CINNAMON

Cinnamomum verum J. Presl

Family

Lauraceae (the laurel or avocado family).

Approximately 250 species have been identified among the cinnamon genus with trees being scattered all over the world.[1] Formerly known by the synonym *Cinnamomum zeylanicum*. Not to be confused with cassia (*Cinnamomum cassia* (L.) J.Presl or synonym *Cinnamomum aromaticum* Nees) which is cheaper, has a stronger flavour and is often marketed as 'cinnamon'. *Cinnamomum aromaticum* J.Graham is a synonym for true cinnamon.[2,3]

Parts Used

Stem bark outer.

Description

Cinnamon has been known since remote antiquity. It is native to Sri Lanka, formerly known by the colonial name Ceylon. Other common names include true cinnamon (*verum* means true) and Sri Lanka, or Ceylon, cinnamon. It also grows throughout India, Bangladesh, Java, Sumatra, West Indies, Brazil, Egypt and Vietnam.

This small, evergreen, tropical tree reaches 10 to 15 metres in height and is covered with a thick, scabrous bark. The branches are numerous, strong, horizontal and declining, and the young shoots are speckled with dark green and light orange colours.[4] The leaves are ovate-oblong and range in size from seven to 18cm long.

The inconspicuous flowers have a green-yellowish colour and can be longer than the leaves. They are arranged in panicles and have a distinct, unpleasant odour. The fruit is a purple-black berry measuring around one centimetre and contains a single seed. Cinnamon sticks are made from the bark of the tree and are rolled naturally into a quill shape when the bark is sun-dried. The oil is traditionally prepared by roughly pounding the bark, macerating it in seawater, and then quickly distilling the whole. It is of a golden-yellow colour with the characteristic odour of cinnamon and a very hot, aromatic taste.[5]

Traditional Use

Cinnamon has a long history of use as a culinary spice in many cultures, being sought after in sweet and savoury dishes alike such as breads, cakes and curries. In ancient times cooks relied on spices such as cinnamon to preserve or disguise bad meat and to prevent food spoiling. It was used in Egypt for embalming, and during the Bubonic Plague sponges were soaked in cinnamon and cloves and placed in sick rooms. It has also been burned as incense.

In addition to its culinary uses, in native Ayurvedic medicine cinnamon is considered a remedy for respiratory, digestive and gynaecological ailments. Cinnamon's history as a medicinal plant goes as far back as the Ancient Egyptians and it was included in Chinese medical texts four thousand years ago for heart problems, influenza, digestive and urinary problems. During the explorations of the fifteenth and sixteenth centuries cinnamon was a highly sought-after spice. The Portuguese found cinnamon trees growing in Sri Lanka (Ceylon) in the early 16th century and they subsequently imported cinnamon to Europe during the 16th and 17th centuries. The Dutch occupied Sri Lanka in the mid-17th century until the British captured the island in 1796. As its availability across Europe increased it was then adopted by herbalists for medicinal uses. It was traditionally used as a warming, flavouring agent (adjuvant) and digestive tonic. Its astringent action has made it useful in cases of diarrhoea. It was also used for rheumatism and menstrual disorders such as menorrhagia.[6,7]

Germany's Commission E approves cinnamon for appetite loss, dyspeptic complaints such a mild, spastic conditions of the gastrointestinal tract, bloating and flatulence.[8]

Constituents

In addition to flavour, a critical difference between true cinnamon and cassia is the coumarin content of cassia. The levels of coumarins in cassia appear to be very high and pose health risks if consumed regularly in higher quantities. Coumarins are plant compounds with strong anticoagulant and suspected carcinogenic and hepatotoxic properties. Coumarin is known to cause liver and kidney damage in rats and mice and there are isolated incidents of similar hepatotoxicity in humans. Cassia contains high levels of coumarin (up to 1%), whereas true cinnamon contains either undetectable levels or only traces of coumarin (0.004%). In addition, according to currently available evidence, coumarin does not seem to play a direct role in the observed biological effects of cassia. Hence, although cassia has also shown many beneficial medicinal properties, its coumarin content is likely to be an obstacle against regular use as a pharmaceutical agent, unlike in the case of true cinnamon.[9,10,11]

