

## CINNAMON- A PROMISING SPICE WITH NUTRACEUTCAL PROPERTIES

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### ABSTRACT

Conventional and organic cinnamon was investigated for their phenolic profile, anti-proliferative, anti-inflammatory and antioxidant properties. Cinnamon seems to be highly bioactive, appearing to mimic the effect of insulin through increased glucose uptake in adipocytes and skeletal muscles. Cinnamon extract would improve insulin action via increasing glucose uptake in vivo, at least in part through enhancing the insulin-signaling pathway in skeletal muscle. Administration of the cinnamon extracts significantly increased the consumption of extracellular glucose in insulin-resistant HepG2 cells and normal HepG2 cells compared with the control group. Both A- and B-type procyanidin oligomers in different cinnamon species have hypoglycemic activities and may improve insulin sensitivity in type 2 DM. The administration of cinnamon extract provides substantial

protection against radiation-induced oxidative and inflammatory damages. Uncontrolled activation of microglia contributes to neuroinflammation, which is highly involved in the development of neurodegenerative diseases. Cinnamon may have a potential therapeutic effect against neurodegenerative diseases and its potent anti-neuroinflammatory capacity was primarily attributed to cinnamaldehyde. *In vitro* and *in vivo* system, cinnamon treatment strongly inhibited the expression of pro-angiogenic factors and master regulators of tumor progression not only in melanoma cell lines but also in experimental melanoma model. Inclusion of 2 g/kg cinnamon can be applied as alternatives to in-feed antibiotics for broiler diets. Though enough basis has been created on the scientific evidence of cinnamon and its components in promoting health as functional foods, research efforts need to be intensified to further substantiate and validate health claims to instil greater confidence of the consumer.

**KEYWORDS:** Cinnamon, Anti-diabetic, Radioprotective, Anti-neuroinflammatory, Anti-tumour, Immune boosting.

## INTRODUCTION



Spices and herbs not only provide flavour but also contribute to the preservation of foods; they exhibit antiseptic and antioxidative activities.<sup>[1-3]</sup> Studies have indicated that various spice principles form an important group of antioxidant. Spices such as ginger, coriander and ajowan are known for stimulating properties. The

pungent compounds present in ginger (*Zingiber officinale Roscob*) are responsible for its anti-emetic properties. Ginger is also used for treatment of asthma, shortness of breath, diarrhea, nausea, motion sickness and appetite loss.<sup>[4-6]</sup> Garlic a popular spice added to several edible preparations and is a remedy for a variety of ailments on consumption reduces certain cancer incidences in the stomach, colon, mammary, cervical, etc.<sup>[7]</sup> Another important spice used in Indian kitchen is Cinnamon, a small tree that grows in India, Sri Lanka, Indonesia, Brazil, Vietnam, and Egypt. It's one of the oldest known spices. The bark of the cinnamon tree is dried and rolled into cinnamon sticks and these are also called quills. The bark of cinnamon can also be dried and ground into a powder. Cinnamonaldehyde is responsible for the characteristic flavor and aroma of cinnamon and this is present in the essential oil of the bark. The other active principles are cinnamyl acetate and cinnamyl alcohol. There are around 250 species of *Cinnamomum* (*Cinnamomum velum* or *C. cassia*) currently recognized. Ceylon cinnamon and Cassia cinnamon are the most popular varieties. Indonesian cinnamon (*Cinnamomum burmanni*) and Vietnamese cinnamon (*Cinnamomum loureiroi*) are the other types.

Ceylon cinnamon is sometimes called true cinnamon and this is more expensive and has a sweet taste. The quills are softer and can be easily ground in a coffee grinder. *Cinnamomum velum* (Ceylon cinnamon) also known as true cinnamon is grown principally in Sri Lanka, the Seychelles, Madagascar and southern part of India. *Cinnamomum Cassia* is also known as Cassia or Chinese cinnamon and is native to southern China and also grown in India, Malaysia, Thailand, Vietnam and Indonesia. Cinnamon available to the consumer may be a mixture of species and grades.

