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File: ■ Cinnamon (*Cinnamomum* spp., Lauraceae)
■ Systematic Review

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RE: Review of the Health Benefits of Cinnamon

Kawatra P, Rajagopalan R. Cinnamon: mystic powers of a minute ingredient. *Pharmacognosy Res*. June 2015;7(Suppl 1):S1-S6.

Historically, the use of cinnamon (*Cinnamomum* spp., Lauraceae) dates back to about 2800 BCE in China. It was used in Biblical anointing oils and to embalm Egyptian mummies. Its desirability and scarcity were major drivers of European exploration in the 15th century CE, motivating the voyages of Christopher Columbus and Vasco da Gama. True or Ceylon cinnamon (*C. verum* syn. *C. zeylanicum*), found in Ceylon (now Sri Lanka), made that nation extremely desirable to Europeans seeking trade supremacy. It was ruled successively by the Portuguese, Dutch, and British before gaining independence in 1948.

Cinnamon is now well known to have several potential health benefits. The authors conducted a systematic review of online publications on health benefits of cinnamon species, including true or Ceylon cinnamon, Saigon cinnamon (*C. loureirii*), and cassia (*C. aromaticum* syn. *C. cassia*). Indonesian cinnamon (*C. burmanni*) and pseudocinnamon (*C. osmophloeum*) also are mentioned. While cinnamon bark, rich in cinnamaldehyde, is most commonly used, pseudocinnamon's leaves contain its cinnamaldehyde component. Cinnamon leaf oil contains eugenol; root-bark oil, camphor; leaves and flowers, trans-cinnamyl acetate. Cassia cinnamon has the highest levels of hepatotoxic, carcinogenic coumarin; true cinnamon and pseudocinnamon have low levels.

Cinnamon may be useful in managing diabetes. While results of several small trials have been conflicting, a meta-analysis of ten randomized, controlled trials (RCTs) including 543 patients found that 120 mg/d to 6 g/d cinnamon taken for approximately four months produced a statistically significant decrease in fasting plasma glucose and an improved lipid profile. Cinnamon is thought to be an insulin-mimetic and insulin-sensitizing agent. Cassia affects phosphorylation of signaling proteins and enhances insulin-sensitive glucose transporter expression. Cinnamon extracts have been shown to increase expression of peroxisome proliferator-activated receptor (PPAR) α and γ, as do thiazolidinediones in type 2 diabetes. Lipid profiles, important in cardiovascular health and diabetes, improved upon exposure to cinnamon extracts in vitro, but were not affected in an animal study. Further studies using human subjects are needed. Cinnamaldehyde and cinnamic acid are thought to be cardioprotective due to their ability to produce nitric oxide. Cinnamaldehyde also inhibits L-type calcium channels in vascular smooth muscles, contributing to vasodilation.

Cinnamon also has antimicrobial, antioxidant, and anti-inflammatory properties. It is used to inhibit growth of *Listeria* spp. and *Escherichia coli* in foods. Cinnamon oil's antimicrobial action is in the range of 10-150 μg ml^{-1}. Cinnamon can alter expression of the gene icaA,

important in formation of bacterial biofilms. While literature on the effects of cinnamon on viruses is limited, it is thought to inhibit viral protein synthesis and was shown to improve survival in mice infected with influenza. A trial of true cinnamon in commercially available preparations against fluconazole-resistant oral candidiasis in five people with HIV found improvement, highlighting a need for additional trials. In combination with clove (*Syzygium aromaticum*, Myrtaceae) oil, cinnamon was effective against the fungus *Aspergillus flavus*.

Lipid oxidation, a challenge during food processing, may be prevented or slowed with the use of cinnamon extracts; a methanolic extract had higher antioxidant properties than either water or ethanolic extracts. In vitro, the eugenol component inhibited peroxynitrite-induced nitration and lipid peroxidation. Cinnamon's antioxidant effects are now being studied in liver diseases, where an ethanolic extract has shown the ability to reduce carbon tetrachloride-induced lipid peroxidation and oxidative stress. A water extract of cinnamon showed anti-inflammatory properties in vitro, reducing levels of tumor necrosis factor-α and interleukin-6. Several compounds in pseudocinnamon also are known to be anti-inflammatory.

Cinnamon's antibacterial activity may also be important in cancer prevention and treatment. Stomach cancer and other serious conditions are often attributed to gram-negative *Helicobacter pylori*; initial research indicates that cinnamon may inhibit this microorganism. In vitro, a cassia extract inhibited the survival, viability, and proliferation of cancer cells without affecting healthy cells. The extract also induced apoptosis in tumor cells and inhibited nuclear factor-kappa B. Two of its derivatives induced apoptosis by raising levels of reactive oxygen species in cancer cells; one of them also made cells more susceptible to oxidative stress by inhibiting proteasome activity. In melanoma cells, cinnamon impeded angiogenesis and increased activity of CD8(+) T cells. The polyphenol components of cinnamon potently inhibited vascular endothelial growth factor.

Finally, cinnamon may also benefit mental cognition by boosting the brain's ability to use glucose. Its ability to reduce oxidative stress and improve insulin resistance are also important mechanisms in brain health.

Highlighting the understudied health effects of one of mankind's most-used spices, this review is marred by its early use of a few words that may be off-putting to some readers; the title offers two examples in *mystic* and *minute*. "The *surplus* health benefits of this *clandestine* ingredient" is also cited in the abstract. (Italics added.) However, the remainder of the report is relatively straightforward.

—Mariann Garner-Wizard

Peer Reviewer Comments:
Data support that *C. verum* has very low coumarin levels, and *C. cassia* the highest, but *C. burmanni* and *C. loureirii* have quite low levels too, as long as they are not adulterated with *C. cassia*. The paper actually says that only *C. verum* has low levels (Table 1).

The authors refer to particular plants as "indigenous" but then fail to identify where the plant is indigenous.

Referenced article can be accessed at http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4466762/.