsible for conditions such as atrophic gastritis, duodenal ulcer, and gastric lymphomas. In a pilot study of fifteen patients, *H. pylori* levels were checked by radiolabelled urea breath test before and after administration of cinnamon alcoholic extract. Though it was not completely effective in eradicating the *H. pylori*, it did decrease the colonization to some extent. Thus, it was suggested that in a concentration of 80 mg/day, it may be valuable with further research.^[38] Since its discovery, nuclear factor kappa B (NFκB), an inducible transcription factor, has become a significant target for treatment of various diseases and malignancies.^[39] Substances acting on pathways involved in its activation has given a new dimension to cancer therapy.^[40] One animal study suggested that *C. cassia* can inhibit the survival, viability and proliferation of tumor cells *in vitro* without having a significant effect on the normal cells. On further detailed analysis, it was found that such an effect could be attributed to the ability of the extract to induce apoptosis in tumor cells and also by inhibiting the activity of NFκB.^[41] Two derivatives: 2'-hydroxycinnamaldehyde (2HCA) and (2'-benzoyl-oxy)cinnamaldehyde also induce mechanism by escalating the levels of reactive oxygen species.^[42] 2HCA also has an additional mechanism whereby it causes apoptosis by stalling the activity of proteasome, thereby making the cell more susceptible to oxidative stress.^[43]

Extensive research has been done to see the effect of cinnamon on melanoma cells. It has been found to impede the activity of pro angiogenic factors which is a major prerequisite for the tumor cells to proliferate and simultaneously increase the activity of CD8(+) T cells.^[44] The polyphenol component of cinnamon extract is a potent inhibitor of Vascular Endothelial growth factor, an eminent factor involved in the growth of endothelial cells, and migration during angiogenesis.^[45]

CINNAMON AND BLOOD PRESSURE

Though the effect of cinnamon has been extensively researched with respect to diabetes, little work has been done regarding its role in maintenance of BP. It causes peripheral vasodilation, resulting in the fall in BP in dogs and guinea pigs.^[46] A systemic review done of three studies have suggested that cinnamon can cause a significant fall in systolic as well as diastolic BP though the precise mechanism remains to be ascertained.^[47] Another study done on 59 subjects,

suggests that the dietary supplementation with cinnamon can lead to significant fall in systolic BP.^[48] The vasorelaxant property of cinnamon due to the production of nitric oxide has said to be the sole cause of this effect. However, an *in vivo* trial hypothesized its effect on KATP channels in the vascular smooth muscles resulting in the fall in BP.^[49,50]

POSSIBLE INTERACTIONS WITH CINNAMON

Cassia cinnamon contains high levels of coumarins, which can prove to be toxic in high doses. A daily intake of more than 0.1 mg/kg body weight can lead to conspicuous effect on the blood coagulation profile if the patient is simultaneously on drugs such as warfarin. However, these results are very contradictory. Coumarin is also a highly hepatotoxic toxin and its addition into food products is prohibited. However, due to the lack of awareness regarding the standard limits of cinnamon in these products, it is advisable for patients of hepatic disorders to avoid cinnamon.

CONCLUSION

The above review highlights the significance of this regularly consumed spice with respect to the cardiovascular system, hematological system, central nervous system, etc.,. Given its broad spectrum of applicability, this particular palatable spice can be used as an adjunct to the regular medications in most of the patients. However, despite all these pleiotropic effects, further research is mandated in order to substantiate the clinical effects of the drug in the dose in which it is being consumed.

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