Three of the main components of the essential oils obtained from cinnamon are trans-cinnamaldehyde, eugenol and linalool, which represent 82.5% of the total composition. Trans-cinnamaldehyde accounts for approximately 49.9 to 62.8% of the total amount of bark oil. Cinnamaldehyde and eugenol are also the major components. *Cinnamomum verum* is stated to contain the highest amount of eugenol.[12] Cassia usually produces only one main type of oil, almost 95% of this oil consists of cinnamaldehyde with slight variation between the different parts of the plant. Other constituents include methoxycinnamaldehyde, benzaldehyde, coumarin, limonene, eugenol and cinnamyl acetate. Methods of distinguishing true cinnamon oil from cassia oil are based on the presence of increased content of benzaldehyde, methoxycinnamaldehyde and coumarin in cassia oil.[13,14]

Other constituents are oligopolymeric procyanidins, cinnamic acid, phenolic acids, pentacyclic diterpenes cinnzeylanol and it's acetyl derivative cinnzeylanine and the sugars mannitol, L-arabino-D-xylanose, L-arabinose, D-xylose, α-D-glucan as well as mucilage polysaccharides. Each 100g contains vitamin A: 260IU, thiamine: 0.02mg, riboflavin: 0.14mg, niacin: 1.3mg, ascorbic acid: 28mg, Ca: 1.228mg, P: 61mg, Fe: 38mg, Mg: 56mg, Na: 26mg, K: 500mg, Zn: 2mg.[15]

Actions

Hypoglycaemic, hypoinsulinaemic, antioxidant, anticancer, antimicrobial, antifungal, antiviral, immunomodulator, astringent, antidiarrhoeal, carminative, hypolipidaemic.

Pharmacological Activity

The available *in vitro* and *in vivo* evidence suggests that cinnamon has many beneficial health effects. However, since data on humans is sparse, randomised controlled trials in humans will be necessary to determine whether these effects have public health implications.[16]

Metabolic Activities: Glucose and Insulin Modulation

The mechanism of action by which cinnamon reduces blood glucose has been well studied *in vitro* and *in vivo*. It seems that cinnamon reduces intestinal glucose absorption by inhibiting enzymes, stimulating cellular glucose uptake, glycogen synthesis, insulin release, potentiating insulin receptor activity and inhibiting gluconeogenesis by effects on key regulatory enzymes.[17]

In 2017 a four month randomised, double blind, placebo controlled clinical trial evaluating the potential effects of true cinnamon extract as a pharmaceutical agent in patients with type 2 diabetes was conducted in Sri Lanka. To the knowledge of the doctors involved this is one of the first randomised controlled trials evaluating the effects of supplementation of true cinnamon in patients with diabetes. Patients received either a cinnamon oral capsule (250mg or 500mg) or an identical placebo daily for four months. While the results have not yet been published one of the doctors involved told the author that for the patients taking cinnamon there was a reduction in fasting blood sugar levels and glycated haemoglobin (HbA1c). For people with diabetes this is important as the higher the HbA1c the greater the risk of developing diabetes related complications. There was also a reduction in total cholesterol and low density lipoprotein (LDL) levels.[18]

Taking 3g of cinnamon daily for 16 weeks resulted in significant improvements in all components of metabolic syndrome in a sample of Asian Indians in north India. In this 2017 double blind randomised controlled trial 116 individuals with metabolic syndrome were randomised to two dietary intervention groups, cinnamon (Six 500g capsules (3g) daily) or placebo. Significantly greater decrease in fasting blood glucose, glycosylated haemoglobin, waist circumference and body mass index was observed in the cinnamon group compared to placebo group. Other parameters which showed significantly greater improvement were waist to hip ratio, blood pressure, serum total cholesterol, low-density lipoprotein cholesterol, serum triglycerides and high-density lipoprotein cholesterol.[19]