Cinnamon has long been considered a "wonder food" in various cultures and science has shown that its active oil components such as cinnamaldehyde, do convey certain health benefits. Cinnamon does have a therapeutic role in certain ailments such as digestive troubles and minor bacterial infections or colds.

### **Folk medicine**

Once upon a time, cinnamon was more valuable than gold because of its potential health benefits that are attributed. Chinese medicine and *Ayurveda* have long revered cinnamon as a superpower that used to treat common cold, indigestion, cramps, vitality, flatulence, nausea, diarrhea, and painful menstrual periods and also believed to improve energy. It's a common ingredient in *chai* tea, and it is believed to improve the digestion of fruit, milk and other dairy products.

### **Phytochemical profile**

Conventional and organic cinnamon was investigated for their phenolic profile, anti-proliferative, anti-inflammatory, and antioxidant properties. Accelerated solvent extraction with 75% acetone was used to extract samples. Catechin, (-)-epigallocatechin gallate, syringic acid, gallic acid, vanillic acid, and *p*-coumaric acid were detected in cinnamon (Table 1). There was no significant difference between conventional and organic spices in the composition of most individual phenolics. All conventional and organic cinnamon extracts exhibited strong anti-proliferative and anti-inflammatory properties. Cinnamon was found to be efficient in inhibiting IL-1 $\beta$  and COX-2 expression. This study indicated that cinnamon may potentially be used as dietary sources of bioactive phytochemicals for improving health (Table 1).

The effect of a water extract of some spices on the *in vitro* activity of the rat jejunal Na<sup>+</sup>-K<sup>+</sup>-ATPase was investigated by Kreydiyyeh *et al.*, 2000.<sup>[8]</sup> Extracts of cinnamon inhibited the ATPase. The extracts of clove and cinnamon had the most potent inhibitory effect on the intestinal ATPase as compared to extracts of other spices. They also inhibited the *in vitro* Na<sup>+</sup>-K<sup>+</sup>-ATPase activity in a crude kidney homogenate and the activity of an isolated dog kidney Na<sup>+</sup>-K<sup>+</sup>-ATPase. The alcoholic extract of cinnamon, compared to the aqueous extract, had a stronger inhibitory action on the jejunal enzyme and a lower IC<sub>50</sub> value, which was not significantly different from the one observed with cinnamaldehyde, the major volatile oil present cinnamon, suggesting that in alcoholic extracts cinnamaldehyde is the major inhibitory component. The aqueous extracts of clove and cinnamon also significantly lowered

the absorption of alanine from the rat intestine. This study showed that the active principle(s) in cinnamon can permeate the membrane of the enterocytes and inhibit the Na<sup>+</sup>-K<sup>+</sup>-ATPase that provides the driving force for many transport processes.

## NUTRACEUTICAL PROPERTIES

### 1. Anti-diabetic properties

Cinnamon has been shown to potentiate the insulin effect through upregulation of the glucose uptake in cultured adipocytes. Qin *et al.*<sup>[9]</sup> evaluated the effect of the cinnamon extract on the insulin action in awaked rats by the euglycemic clamp and further analyzed possible changes in insulin signaling occurred in skeletal muscle. The rats were divided into saline and cinnamon extract (30 and 300 mg/kg BW-doses: C30 and C300) oral administration groups. After 3-weeks, cinnamon extract treated rats showed a significantly higher glucose infusion rate (GIR) at 3 mU/kg per min insulin infusions compared with controls (118 and 146% of controls for C30 and C300, respectively). At 30 mU/kg per min insulin infusions, the GIR in C300 rats was increased 17% over controls. There were no significant differences in insulin receptor (IR)- $\beta$ , IR substrate (IRS)-1, and phosphatidylinositol (PI) 3-kinase protein content between C300 rats and controls. However, the skeletal muscle insulin-stimulated IR- $\beta$  and the IRS-1 tyrosine phosphorylation levels in C300 rats were 18 and 33% higher, respectively, added to 41% higher IRS-1/PI 3-kinase association. These results suggested that the cinnamon extract would improve insulin action via increasing glucose uptake *in vivo*, at least in part through enhancing the insulin-signaling pathway in skeletal muscle.

