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Cinnamon and Health

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Cinnamon has been used as a spice and as traditional herbal medicine for centuries. The available in vitro and animal in vivo evidence suggests that cinnamon has anti-inflammatory, antimicrobial, antioxidant, antitumor, cardiovascular, cholesterol-lowering, and immunomodulatory effects. In vitro studies have demonstrated that cinnamon may act as an insulin mimetic, to potentiate insulin activity or to stimulate cellular glucose metabolism. Furthermore, animal studies have demonstrated strong hypoglycemic properties. However, there are only very few well-controlled clinical studies, a fact that limits the conclusions that can be made about the potential health benefits of cinnamon for free-living humans. The use of cinnamon as an adjunct to the treatment of type 2 diabetes mellitus is the most promising area, but further research is needed before definitive recommendations can be made.

Keywords Cinnamomum, spice, insulin, diabetes, cinnamon

INTRODUCTION

The purpose of this paper is to provide a comprehensive summary of the current scientific literature on the effect of cinnamon on several physiological and health-related conditions.

Cinnamon has been used as a spice in several cultures for centuries. In addition to its culinary uses, cinnamon has been employed as a stomachic and carminative for gastrointestinal complaints as well as other ailments and is still used for these conditions in many countries (Teuscher, 2003). The German Commission E and the European Scientific Cooperative on Phytotherapy (ESCOP) approved two medicinal herbs of the genus *Cinnamomum*: *C. zeylanicum* (Blumenthal et al., 1998a; European Scientific Cooperative on Phytotherapy, 2003) and *C. cassia* (Blumenthal et al., 1998b). The bark is the only part of these plants that is used as a spice or for medical purposes (*Cinnamomi cortex*) (Blumenthal et al., 1998a; 1998b).

The volatile oils obtained from the bark, leaf, and root bark of *Cinnamomum zeylanicum* and *C. cassia* vary significantly in chemical composition which suggests that they vary in their pharmacological effects as well (Shen et al., 2002; Wijesekera, 1978). These oils of three different plant parts possess the same array of monoterpene hydrocarbons in different proportions. However, each oil has a different primary constituent: cinnamaldehyde (in the bark oil), eugenol (in the leaf oil), or camphor (in the root-bark oil).

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Three of the main components of the essential oil obtained from the bark of *C. zeylanicum* are *trans*-cinnamaldehyde, eugenol, and linalool, which, according to Chericoni et al. (2005) represent 82.5% of the total composition. *Trans*-cinnamaldehyde, the major component of *C. zeylanicum* bark oil, accounts for approximately 49.9% (Singh et al. 2007) to 62.8% (Simic et al., 2004) of the total amount. Cinnamaldehyde and eugenol also are the major components of cinnamon extract (Usta et al., 2002; 2003). The dried stem bark of *C. cassia* contains four characteristic components—cinnamaldehyde, cinnamic acid, cinnamyl alcohol, and coumarin. He et al. (2005) identified high contents of cinnamaldehyde (13.01–56.93 mg/g) in *C. cassia* bark. Friedman et al. (2000) found that eugenol and linalool in foods are stable to heat, unlike pure cinnamaldehyde, which undergoes a temperature-dependent transformation to benzaldehyde under the influence of heat starting at approximately 60°C.

According to the U. S. Department of Agriculture (USDA) Economic Research Services, 1,797,000 pounds of cinnamon were imported into the U.S. for consumption in 2005.

DATA AND METHODS

An extensive database search was performed using the databases PubMed, MEDLINE, EMBASE, BIOSIS, TOXLINE and Google Scholar. Search terms used were as follows: "cinnamon," "Cinnamomum," "cinnam*" combined with "anti-inflammatory," "antioxidant," "antiviral," "viral," "cancer," "cholesterol," "dietary," "diabetes," "heart," "immunomodul*,"

"Alzheimer," "Parkinson." Species of the genus *Cinnamomum* other than *C. zeylanicum* (syn. *C. verum*) and *C. cassia* were excluded as well as most studies on plant parts other than the bark. Retrieved abstracts were searched manually and more than 200 articles relevant to the efficacy of *C. zeylanicum* and *C. cassia* were evaluated.