A recent meta-analysis, and a systematic review, on the effects of cinnamon on diabetes demonstrate numerous beneficial effects both *in vitro* and *in vivo*. The beneficial effects of cinnamon *in vivo* include attenuation of weight loss associated with diabetes, reduction of Fasting Blood Glucose, reducing LDL and increasing HDL cholesterol, reducing HbA1c and increasing circulating insulin levels. *In vitro* cinnamon has demonstrated a potential for reducing post-prandial (following a meal) intestinal glucose absorption by inhibiting the activity of enzymes involved in carbohydrate metabolism (pancreatic α–amylase and α–glucosidase), stimulating cellular glucose uptake by membrane translocation of glucose transporter 4 (GLUT4) and stimulating glucose metabolism. Cinnamtannin B1 was identified as the potential active compound responsible for these effects. In addition, cinnamon also showed beneficial effects against diabetic neuropathy and nephropathy.[20,21]

The results of a 2014 study suggest that cinnamon may provide a natural and safe solution for the reduction of postprandial hyperglycaemia (high blood sugar after eating) and therefore help to reduce the risks of developing metabolic disorders. Postprandial hyperglycaemia is a known risk factor for the development of several health disorders including type 2 diabetes, obesity, oxidative stress and cardiovascular diseases. One encouraging approach for better control of postprandial hyperglycaemia is to reduce carbohydrate digestion. Cinnamon extracts have been known for managing blood glucose. However, their effects on inhibiting digestion of carbohydrate have been poorly analysed. The aim of this study was to investigate the acute effect of a specific Ceylon cinnamon hydro-alcoholic extract (CCE) on carbohydrate

digestion and post-meal blood glucose reduction. *In vitro* enzymatic assays and *in vivo* starch tolerance tests in rats were designed as preclinical assays. Then a randomised, double-blind, placebo-controlled, cross-over clinical trial was conducted in 18 healthy female and male volunteers. Following the intake of one gram of CCE the subjects ate a standardised meal. Blood samples were collected during the two hours following the meal to measure glucose and insulin concentrations. In the *in vitro* study CCE demonstrated that it inhibited pancreatic α-amylase activity with an IC50 of 25µg/mL. In the *in vivo* study, CCE was shown to acutely reduce the glycaemic response to starch in a dose-dependent manner in rats. This effect was significant from the dose of 12.5mg/kg of body weight. In both the *in vitro* and *in vivo* studies the hydro-alcoholic extract was more efficacious than the aqueous extract. In the human clinical trial, one gram of CCE lowered the area under the curve of glycaemia between 0 and 120 minutes by 14.8% ($p = .15$) and between 0 and 60 minutes by 21.2% ($p < .05$) compared to the placebo. This effect occurred without stimulating insulin secretion. No adverse effects were reported.[22]

Non-alcoholic fatty liver disease (NAFLD) is the most prevalent cause of hepatic injury in the world. One of the most important therapeutic strategies for this disease is modulating insulin resistance and oxidative stress. A 2014 study investigated the hypothesis that supplementation with cinnamon exerts an insulin sensitiser effect in patients with NAFLD. The study suggests that taking 1500mg cinnamon daily may be effective in improving NAFLD characteristics. In a double-blind, placebo-controlled trial with two parallel groups, fifty patients with NAFLD were randomised to receive daily supplementation with either two capsules of cinnamon (each capsule contain 750mg cinnamon) or two placebo capsules, daily for 12 weeks. During the intervention, all patients were given advice on how to implement a balanced diet and physical activity into their daily lives. In the treatment group ($p < .05$), significant decreases in HOMA (Homeostatic Model Assessment) index, FBS (fasting blood glucose), total cholesterol, triglyceride, ALT (alanine aminotransferase), AST (aspartate aminotransferase), GGT (gamma glutamine transpeptidase), and high-sensitivity C-reactive protein were seen, but there was no significant change in serum high-density lipoprotein levels ($p = .122$). In both groups, low-density lipoproteins decreased significantly ($p < .05$).[23]