Cinnamon and vinegar or acetic acid was reported to reduce the postprandial blood glucose response. It was hypothesized that the combination of these substances might result in an additive effect.<sup>[10]</sup> The significant effect of the combination of cinnamon and acetic acid on blood glucose and satiety immediately after meal intake indicated an additive effect of the 2 substances. Further studies on larger doses of cinnamon and acetic acid which may result in a more substantial additive effect on blood glucose or satiety remains to be investigated.

Cinnamon seems to be highly bioactive, appearing to mimic the effect of insulin through increased glucose uptake in adipocytes and skeletal muscles. A systematic review and meta analysis examined the effect of cinnamon on glycaemic control in patients with Type 2 Diabetes mellitus. A total of 6 clinical trials met the strict inclusion criteria and considered a total of 435 patients; follow up between 40 days–4 months, doses ranging from 1 g to 6 g per day. Meta-analysis of RCTs showed a significant decrease in mean HbA1c [0.09%; 95% CI

was 0.04–0.14] and mean FPG [0.84 mmol/l; 95% CI was 0.66–1.02]. Use of cinnamon showed a beneficial effect on glycaemic control (both HbA1c and FPG) and the short term (<4 months) effects of the use of cinnamon on glycaemic control looks promising<sup>[11]</sup>. In a study conducted recently by Lu *et al.*, 2012<sup>[12]</sup> a phytochemically-enhanced functional food ingredient that captures water soluble polyphenols from aqueous cinnamon extract onto a protein rich matrix was developed. Cinnamon extract and cinnamon polyphenol-enriched defatted soy flour were effective in acutely lowering fasting blood glucose levels in diet induced obese hyperglycemic mice at 300 and 600 mg/kg, respectively. To determine mechanisms of action, rat hepatoma cells were treated with cinnamon extract and eluates of cinnamon polyphenol-enriched defatted soy flour at a range of 1–25 µg/ml. Cinnamon extract and eluates of cinnamon polyphenol-enriched defatted soy flour demonstrated dose-dependent inhibition of hepatic glucose production with significant levels of inhibition at 25 µg/ml. Furthermore, cinnamon extract decreased the gene expression of two major regulators of hepatic gluconeogenesis, phosphoenolpyruvate carboxykinase and glucose-6-phosphatase. Hence the hypoglycemic and insulin-like effects of cinnamon extract and cinnamon polyphenol-enriched defatted soy flour might help to ameliorate type 2 diabetes conditions.

Procyanidin oligomers in cinnamon are thought to be responsible for the biological activity in the treatment of diabetes mellitus. To clarify types of procyanidin oligomers in different Cinnamon species and investigate their different effects, a study by Lu *et al.*, 2011<sup>[13]</sup> investigated procyanidin oligomers in polyphenolic oligomer-rich extracts of three Cinnamon samples by LC–MS methods, and their hypoglycemic activities were detected *in vivo* and *in vitro*. The results showed that two of the three samples from *Cinnamomum cassia* were rich in B-type procyanidin oligomers, and the other sample was rich in A-type procyanidin oligomers. The Cinnamon extracts were administered at doses of 200 and 300 mg/kg body wt. in high-fat diet-fed and low-dose streptozotocin -induced diabetic mice for 14 days. The results showed that blood glucose concentrations were significantly decreased in all Cinnamon extract groups compared with the control group ( $p < 0.05$ ). Administration of the Cinnamon extracts significantly increased the consumption of extracellular glucose in insulin-resistant HepG2 cells and normal HepG2 cells compared with the control group. These results suggest that both A- and B-type procyanidin oligomers in different Cinnamon species have hypoglycemic activities and may improve insulin sensitivity in type 2 DM.