Results

Summary of Human Trials

Few human trials have been published that investigated the efficacy of cinnamon on physiological parameters and health-related conditions. However, recent *in vitro* and *in vivo* research has discovered new properties of *C zeylanicum* and *C. cassia*, which may be of interest for clinical use. The treatment of diabetes (type 2) has been investigated in several clinical trials (Blevins et al., 2007; Khan et al., 2003; Mangold et al., 2006; Suppapitiporn et al., 2006; Vanschoonbeek et al., 2006) and is probably the most well-documented health benefit of this spice for humans. Nevertheless, additional research is needed to determine whether cinnamon can help control this disease in free-living patients. Furthermore, some evidence suggests that cinnamon may be effective in the supportive treatment of cancer, infectious diseases, and complaints associated with modern life style due to its anti-inflammatory, antimicrobial, antioxidant, and blood pressure-lowering effects. Unfortunately, human data in this area is limited. One trial on *Helicobacter pylori* infection (Nir et al., 2000) yielded negative results for cinnamon ingested at daily doses of 80 mg as did a pilot trial (Quale et al., 1996) on candidiasis in HIV-patients (daily dosage of cinnamon not reported).

Dose-response trials are of paramount importance, as the clinical studies on the hypoglycemic properties of cinnamon have shown. The studies which did not yield statistically significant results were carried out with a daily dose of $\leq$1.5 g of cinnamon. Significant positive effects were only found in studies utilizing 3 to 6 g of cinnamon daily. One teaspoonful of cinnamon powder weighs approximately 1.5 g. It seems reasonable that up to 2 teaspoons of this spice could easily be integrated into a normal diet.

Preclinical and Clinical Evidence

Anti-inflammatory properties. The studies cited in this section refer to the ability of cinnamon to affect inflammation, e.g., by counteracting the cyclooxygenase (COX) enzyme. Studies dealing with related mechanisms of action are cited in the appropriate sections—for example, the antioxidant activity may influence the immunomodulary properties of a drug, which in turn may cause an anti-inflammatory effect.

The inhibitors of prostaglandin biosynthesis and nitric oxide production are potential anti-inflammatory and cancer chemopreventive agents. *Cinnamomum cassia* extracts showed potent inhibition of cyclooxygenase-2 (COX-2) activity in lipopolysaccharide (LPS)-induced mouse macrophage RAW264.7 cells (Hong et al., 2002). The main constituents of cinnamon, eugenol, and cinnamaldehyde, were found to inhibit COX-2 *in vitro* in a rapid semi-homogeneous COX-2 enzymatic assay (Huss et al., 2002).

The redox sensitive, pro-inflammatory nuclear transcription factor NF-kappaB plays a key role in inflammation. Cinnamaldehyde derivatives based on 2′-hydroxycinnamaldehyde isolated from the bark of *C. cassia* significantly inhibited lipopolysaccharide (LPS)-induced nitric oxide (NO) production and NF-kappaB transcriptional activity in a dose-dependent manner (Lee et al., 2005). 2′-Hydroxycinnamaldehyde had the strongest inhibitory effect on NO production among the cinnamaldehyde derivatives through inhibition of NF-kappaB activation, and thus could be used as an anti-inflammatory agent due to its antioxidant properties.

Kim et al. (2007) recently examined cinnamaldehyde further for its molecular modulation of inflammatory NF-kappaB activation via the redox-related NF-kappaB/IχB kinases (NIK/IKK) and mitogen-activated protein kinase (MAPK) pathways through the reduction of oxidative stress. Results show that age-related NF-kappaB activation upregulated NF-kappaB targeting genes, inflammatory iNOS, and COX-2, all of which were effectively inhibited by cinnamaldehyde. Cinnamaldehyde furthermore inhibited the activation of NF-kappaB via three signal transduction pathways—NIK/IKK, extracellular signal-regulated kinases, and p38 MAPK. It is likely that the antioxidative effect of cinnamaldehyde and the restoration of redox balance are responsible for its anti-inflammatory action.

As this section has suggested, the bark of *C. cassia*, probably due to its cinnamaldehyde content, demonstrates clear anti-inflammatory properties *in vitro*. Additional information is provided below in the sections on "antioxidant properties" and "immunomodulatory properties."

Antimicrobial Properties

Antibacterial properties. Spices have been traditionally used since ancient times for their antiseptic and disinfectant properties. De et al. (1999) carried out a preliminary screening for antimicrobial activities of 35 different Indian spices. Cinnamon, among others, has potent antimicrobial activity against the test organisms *Bacillus subtilis* and *Escherichia coli*.