Treatment of diabetic subjects with cinnamon has demonstrated an improvement in blood glucose concentrations and insulin sensitivity but the underlying mechanisms remain unclear. A 2014 study intending to elucidate the impact of cinnamon effects on the brain, by using isolated astrocytes and an obese and diabetic mouse model, has found that cinnamon extract improved insulin action in the brain, as well as brain activity and locomotion. This specific effect may represent an important central feature of cinnamon in improving insulin action in the brain, and mediates metabolic alterations in the periphery to decrease liver fat and improve glucose homeostasis.[24]

The results of a study in 2014 indicate that cinnamon ameliorates type 2 diabetes by inducing GLUT4 translocation via the AMPK (an enzyme) signalling pathway. The study also found insulin antagonistically regulates the activation of AMPK. It was previously demonstrated that cinnamon ameliorates type 1 diabetes induced by streptozotocin in rats through the up-regulation of GLUT4 translocation in both muscle and adipose tissues. This study was aimed at clarifying the detailed mechanisms with which cinnamon increases the glucose uptake *in vivo* and in cell culture systems. The results showed that cinnamon stimulated the phosphorylation of AMPK and acetyl-CoA carboxylase. For the first time it was found that insulin suppressed AMPK activation in the adipocyte.[25]

Cinnamon has been studied in randomised controlled trials (RCTs) for its glycaemic-lowering effects but studies have been small and show conflicting results. A prior meta-analysis did not show significant results but several RCTs have been published since then. In 2013 an updated systematic review and meta-analysis of RCTs evaluating cinnamon's effect on glycaemia and lipid levels was conducted. In a meta-analysis of 10 RCTs (N = 543 patients), cinnamon doses of 120mg/d to 6g/d for four to 18 weeks reduced levels of fasting plasma glucose, total cholesterol, LDL-C and triglycerides. Cinnamon also increased levels of HDL-C. The consumption of cinnamon is associated with a statistically significant decrease in levels of

fasting plasma glucose, total cholesterol, LDL-C and triglyceride levels, and an increase in HDL-C levels however no significant effect on haemoglobin A1c was found. The high degree of heterogeneity may limit the ability to apply these results to patient care because the preferred dose and duration of therapy are unclear.[26]

A study suggested that cinnamon would improve insulin action via increasing glucose uptake *in vivo*, at least in part through enhancing the insulin-signalling pathway in skeletal muscle.[27] Early administration of cinnamon to rats fed a high fructose diet prevented the development of insulin resistance at least in part by enhancing insulin signalling.[28]

Some studies have examined the effects of chromium and cinnamon in metabolic syndrome and diabetes. In a double-blind placebo-controlled study it has been demonstrated that glucose, insulin, cholesterol and HbA1c are all improved in patients with type 2 diabetes following chromium supplementation. It has also been shown that cinnamon polyphenols improve insulin sensitivity in *in vitro*, animal and human studies. Subjects with metabolic syndrome who consume an aqueous extract of cinnamon have been shown to have improved fasting blood glucose, systolic blood pressure, body fat and increased lean body mass compared with the placebo group.[29]

Positive results were found in one trial examining cinnamon in 60 people with type 2 diabetes. Groups consumed between 1 to 6g of cinnamon daily or placebo. The results found 1, 3, or 6g of cinnamon per day reduces serum glucose, triglyceride, LDL cholesterol, and total cholesterol in people with type 2 diabetes and suggest that the inclusion of cinnamon in the diet of people with type 2 diabetes will reduce risk factors associated with diabetes and cardiovascular diseases.[30]

Cinnamon equivalent to three grams of powder per day was examined for its effects on fasting plasma glucose level compared to placebo. There was a significantly higher reduction in the cinnamon group (10.3%) than in the placebo group (3.4%). No significant differences were observed regarding HbA1c or lipid profiles. The decrease in plasma glucose correlated significantly with the baseline concentrations, indicating that subjects with a higher initial plasma glucose level may benefit more from cinnamon intake. No adverse effects were observed. The cinnamon extract seems to have a moderate effect in reducing fasting plasma glucose concentrations in diabetic patients with poor glycaemic control.[31]

