Cinnamon (*Cinnamomum spp.)*

Common Indications:

- Blood sugar regulation
- Metabolic syndrome
- Hypertension
- Polycystic Ovarian Syndrome
- Antioxidant
- Immune support, Allergy and Asthma
- Infections, Antibacterial and Fungicidal
- Dyspepsia and Flatulence
- Dyslipidemia
- Tumor

Additional potential indications:

- Depression
- Inflammation, Pain Relief and Fever
- Neuroprotection
- Osteopenia

General Comments:

Cinnamon is often thought of in regard to its impact on glucose regulation but as you will read, it has many other functions of importance. Cinnamon has a long history of use in medical applications. Like most spices, cinnamon is an excellent antioxidant and so has a therapeutic role in metabolic syndrome, blood glucose regulation, blood pressure, and gut and immune issues. *Cinnamomum zeylanicum as well as other cinnamomum* species grow all over the world and it is from the bark of this plant that we derive the spice.

Benefits & Mechanism of Action:

Blood Sugar Regulation

Cinnamon improves blood glucose levels and insulin sensitivity in laboratory and human studies. Enhanced GLUT-4 activity and sensitivity creates this improved glucose control. Enhanced insulin response via increased glucagon-like peptide-1 (GLP-1) concentrations was seen with doses of 3 grams of cinnamon without significantly affecting gastric

inhibitory peptide (GIP), the ghrelin concentration, satiety, or gastric emptying rate (GER).[1] Cinnamon in the diet reduced the postprandial glucose response without affecting satiety. Additional studies have found that the cinnamon improved glycemic control and insulin sensitivity.[2,3]

An in vitro study of a water-soluble extract improved the postprandial overproduction of intestinal apoB48-containing lipoproteins by ameliorating intestinal insulin resistance.[4] Studies utilizing 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.[5]

A 2013 Cochrane Database System Review of cinnamon reported that there was insufficient evidence that cinnamon helps those with type 1 or type 2 diabetes.[6] However, this study included research using *Cinnamomum cassia* and *Cinnamomum zeylanicum*. Most clinical positive research uses the species *Cinnamomum zeylanicum*. A 2012 comprehensive systematic review and meta-analysis reported that *Cinnamomum zeylanicum* demonstrated numerous beneficial effects both *in vitro* and *in vivo* as a potential therapeutic agent for diabetes mellitus.[7]

Since the Cochrane review, there have been 3 additional studies that have all had positive results using cinnamon for glycemic control.[8,9,10]

Metabolic syndrome

There are two studies that showed a positive effect on percentage of body fat and lean body mass when consuming the aqueous extract of cinnamon. The effect is attributed to high levels of polyphenol compounds in the aqueous extract.[11,12]

Hypertension

When studied in patients with Type 2 Diabetes, cinnamon has been shown to statistically significantly lower systolic and diastolic blood pressure regardless of concurrent antihyperglycemic or antihypertensive medication use or diet. [13,14]

Polycystic Ovarian Syndrome

A pilot study of non-diabetic women with polycystic ovarian syndrome showed a significant reduction in fasting glucose and insulin resistance.[5]

Antioxidant

Multiple studies have shown that the polyphenols found in cinnamon have a powerful antioxidant effect.[15,16] An animal study in India showed that when being fed a high fat diet along with cinnamon, glutathione content was markedly increased and lipid conjugated

dienes and hydroperoxides (the primary products of lipid peroxidation) were reduced.[17] This supports antioxidant activity through the ability to activate antioxidant enzymes.[17]

Immune support, Allergies and Asthma

Cinnamon extract has been shown to reduce degranulation, reduce cysteinyl leukotriene production, and reduce the expression of proinflammatory cytokines and proteases in human mast cells.[18] These are all anti-allergy activities. Animal studies have also shown a reduction in lung inflammation, increased oxygen supply to cells, reduced goblet cell hyperplasia, reduced mucous secretion, reduced eosinophil infiltrates, and mast cell stabilization.[19] This could be beneficial in asthma management.

Infections, Antibacterial and Fungicidal (including *Helicobacter pylori*)

Antibacterial and fungicidal activity of cinnamon, all varieties, is attributed to cinnamaldehyde, eugenol, caryophyllene, and 1,8 cineole. Cinnamon has been reported to have antifungal activity and cause marked improvement in symptoms associated with oral candidiasis.[20] The study also found in an *in vitro* test that cinnamon (specifically *C. zeylanicum*) was highly active against fluconazole-resistant and- susceptible Candida isolates.[20]

Cinnamomum verum has shown activity against *Bacillus subtilis, Escherichia coli, Saccharomyces cerevisiae, Candida albicans, Listeria monocytogenes,* and *Salmonella enterica.*[21,22,23,24,25] It has been recommended as a treatment for candidiasis.[26]

Cinnamomum cassia extracts significantly inhibited *Helicobacter pylori* and produced zones of inhibition greater than or equal to those from commonly used antibiotics.[27] One small study (15 patients) found that 40mg of cinnamon twice daily for four weeks was ineffective in eradicating the *H. pylori*.[28] *C. cassia* oil showed antifungal properties, requiring less amphotericin per dose in a 2006 study.[29] *C. cassia* has also shown effectiveness against *Escherichia coli* and *Staphylococcus aureus*.[30]