Cinnamon bark oil as well as cinnamaldehyde and eugenol showed potent antibacterial effects against *Bacillus cereus, Campylobacter jejuni, Enterococcus faecalis, Escherichia coli, Listeria monocytogenes, Haemophilus influenzae, Salmonella choleraesuis, S. enterica, Pseudomonas aeruginosa, Staphylococcus aureus, Streptococcus pneumoniae, and S. pyogenes,* as well as *Yersinia enterocolitica* (Friedman et al., 2002; Inouye et al., 2001; López et al., 2005; Smith-Palmer et al., 1998). In general, Gram-positive bacteria were more sensitive to inhibition by the plant essential oil than Gram-negative bacteria. *Campylobacter jejuni* was the most resistant of the bacteria investigated (Smith-Palmer et al., 1998).

Cinnamaldehyde showed the strongest antibacterial effectiveness of the constituents examined (López et al., 2007).

Oussalah et al. (2006) studied the mechanism of the antimicrobial action of the essential oil of *C. cassia* against cell membranes and walls of bacteria by measurement of intracellular pH and ATP concentration, the release of cell constituents, and electronic microscopy of the cells when the essential oil at its minimum inhibitory concentration was in contact with *E. coli* and *L. monocytogenes*. A significantly ($p \leq 0.05$) higher cell constituent release compared to untreated controls was observed in the supernatant when *E. coli* and *L. monocytogenes* cells were treated with *C. cassia* oil. The oil reduced the intracellular pH of *E. coli* and decreased the intracellular pH of *L. monocytogenes* significantly ($p \leq 0.05$ for both). Electronic microscopy observations revealed that the cell membrane of both treated bacteria was significantly damaged. These results suggest that the cytoplasmic membrane is involved in the toxic action of essential oils. Senhaji et al. (2007) found that in the presence of 0.05% of the essential oil from *C. zeylanicum*, most of *E. coli* cells were killed after 30 min, suggesting that the antimicrobial activity of essential oil is bactericidal.

Aqueous and ethanolic *C. cassia* extracts exhibited strong inhibitory effects on collagenolytic activity of *Porphyromonas gingivalis* (Osawa et al., 1991). These extracts are effective in reducing the pathogenicity of periodontopathic bacteria. The extracts of *C. cassia* also had relatively strong anti-cytotoxic activity. Azumi et al. (1997) found a substance in cinnamon bark that inhibits the activity of bacterial endotoxin (LPS). Furthermore, the inhibitor abrogated the pyrogenicity of the LPS. Watt et al. (2007), however, found no antibacterial activity in *C. zeylanicum* tincture using luminescent bacterial biosensors (*E. coli* strains).

Antifungal properties. The essential oils of several *Cinnamomum* species have been shown to have anticandidal (*Candida albicans, C. glabrata*) and antidermatophytic (*Microsporum canis, Trichophyton mentagrophytes, T. rubrum*) activity *in vitro* (Mastura et al., 1999). The essential oil of the leaves of *C. zeylanicum* demonstrated only modest antifungal properties. However, according to Simic et al. (2004), the essential oil of *C. zeylanicum* (plant part not specified) showed the strongest antifungal activity compared to *Aniba roaeodora, Laurus nobilis* and *Sassafras albidum* against 17 micromycetes (*Aspergillus niger, A. ochraceus, A. versicolor, A. flavus, A. terreus, Alternaria alternata, Aureobasidium pullulans, Penicillium ochrochloron, P. funiculosum, Cladosporium cladosporioides, C. Fulvium, Trichoderma viride, Fusarium tricinctum, F. sprortrichoides, Phoma macdonaldii, Phomopsis helianthi, Mucor mucedo*) *in vitro*. Transcinnamaldehyde was the most active component in the oil of *C. zeylanicum*.

Singh et al. (1995) identified cinnamic aldehyde as the active fungitoxic constituent of *C. zeylanicum* bark oil. The fungitoxic properties of the vapors of the oil/active constituent were established against fungi involved in respiratory tract infections (mycoses), i.e., *Aspergillus niger, A. fumigatus, A. nidulans A. flavus, Candida albicans, C. tropicalis, C. pseudotropicalis*, and *Histoplasma capsulatum*. The authors concluded that these inhalable vapors appear to approach the ideal chemotherapy for respiratory tract mycoses.