Studies utilising an aqueous extract of cinnamon, high in type A polyphenols, have also demonstrated improvements in fasting glucose, glucose tolerance and insulin sensitivity in women with insulin resistance associated with the polycystic ovary syndrome.[32]

Unfortunately, other human trials have found less favourable effects but may have been limited by specific variables (diet, ethnicity, BMI, glucose levels, cinnamon dose and concurrent medication). The effect of cinnamon (1g/day) or placebo on glycaemic control in adolescents with type 1 diabetes was examined. No significant differences in final A1C, change in A1C, total daily insulin intake, or number of hypoglycaemic episodes were found between the cinnamon and placebo arms.[33] Another study examined the effect of cinnamon (1g/day) on glucose and lipid levels in American adults. There was no difference between the cinnamon group and placebo after three months.[34]

The effect of cinnamon on the rate of gastric emptying, the postprandial blood glucose response, and satiety was examined in healthy subjects. The addition of cinnamon to the meal (rice pudding) significantly delayed gastric emptying and lowered the postprandial glucose response. The effect of cinnamon on satiety was not significant. Inclusion of cinnamon in the diet lowers the postprandial glucose response, a change that is at least partially explained by a delayed gastric emptying.[35]

Cholesterol Lowering Activity

The mechanism for the lipid lowering effects of cinnamon is not clearly described in literature. Its high dietary fibre content could result in reduced intestinal lipid absorption and the high vitamin/anti-oxidant content is likely to result in increased lipid metabolism. Insulin plays a key role in lipid metabolism and it is possible that increased serum insulin levels following cinnamon administration also contribute towards reducing lipid levels.[36]

A recent study demonstrated that cinnamon reduced total cholesterol, LDL cholesterol and triglycerides while increasing HDL cholesterol

in diabetic rats. Similar results have also been observed in hyperlipidaemic albino rabbits. However, feeding cinnamon to animals at levels corresponding to the average human dietary intake has not shown to reduce lipid levels significantly.[37,38,39]

Another recent study examined the effects of cinnamon on mean arterial blood pressure (BP) of normotensive (normal blood pressure-NR) rats, salt-loaded hypertensive rats (SLHR), L-NAME hypertensive rats (LNHR) and spontaneously hypertensive rats (SHR). Immediately after intravenous administration a significant drop of BP was shown in NTR, SLHR and LNHR in a dose dependent manner, the drop in BP was not dose dependent in SHR.[40]

Similar effects were demonstrated in another study in NTR and SLHR, they also showed that cinnamon has a vaso-relaxant effect on the rat thoracic aortic ring segments, suggesting that cinnamon might be inhibiting extracellular Ca 2+ through L-type voltage-sensitive channels.[41]

Anti-inflammatory and Antioxidant Activity

To ease menstruation and menstrual pain was the most common use of cinnamon as reported by the public in a 2018 study on the ethnopharmacological uses of cinnamon in Khobar, Saudi Arabia. Studies have reported cinnamon as an aid for the ease of menstruation and in reducing the intensity of pain associated with menstrual cycle (see below). The second most common use reported was in the regulation of blood sugar level. A small fraction used it as a digestive aid and for weight loss. The uses of cinnamon in the study were found to be attributed to the use by family or relatives and the knowledge from them.[42]

Cinnamon can be regarded as a safe and effective treatment for dysmenorrhea in young women (aged 18 to 30) following a recent randomised double-blind trial. In the study 38 received capsules containing 420mg cinnamon three times a day in 24 hours during the first three days of the menstrual cycle. Cinnamon reduced the severity of primary dysmenorrhea had a significant effect on reduction of pain, menstrual bleeding, nausea and vomiting without side effects.[43]

The results of a 2014 study suggest that cinnamon can induce cognitive improvement in scopolamine (SCOP)-treated rats and this effect can be attributed to a certain extent to decreased oxidative stress. The study was designed to assess the effect of extract of cinnamon bark on cognitive performance of SCOP-treated rats and on associated altered oxidative stress markers in the brain of rats. The SCOP-treated group showed significantly impaired acquisition and retention of memory as compared to the saline- and vehicle-treated groups. Pre-treatment with cinnamon extract (200 and 400mg/kg) for 21 days significantly reversed SCOP-induced amnesia.[44]