Dyspepsia and Flatulence

Cinnamaldehyde, found in cinnamon, has been shown in animal studies to decrease smooth muscle contractions in the trachea, ileum, and colon.[31] It has also showed antifoaming activity.[32] The German Commission E has approved cinnamon bark and Chinese cinnamon for the treatment of loss of appetite, mild gastrointestinal spasms, bloating, and flatulence.[33]

Dyslipidemia

Weight gain and obesity leads to increased levels of proinflammatory cytokines, such as TNF-alpha, which in turn stimulates the overproduction of intestinal apolipoprotein (apo) B48 containing lipoproteins leading to further weight gain. Water-soluble cinnamon

extract reverses TNF-alpha-induced overproduction of intestinal apoB48 by regulating gene expression involving inflammatory, insulin, and lipoprotein signaling pathways.[34,35] There appeared to be a reduction in the inflammatory driven intestinal dyslipidemia. HMG-CoA reductase activity is also reduced with cinnamon extracts thus having a possible role in addressing lipid and metabolic syndrome problems. Reservation exists here due to one study in rate that showed an actual rise in cholesterol levels.[36] In vitro studies have shown that hydrophilic cinnamon extracts inhibit copper-mediated LDL oxidation and LDL phagocytosis by macrophages, exhibit strong anti-glycation activity, have some ferric ion removal ability, and have hypolipidemic activity.[37]

Tumor

Cinnamon has shown anticancer activity through multiple pathways, including cytotoxicity.[38] When administered orally or by intramuscular injection, cinnamon significantly inhibited the expression of pro-angiogenic factors and master regulators of tumor progression.[39] The effects were seen in melanoma cell lines and in a melanoma experimental model. An additional study also showed an increase in the anti-tumor activities of $CD8^+$ T cells by increasing the levels of the cytotoxic molecules, increasing their activity.[40] These studies highlight the importance of cinnamon in types of cancer associated with tumor angiogenesis.

An animal study looking at human melanoma cells showed that cinnamon worked in multiple ways, including G1 cell-cycle arrest, elevated intracellular ROS, and impairing invasiveness.[41]

Aqueous extract of cinnamon has also been shown to disrupt cell proliferation in leukemic cells by disrupting the G2/M phase.[42] Cinnamon interrupts a critical phosphorylating/dephosphorylating signaling event that, when not disrupted, propels cells through the G2/M phase.

Depression

Preclinical model showed that animal behavior on varying doses of *C. zeylanicum* had effects similar to imipramine (a tricyclic antidepressant).[43]

Inflammation, Pain Relief and Fever

Cinnamon exhibits anti-inflammatory activity by inhibiting nitric oxide production via inhibition of NF-kappaB.[44] Cinnamon bark oil has shown potent antioxidant and anti-inflammatory activity.[32,45,46,47]

Cinnamomum zeylanicum has shown dose-dependent antinociceptive effects.[48] Antipyretic activity and reduced occurrence of ulcers was shown with dose-dependent aqueous *Cinnamomum cassia*.[49]

Neuroprotection

Aqueous extract of cinnamon inhibited tau aggregation and filament formation, hallmarks in Alzheimer's disease, in a 2009 study.[50] Another study in 2013 demonstrated neuroprotective effects of type A cinnamon polyphenols through their actions of upregulating prosurvival proteins, activating mitogen-activated protein kinase pathways and decreasing proinflammatory cytokines.[51]

Osteopenia

In a 2008 study, *Cinnamomum zeylanicam* exhibited strong inhibitory effects on osteoclast-like cell formation without affecting cell viability.[52]

Dose:

General

- Dried bark (crushed cinnamon)*: 1.5-6 g (¼-1 teaspoonful) taken up to four times daily
- Fluid extract (1:1)*: 0.5-1 mL taken up to three times daily
- Fluid extract (20:1), Cinnulin PF®: 250 mg taken up to 2 times daily, 1 hour before meals
- Tea*: half to three-quarters teaspoon of powdered cinnamon in a cup of boiling water 2-3 times daily with meals
- Essential oil*: 0.05-0.2 mL diluted in a carrier oil

*Note: There are various products with different dosages and standardizations to choose from. When choosing a dietary supplement, select those from reputable manufacturers.

Type 2 Diabetes

- 1-6 grams daily for a minimum of 12 weeks to assess response

Cautions and Side Effects:

- Cinnamon has been reported to be safe in recommended doses.
- An oral lethal dose (in rats), LD_{50}, has been calculated at 4.16g/kg and 3.4mL/kg body weight.
- When applied topically, allergic contact dermatitis in response to cinnamaldehyde may occur[53,54,55]
- Mouth irritation and cinnamon-induced stomatitis may occur[56]

Cinnamon is contraindicated in people with an allergy to cinnamon or Peru balsom, in cases of fever of unknown origin, or active stomach or duodenal ulcers.[31]

Cinnamon should not be used therapeutically during pregnancy, however usual dietary intake is likely safe. Studies are contradictory as to possible teratogenicity from therapeutic doses of cinnamon.

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