Cinnamon oil demonstrated inhibitory activity against *Aspergillus flavus, A. parasiticus, A. ochraceus, Fusarium moniliforme, F. graminearum* and *F. proliferatum* as well as *Saccharomyces cerevisiae* in several further studies (De et al., 1999; Soliman and Badeaa, 2002; Ranasinghe et al., 2002; Bartine and Tantaoui-Elaraki, 1997; Velluti et al., 2003; Velluti et al., 2004). Furthermore, oils obtained from *C. zeylanicum* were found to be most active *in vitro* tested against dermatophyte strains isolated from patients with dermatophytosis inhibiting 80% of the dermatophyte strains tested (Lima et al., 1993).

Oral candidiasis is a frequent occurance in patients with HIV-infection. Treatment of this condition with an oral azole is generally effective. However, fluconazole-resistant *Candida* species are an emerging problem. *C. zeylanicum* shows *in vitro* activity against fluconazole-resistant and -susceptible *Candida* isolates (Quale et al., 1996).

CLINICAL TRIALS

Quale et al. (1996) conducted a pilot study in five patients with HIV infection and oral candidiasis to investigate the activity of cinnamon (*Cinnamomum zeylanicum*) against fluconazole-resistant and –susceptible *Candida* isolates. All patients studied had pseudomembranous candida infection confirmed by culture. Patients were given eight lozenges of a cinnamon candy daily (no further information given). The commercially available extract was administered for one week. Three of the five patients had improvement of their oral candidiasis (no further details given). The pilot study was neither randomized nor blinded, and the sample size was very small. Further clinical trials will be necessary to determine the usefulness of cinnamon for the treatment of mucosal candidiasis.

Antiviral Properties

A *Cinnamomum cassia* bark extract was highly effective against HIV-1 and HIV-2 replication in terms of inhibition of virus-induced cytopathogenicity in MT-4 cells infected with HIV (Premanathan et al., 2000). Cinnamaldehyde derived from cinnamon bark has an inhibitory effect on the growth of influenza A/PR/8 virus in *vitro* (Madin-Darby canine kidney cells) and *in vivo* (mice infected with the lung-adapted PR-8 virus; Hayashi et al., 2007).

The available *in vitro* data demonstrate that C. *cassia* bark oil as well as aqueous and ethanolic extracts have potent antibacterial and highly effective antiviral properties against Gram-positive and Gram-negative bacteria as well as HI- and influenza virus, respectively. These properties have not been reported for *C. zeylanicum*, even though the two cinnamon species have

similar constituents. The essential oil of *C. zeylanicum*, however, demonstrated potent antifungal activity. Further *in vitro* and *in vivo* research in addition to human data is needed to confirm the antimicrobial properties of cinnamon in free-living individuals.

Antioxidant Properties

Spices and vegetables possess antioxidant activity that can reduce lipid peroxidation in biological systems (Shobana and Naidu, 2000). Reactive oxygen species have been implicated in a range of human diseases such as atherosclerosis and certain cancers (Halliwell, 2007). Oxidative processes generally play a key role in inflammatory and immune processes. As oxidative stress has been implicated in the pathogenesis of many human diseases, the use of antioxidants in pharmacology is widely studied (Clark, 2002). Dragland et al. (2003) found very high concentrations of antioxidants (i.e., >75 mmol/100 g) in the medicinal herb *Cinnamomi cortex*. The authors speculate that several of the effects of this herb are mediated by their antioxidant activities.

A water and alcoholic extract (1:1) of cinnamon showed significant inhibition of lipoxygenase-dependent enzymatic lipid peroxidation in an *in vitro* lipid peroxidation assay (Shobana and Naidu, 2000). Etheric, methanolic, and aqueous cinnamon extracts, inhibited *in vitro* oxidation in a beta-carotene/linoleic acid system (Mancini-Filho et al., 1998).

Ethanol extracts of dry bark of *C. cassia* exhibited a greater inhibition of lipid peroxidation of rat liver homogenate *in vitro* than alpha-tocopherol, high superoxide anion scavenging activity, strong anti-superoxide formation activity ($P < 0.05$), and excellent antioxidant activity in enzymatic and nonenzymatic liver tissue oxidative systems (Lin et al., 2003). Cinnamon exhibited a higher percentage of inhibition of oxidation than butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate as tested by the lipid peroxidation assay (Murcia et al., 2004). *Cinnamomi cortex* also has inhibitory effects on lipid peroxidation and protein oxidative modification by copper (Toda, 2003).

Cinnamon oil exhibited superoxide dismutase (SOD)-like activity measured by the inhibition of pyrogallol autoxidation that is catalyzed by the superoxide radical (Kim et al., 1995). The volatile extracts of cinnamon showed moderate antioxidant activities in the aldehyde/carboxylic acid assay and in the conjugated diene assay (Lee and Shibamoto, 2002).