## 2. Radio-protective properties

In another study<sup>[14]</sup> rats were subjected to fractionated doses of gamma radiation. Cinnamon extract were daily administrated before starting irradiation and continued after radiation exposure. The results obtained revealed that the administration of cinnamon extract to irradiated rats significantly ameliorated the changes induced in liver antioxidant system; catalase, superoxide dismutase and glutathione peroxidase activities as well as reduced glutathione concentration. The liver's lipid peroxidation and protein oxidation indices were significantly decreased when compared with their equivalent values in irradiated rats. Furthermore, the changes induces in xanthine oxidoreductase system were significantly diminished. In addition, the changes in liver nitric oxide contents, serum tumor necrosis factor alpha and C-reactive protein levels were markedly improved. In this study, it was suggested that the administration of cinnamon extract provides substantial protection against radiation-induced oxidative and inflammatory damages.

## 3. Anti-neuro-inflammatory properties

Uncontrolled activation of microglia contributes to neuroinflammation, which is highly involved in the development of neurodegenerative diseases. The composition of cinnamon extract was analyzed by LC-MS and the ability of cinnamon and its main constituents to inhibit neuro-inflammation was evaluated using a lipopolysaccharide (LPS)-activated BV2 microglia culture system. In total, 50µg/mL cinnamon extract decreased significantly the production and expression of nitric oxide (NO), interleukin (IL)-1β, IL-6, and tumor necrosis factor (TNF)-α in LPS-activated BV2 microglia. Blocking of nuclear factor-κB (NF-κB) activation was the most likely mechanism responsible for inhibition by cinnamon of neuroinflammation. Among the eight tested compounds, cinnamaldehyde had the greatest anti-neuroinflammatory capacity. These results suggest that cinnamon may have a potential therapeutic effect against neurodegenerative diseases and its potent anti-neuroinflammatory capacity was primarily attributed to cinnamaldehyde.<sup>[15]</sup>

For thousands of years, cinnamon has been used as a traditional treatment in China. Recently a study was conducted to investigate whether cinnamon supplements are able to aid in the treatment of type 2 diabetes in Chinese subjects. It was hypothesized that cinnamon should be effective in improving blood glucose control in Chinese patients with type 2 diabetes. To address this hypothesis, work was done in a randomized, double-blinded clinical study to analyze the effect of cinnamon extract on glycosylated hemoglobin A<sub>1c</sub> and fasting blood

glucose levels in Chinese patients with type 2 diabetes. A total of 66 patients with type 2 diabetes were recruited and randomly divided into 3 groups: placebo and low-dose and high-dose supplementation with cinnamon extract at 120 and 360 mg/d, respectively. Patients in all 3 groups took gliclazide during the entire 3 months of the study. Both hemoglobin A<sub>1c</sub> and fasting blood glucose levels were significantly reduced in patients in the low- and high-dose groups, whereas they were not changed in the placebo group. The blood triglyceride levels were also significantly reduced in the low-dose group. The blood levels of total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and liver transaminase remained unchanged in the 3 groups. This study indicated that cinnamon supplementation is able to significantly improve blood glucose control in Chinese patients with type 2 diabetes.<sup>[12]</sup>

#### 4. Anti-tumour properties

*In vitro* and *in vivo* system, cinnamon treatment strongly inhibited the expression of pro-angiogenic factors and master regulators of tumor progression not only in melanoma cell lines but also in experimental melanoma model. In addition, cinnamon treatment increased the anti-tumor activities of CD8<sup>+</sup> T cells by increasing the levels of cytolytic molecules and their cytotoxic activity. This work showed that cinnamon extract has the potential to be an alternative medicine for tumor treatment<sup>[16]</sup>