Eighteen operating room personnel were treated with cinnamon (100mg/300mL tea) daily for 10 days and blood samples were analysed for biomarkers of oxidative stress including Lipid Peroxidation Level (LPO), Total Antioxidant Power (TAP) and Total Thiol Molecules (TTM). Treatment of subjects with cinnamon induced a significant reduction in plasma LPO, however no statistically significant alteration was found for plasma TAP and TTM after 10 days treatment with cinnamon.[45]

Treatment of 54 healthy volunteers with cinnamon (100mg/30mL of tea) daily were significantly effective in the reduction of lipid peroxidation and increasing TAP and TTM in comparison with controls. The extent of increase in plasma TBARS and TAP for the cinnamon group was significantly higher than in those given regular tea only.[46]

Cinnamon was found to be potent in free radical scavenging activity especially against DPPH radicals and ABTS radical cations, while the hydroxyl and superoxide radicals were also scavenged by the tested compounds.[47] Similar findings were found in another study which showed that cinnamon has 65.3% anti-oxidant activity and strong free radical scavenging activity.[48]

Cinnamon has been found in many studies to have antioxidant actions making it a suitable and palatable addition to preserve food and promote health. The etheric (0.69mg), methanolic (0.88mg) and aqueous (0.44mg) cinnamon extracts inhibited the oxidative process in 68%, 95.5% and 87.5% respectively.[49,50]

Anticancer Activity

Cinnamon compounds strongly inhibited *in vitro* growth of 29 kinds of human cancer cells and *in vivo* growth of human tumour xenograft without the loss of body weight in nude mice.[51]

In vitro and *in vivo* cinnamon was found to strongly inhibit the expression of pro-angiogenic factors and master regulators of tumour progression not only in melanoma cell lines but also in experimental melanoma model. In addition, cinnamon treatment increased the anti-tumour activities of CD8+ T cells by increasing the levels of cytolytic molecules and their cytotoxic activity.[52]

Antimicrobial, Antifungal and Antiviral Activity

In 2014 there were more than 30 different studies evaluating the *in vitro* anti-microbial properties of cinnamon. It has shown potential antimicrobial action against a wide variety of bacteria including *Escherichia coli, Helicobacter pylori, Listeria monocytogenes, Salmonella typhi, Staphylococcus aureus* and *Streptococcus agalactiae*. In addition there seems to be activity against numerous fungi including *Aspergillus fiavus* and *Candida albicans*. Cinnamon has also demonstrated activity against the human rota-virus.[53]

Cinnamon has been shown to have antifungal activity against some strains of *Candida* spp.[54] A small trial of five patients with HIV infection and oral candidiasis received a commercially available cinnamon preparation for one week. Three of the five patients had improvement of their oral candidiasis. Further clinical trials will be necessary to determine the usefulness of cinnamon for the treatment of mucosal candidiasis.[55]

Cinnamon was one herb studied for its effects against three strains of *Mycobacterium avium subsp. paratuberculosis*. The most effective compound was trans-cinnamaldehyde followed by cinnamon oil.[56]

Indications

- Digestive disorders including flatulent dyspepsia, nausea and diarrhoea
- Bacterial and viral infections including the common cold and influenza
- Fungal infections including tinea pedis and candida
- Diabetes, obesity and metabolic syndrome
- Hyperlipidaemia
- Possible cancer prophylaxis and treatment adjuvant
- Oxidative stress and inflammatory disorders

Energetics

Pungent, sweet, astringent, heating.

Use in Pregnancy

There are no known problems with the use of cinnamon during pregnancy and lactation provided that doses do not greatly exceed the amounts used in food.[57]

Contraindications

None known.

Drug Interactions

Caution with antidiabetic drugs.

Administration and Dosage

Liquid Extract:	1:2
Alcohol:	50%
Weekly Dosage:[58]	20 to 40mL

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