The essential oil obtained from the bark of *C. zeylanicum* and three of its main components, eugenol, (E)-cinnamaldehyde, and linalool, were tested in two *in vitro* models of peroxynitrite-induced nitration and lipid peroxidation. The essential oil and eugenol showed very powerful activities. (E)-cinnamaldehyde and linalool were completely inactive (Chericoni et al., 2005). However, *C. cassia* bark-derived trans-cinnamaldehyde showed potent inhibitory effects on NO production in RAW 264.7 cells, determined through the evaluation of NO production and expression of inducible nitric oxide. Little or no activity was observed for cinnamic acid and eugenol (Lee et al., 2002).

Several flavonoids obtained from cinnamon that were reported to exhibit antioxidant and free radical scavenging activities were tested for their 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity (Okawa et al., 2001). Recently, Prakash et al. (2007) found strong free radical-scavenging activities in the bark of *C. zeylanicum* as indicated by a very low inhibitory concentration value, efficiency concentration value (DPPH), and reducing power value (ascorbic acid equivalents) as well as a reasonably high value of anti-radical power. These findings confirm earlier results by Shan et al. (2005), which indicate very strong activity for *C. zeylanicum* and a relatively high activity for *C. cassia*.

Animal Studies

Dhuley (1999) assessed the antioxidant properties of *C. zeylanicum in vivo* through the measurement of hepatic and cardiac antioxidant enzymes, glutathione (GSH) content and lipid conjugated dienes in rats fed a high fat diet containing 10% cinnamon. The antioxidant enzyme activities were significantly enhanced whereas the GSH content was markedly restored in rats fed a high-fat diet containing spices. In addition, cinnamon partially counteracted the primary products of lipid peroxidation (i.e., increase in lipid conjugated dienes and hydroperoxides) in this system. These observations suggest that this spice exerts antioxidant protection through its ability to activate antioxidant enzymes. *C. cassia* pretreatment decreased liver cytochrome P450 content, but increased GSH content and the activity of the glutathione-dependent antioxidant enzymes glutathione S-transferase, glutathione reductase, and glutathione peroxidase. Hence, the antimutagenic potential of *C. cassia* could be attributed to its modulatory effect on the xenobiotic bioactivation and detoxification processes.

High fructose feeding in normal rats facilitates oxidative damage. Suganthi et al. (2007) evaluated a spice mixture containing 1.0 g/100 g of cinnamon bark for its effect on oxidative stress markers and antioxidant potential in tissues of high fructose-fed insulin-resistant rats. Administration of the spice mixture along with dietary fructose reduced the levels of peroxidation markers in tissues and improved the antioxidant status compared to rats receiving dietary fructose alone.

In conclusion, numerous *in vitro* studies and one *in vivo* trial demonstrate the antioxidant potential of *Cinnamomum cassia* and *C. zeylanicum*. However, the *in vivo* data are scarce and no human data are available to confirm the beneficial effects of cinnamon with respect to its antioxidant properties. Halvorsen et al. (2006) generated a ranked food table with values for total content of redox-active compounds (i.e., antioxidants). Ground cinnamon ranked fourth with regard to total antioxidant content (17.647 mM/100 g) but was not among the 50 foods with the highest antioxidant contents per serving size. Based on the work of Wu et al. (2004), the USDA published the oxygen radical

absorbance capacity (ORAC) of selected foods. Both lipophilic (L-ORAC) and hydrophilic (H-ORAC) antioxidant capacities were determined. Ground cinnamon had values of 34.53 μM of Trolox equivalent (TE)/g and 2640.83 μM TE/g for L- and H-ORAC, respectively. Total ORAC was 2675.36 μM TE/g. These data show that cinnamon used as a spice has potentially high antioxidant content, and can contribute to the total antioxidant content of the diet.

Antitumor Properties

As has been stated above, antitumor and anti-cancer properties of a substance are closely related to its antioxidant and immunomodulatory properties. Studies on the antioxidant and immunomodulatory properties of *C. zeylanicum* and *C. cassia* may imply antitumor properties. However, additional studies on cinnamon bark and its main constituent cinnamaldehyde are needed in order to investigate their precise antitumor properties.