#### 5. Immune boosting properties

A study was performed to investigate the effect of dietary supplementation with cinnamon and garlic powder as growth promoter agents on performance, carcass traits, immune responses, serum biochemistry, haematological parameters and thigh meat sensory evaluation in broilers.<sup>[17]</sup> A total of 288, day-old male broilers (Ross 308) were randomly assigned to six treatments with four replicates. The dietary treatments consisted of the basal diet as control, antibiotic group receiving 3 mg/kg flavophospholipol, 2 and 4 g/kg cinnamon or garlic powder added to the basal diet. Body weights of broilers were measured at 1, 14, 28 and 42 days, feed intake was measured at the same periods and feed conversion was calculated, accordingly. At day 42 two birds per replicate were slaughtered for determination of carcass and organ weights and also meat sensory evaluation. Supplementing 2 g/kg cinnamon increased body weight of broilers at 28 and 42 days of age. FCR was calculated to be significantly lower in all treatments compared to the control birds at 28 day period. Feed intake, feed efficiency, internal organ weights and carcass characteristics were not

significantly influenced by the dietary treatments at 42 day. None of the immune related parameters was statistically different among treatments. Broilers fed 4 g/kg garlic powder, had a significantly lower concentration of serum LDL cholesterol and elevated HDL cholesterol at day 42. Serum SGPT enzyme was reduced markedly in 4 g/kg cinnamon group but serum protein, albumin, triglyceride and SGOT were not affected by dietary treatments. Garlic powder significantly increased red blood cell count, haemoglobin concentration and haematocrit percentage compared to the control group. Sensory evaluation of thigh meat displayed no abnormal odor or flavour in meat induced by feed additives. The results suggested that dietary inclusion of 2 g/kg cinnamon can be applied as alternatives to in-feed antibiotics for broiler diets.

## 6. Anti-microbial properties

Ethanol and methylene chloride extracts of cinnamon were compared for their effect on *Helicobacter pylori* growth and urease activity.<sup>[18]</sup> Methylene chloride extract was found to inhibit growth of *H. pylori*, while ethanol extract counteracted its urease activity. Cinnamon extract (from methylene chloride) inhibited *H. pylori* at concentration range of common antibiotics. Complete inhibition in vitro was achieved by 50 µg/ml in solid medium (egg yolk emulsion agar) and by 15 µg/ml in liquid medium (supplemented brain heart infusion broth). The cinnamon extracts were more inhibitory on free urease than on whole cell urease.

## Chemical constituents

Cinnamon contains proteins, carbohydrates, vitamins (A, C, K, niacin), minerals like calcium, iron, magnesium, manganese, phosphorous, sodium and zinc.

The major compounds present in different parts of the tree are the following.<sup>[19]</sup>

Bark: Cinnamaldehyde – 65 to 80%, Eugenol – 5 to 10%.

Leaves: Cinnamaldehyde – 1 to 5% Eugenol – 70 to 95%

Root Bark: Camphor – 60%

Fruit: Trans – cinnamyl acetate and β – caryophyllene

Buds: Terpene hydrocarbons - 78% Alpha Bergamotene - 27.38% Alpha - Copaene - 23.05% Oxygenated terpenoids - 9%

Flowers: (E)-Cinnamyl acetate - 41.98% Trans-alphabergamotene - 7.97% Caryophyllene oxide - 7.2%.