Ka et al. (2003) investigated the effects of cinnamaldehyde on the cytotoxicity, induction of apoptosis and putative pathways of its actions in human promyelocytic leukemia cells. Cinnamaldehyde was a potent inducer of apoptosis in these studies. The authors concluded that the anticancer effects of cinnamaldehyde result from induction of reactive oxygen species (ROS)-mediated mitochondrial permeability transition and resultant cytochrome C release. Nishida et al. (2003) found that *C. cassia* induced death of HL-60 cells as demonstrated by the reduction of mitochondrial transmembrane potential and increased caspase-3 activity. According to the authors, the apoptosis induced by *C. cassia* occurred via the mitochondrial route and the apoptosis-conducting mechanism acted through a cascade involving caspase-3.

Kwon et al. (1998) synthesized cinnamaldehydes and related compounds from various cinnamic acids based on the 2′-hydroxycinnamaldehyde isolated from the bark of *C. cassia*. Cinnamic acid, cinnamates, and cinnamyl alcohols did not show cytotoxicity against several human solid tumor cells. HCT15 and SK-MEL-2 cells, however, were much more sensitive to these cinnamaldehyde analogues. Cytotoxicity of the saturated aldehydes was much weaker compared to their unsaturated counterparts.

Matrix metalloproteinase-9 (MMP-9) degrades type IV collagen, the major structural component of the basement membrane and the extra cellular membrane (Seo et al., 2005). The activity of this enzyme is found to be elevated in tumor tissues. The hexane and chloroform fractions as well as water extracts of *C. cassia* showed a weak inhibitory effect on MMP-9 activity. However, a strong MMP-9 inhibition was found in the butanol fraction of *C. cassia*.

2′-Hydroxycinnamaldehyde (HCA) and 2′-benzoyloxycinnamaldehyde (BCA) isolated from *C. cassia* strongly inhibited *in vitro* growth of 29 kinds of human cancer cells and *in vivo* growth of SW-620 human tumor xenograft without loss of body weight in nude mice (Lee et al., 1999). HCA prevented adherence of SW-620 cells to the culture surface but did not inhibit oncogenic K-Ras processing, implying its antitumor mechanisms are at the cellular level.

Haranaka et al. (1985) suggested that one mechanism underlying the antitumor activity of *Cinnamomi cortex* is based on stimulation of the reticuloendothelial system (RES) and is closely related to tumor necrosis factor (TNF) production. The drug was given to DDY mice in drinking water before and after transplantation of Ehrlich tumors. A good survival rate was found in the group administered *Cinnamomi cortex*. Relatively high levels of TNF activity were noted in the group given cinnamon. The TNF capacity for production broadly paralleled the survival rate of the mice transplanted to Ehrlich tumors.

Abraham et al. (1998) assessed antigenotoxic effects and changes in glutathione S-transferase (GST) activity in mice after oral co-administration of urethane (URE), a carcinogenic substance, with an aqueous extract of cinnamon. The results of the genotoxicity assay (micronucleus test) demonstrated dose-related antigenotoxic effects after URE was co-administered with the extract. Furthermore, an aqueous extract prepared from cinnamon seemed to interact with phosphorylation/dephosphorylation signaling activities in three myeloid cell lines (Jurkat, Wurzburg, and U937), thus reducing cellular proliferation and blocking the G2/M phase of the cell cycle (Schoene et al., 2005).

Furthermore, *C. cassia* exerted significant antimutagenic effects against benzo[a]pyrene and cyclophosphamide in mice pretreated with the plant extract as shown by the Ames test, the bone marrow chromosomal aberration assay, and the micronucleus test (Sharma et al., 2001).

In conclusion, the available *in vitro* and *in vivo* data suggest that cinnamon has antitumor properties that are probably related to its antioxidant activity.

Blood Pressure-Lowering Properties

Cinnamomum cassia bark affects the blood and cardiovascular system (Chen 1981). The cardiovascular properties of cinnamon are closely connected to its effects on blood lipids and glucose metabolism. Many agents (nutrients, nutraceuticals, and drugs) that enhance insulin sensitivity and/or reduce circulating insulin concentrations also lower blood pressure (Preuss et al., 2006). Cinnamon (8% w/w) in the diet reduced the systolic blood pressure of spontaneously hypertensive rats (SHR) eating sucrose-containing diets to virtually the same levels as SHR consuming diets containing non sucrose. The presence of cinnamon in the diet also decreased the systolic blood pressure of SHR consuming a non sucrose-containing diet, suggesting that cinnamon reduces more than just sucrose-induced blood pressure elevations.

Cinnamomum cassia bark increases the level of atrial natriuretic factor (ANF) in the plasma of mice (Zhou et al., 1995). ANF acts to reduce the water, sodium, and adipose loads on the circulatory system, thereby reducing blood pressure. ANF was

significantly higher in the plasma of mice after giving *C. cassia* orally, compared with control ($p < 0.001$).

In conclusion, available *in vivo* data strongly support the hypothesis that cinnamon lowers systolic blood pressure in experimental animals.

Cholesterol- and Lipid-Lowering Properties

Several spices, e.g. garlic or ginger, have been shown to have beneficial hypolipidemic or hypocholesterolemic properties (Sambaiah and Srinivasan, 1991). In a study undertaken to screen several spices, *C. zeylanicum* did not lower serum or liver cholesterol concentrations of rats when included in the diet at about 5-fold the normal human intake level (i.e., 0.05% of the diet). In contrast, cholesterol concentrations were increased by 25% in cinnamon fed animals (Sambaiah and Srinivasan, 1991). However, hypocholesterolemic effects were reported in a very recent study conducted to isolate and identify the putative antidiabetic compounds of *C. zeylanicum* based on bioassay-guided fractionation. It was found that cinnamaldehyde significantly ($p < 0.05$) decreased plasma glucose concentration in a dose-dependent manner (63.29%) compared to the control in streptozotocin-induced male diabetic Wistar rats (Subash Babu et al., 2007). The results of this study indicate that cinnamaldehyde possesses hypolipidemic effects in streptozotocin-induced diabetic rats.

Kim et al. (2006a) demonstrated the effect of *C. cassia* extract on blood lipids in an *in vivo* study. HDL-cholesterol concentrations were significantly higher ($p < 0.01$) in mice fed with cinnamon extract, and the concentrations of triglyceride and intestinal alpha-glycosidase activity were significantly lower ($p < 0.01$), after 6 weeks. These results suggest that cinnamon extract has a regulatory role in blood lipids and it may also exert a blood glucose-suppressing effect by improving insulin sensitivity or slowing absorption of carbohydrates in the small intestine.

In conclusion, several *in vivo* studies strongly suggest that *C. zeylanicum* and *C. cassia* have cholesterol-lowering properties. Khan et al. (2003) determined whether cinnamon improves blood glucose, triglyceride, total cholesterol, HDL cholesterol, and LDL cholesterol levels in people with type 2 diabetes (see "Hypoglycemic properties (including diabetes (type 1, type 2))" below). After 40 days, 1, 3, or 6 g of cinnamon daily reduced mean fasting serum glucose (18–29%), triglyceride (23–30%), LDL cholesterol (7–27%), and total cholesterol (12–26%) levels; no significant changes were noted in the placebo groups. Changes in HDL cholesterol were not significant. However, more clinical trials, especially with healthy volunteers and people suffering from hyperlipidemia, are needed to confirm the cholesterol- and lipid-lowering effects for humans.

Gastroprotective Properties (including H. pylori Infection)

Helicobacter pylori has been associated with the pathogenesis of antral gastritis, duodenal ulcer, and gastric lymphoma, and the eradication of this organism has been shown to reverse or prevent relapse of these diseases. Antimicrobials employed in the eradication of *H. pylori* are not without adverse effects (Chiba et al., 1992). Newer treatment modalities, therefore, are required (Nir et al., 2000).

Cinnamon extract (from methylene chloride) inhibited *H. pylori* growth at a concentration range typical of common antibiotics (Tabak et al., 1999). The efficiency of cinnamon extracts in liquid medium and its resistance to low pH levels may enhance its effect in an environment such as the human stomach.

Animal Studies

Tanaka et al. (1989) showed that 3-(2-hydroxyphenyl)-propanoic acid and its O-glucoside isolated from the stem bark of *C. cassia* prevented serotonin-induced ulcerogenesis in rats after per oral (p.o.) administration. The former compound, administered orally or parenterally to rats at a remarkably low dose (40 μg/kg body weight), also inhibited gastric ulcers induced by phenylbutazone, ethanol, and water immersion stress. The authors suggest that the antiulcerogenicity of 3-(2-hydroxyphenyl)-propanoic acid may be due to cytoprotection comparable to prostaglandin E_2.