The other chemical constituents identified in cinnamon are: cinnamaldehyde, eugenol, camphor, cinnamyl acetate, β – caryophyllene, terpene hydrocarbons, α -bergamotene, α –

copaene, oxygenated terpenoids, trans- $\alpha$ -bergamotene, caryophyllene oxide, borneo, cinnamic acid, coumarin,  $\alpha$ -thafone,  $\alpha$ -pinene, benzaldehyde, heptanol, sabinene, 1-octen-3-ol, methyl eugenol, isoeugenol, cis-caryophyllene, t-cinnamic acid, cinnamyl acetate,  $\alpha$ -caryophyllene, e-ethyl cinnamate, terpinen-4-ol, linalool,  $\beta$ -pinene, myrcene, p-cymene, limonene,  $\beta$ -phellandrene, 1,8-cineole,  $\gamma$ -terpinene, octanol,  $\alpha$ -terpineol, trans-carveol, nerol, neral, geraniol, geranial, neryl acetate, trans-cinnamaldehyde, cinnamyl alcohol, dihydroeugenol, ethylcis-cinnamate, t-methyl cinnamate, cinnamyl alcohol.<sup>[20]</sup>

### Recent trends in research on cinnamon

It was found that cinnamon taken at a dose of 1 g daily for 3 months produced no significant change in fasting glucose, lipid, A1C, or insulin levels.<sup>[21]</sup> They concluded that the effects of cinnamon differ by population. Studies should be conducted to determine how specific variables (diet, ethnicity, BMI, glucose levels, cinnamon dose, and concurrent medication) affect cinnamon responsiveness. Until then, cinnamon cannot be generally recommended for treatment of type 2 diabetes in an American population. Recently many trials have explored the beneficial effects of cinnamon in Parkinsons, diabetes, blood, and brain. A recent systematic review underlines the surplus health benefits of this clandestine ingredient in the food and the scope of further research in the clinical scenarios viz. Parkinsons, diabetes, etc.<sup>[22]</sup> Nabavi S *et al.*<sup>[23]</sup> provided a brief summary of the history, traditional uses, phytochemistry and clinical impacts of cinnamon to provide a better view of this spice and herbal medicine. They recommended that further studies should be performed on the toxicity of cinnamon prior to its clinical use; studies on the mechanism of the antibacterial effects of its extracts and essential oils; on the separation, purification and identification of the most effective antibacterial constituents of cinnamon and their food- and drug-interactions. Clinical studies are also important to examine the antibacterial effects of extracts and essential oils of cinnamon and its bioactive constituents in different infectious diseases. A recent study showed that cinnamon may aid in improving learning ability.<sup>[24]</sup>

**Table 1: Pharmaceutical/nutraceutical properties of cinnamon**

PROPERTIES	REFERENCES
Anti-diabetic	[25-27]
Anti-microbial	
Immunomodulatory	[30-32]
Alzheimer's disease prevention	[30]
Anti-melanoma activity	[16]
Urinary tract diseases treatment	[31-32]

Anti coagulant	[31]
Food preservative	[33]
Enhances blood circulation	[32]
Anti-ulcer	[34]
Gastro-intestinal diseases treatment	[35]
Anti-cancer	[36-38]
Memory enhancing	[39]
Cardio-protective	[40]
Antioxidant	[37, 20]
Anti-inflammatory	[37,41]
Anti-bacterial	[20]
Anti-fungal	[20]
Anti-obese	[42]
Anti- allergic	[35, 43]

## CONCLUSION

Because of the increasing focus on shifting to positive approach to stay healthier and fit, the market potential for phytonutrients and pharmacologically important non-nutrients is increasing at a faster pace. Today's consumer is much concerned with weight management, healthy heart, immunomodulation, neuroprotection, protection from life style diseases, etc. This scope is offering huge economic potential for manufacturing and marketing of therapeutic foods. Cannamon, being easily available has the potential to serve the nutraceutical industry as a prophylactic food. Isolation and concentration of bioactive constituents of cinnamon as nutraceuticals and its incorporation into other foods as spice supplements offer exciting prospects for spice entrepreneurs of the country as India has already emerged as the leading producer of spices in the world. At the same time, the nutraceutical products available in market based on cinnamon is very less. Though enough basis has been created on the scientific evidence of cinnamon and its components in promoting health as functional foods with its nutraceutical properties, research efforts need to be intensified to further substantiate and validate health claims to instil greater confidence of the public.

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