Clinical Trials

A pilot study (Nir et al., 2000) was conducted to test the activity of an alcoholic extract of cinnamon in a group of patients infected with *H. pylori* (see Table 1). This study found that cinnamon extract, at a concentration of 80 mg/day as a single agent, was ineffective in eradicating *H. pylori*. The authors concluded that a combination of cinnamon with other antimicrobials, or a higher concentration of cinnamon extract may have had an effect. Further studies are needed to test this hypothesis.

An *in vivo* study (Tanaka et al., 1989) supports the hypothesis that cinnamon may have gastroprotective properties via inhibition of gastric ulcers. However, despite the positive outcomes of an *in vitro* study (Tabak et al., 1999), there is no direct evidence to suggest that cinnamon can affect *H. pylori* infection in humans.

Hypoglycemic Properties (including Diabetes (type 1, type 2))

Diabetes mellitus is the sixth leading cause of death in the United States where it affects an estimated 20.8 million people (Chase and McQueen, 2007). The prevalence of adult onset (type 2) diabetes greatly exceeds that of juvenile onset (type 1) diabetes in this population (Pham et al., 2007). Over the past several years, the effectiveness of cinnamon supplementation for the management of diabetes has received worldwide media attention. Several *in vitro* (Anderson et al., 2004; Berrio et al., 1992; Broadhurst et al., 2000; Cao et al., 2007;

Table 1 Clinical trials of cinnamon extracts (*Cinnamomum zeylanicum, C. cassia*)

Disease	Study design	No. of patients	Dosage	Duration	Main result	Facility	Reference
Oral candidiasis	Pilot study	5 with HIV infection	—	1 week	Three of the five patients had improvement of their oral candidiasis (no further details given).	Department of Veterans Affairs Medical Center at Brooklyn, New York, U.S.A.	Quale et al., 1996
Helicobacter pylori infection	Pilot study	23	80 mg/day	4 weeks	The cinnamon extract was ineffective.	Bnai Zion Medical Center, Technion, Haifa, Israel	Nir et al., 2000
Insulin resistance	Pilot study (RCT)	15 women with polcystic ovary syndrome	999 mg/day	8 weeks	Comparisons of post-treatment to baseline insulin sensitivity indices using fasting and 2-hour oral glucose tolerance tests showed significant ($p < 0.05$) reductions in insulin resistance in the cinnamon group but not in the placebo group.	College of Physicians and Surgeons, Columbia University, New York, New York, U.S.A.	Wang et al., 2007
Adolescent type 1 diabetes	RCT	72	1 g/day	90 days	No significant differences in final HbA1C, change in HbA1C, total daily insulin intake, or no. of hypoglycemic episodes between the cinnamon and placebo groups.	Dartmouth College, Hanover, New Hampshire, U.S.A.	Altschuler et al., 2007
Type 2 diabetes	RCT	60	1.5 g *C. cassia* powder daily	12 weeks	*C. cassia* powder did not significantly reduce fasting plasma glucose, HbA1c or serum lipid profile.	King Chulalongkorn Memorial Hospital, Bangkok, Thailand	Suppapitiporn et al., 2006
Type 2 diabetes	RCT	58	1 g/day	12 weeks	No significant changes in fasting glucose, lipid, HbA1c, or insulin levels.	University of Oklahoma, Oklahoma City, Oklahoma, U.S.A.	Blevins et al., 2007
Type 2 diabetes	RCT	25 post-menopausal women	1.5 g/day	6 weeks	No interactions for plasma HbA1c, fasting glucose, insulin concentrations, or fasting blood lipid concentrations.	Maastricht University, Maastricht, The Netherlands	Vanschoonbeek et al., 2006
Type 2 diabetes	RCT	79	3 g cinnamon powder daily	4 months	There was a significantly ($p = 0.046$) higher reduction of fasting plasma glucose concentration in the cinnamon group (10.3%) than in the placebo group (3.4%). No significant differences were observed regarding HbA1C, and lipid profiles.	University of Hannover, Hannover, Germany	Mang et al., 2006
Type 2 diabetes	RCT	60	1-6 g/day	40 days	Cinnamon reduced mean fasting serum glucose (18–29%), triglyceride (23–30%), LDL cholesterol (7–27%), and total cholesterol (12–26%) levels ($P < 0.05$ for each). No significant changes were noted in the placebo groups. Changes in HDL cholesterol concentrations were not significant.	NWFP Agricultural University, Peshawar, Pakistan	Khan et al., 2003

Imparl-Radosevich et al., 1998; Jarvill-Taylor et al., 2001; Khan et al., 1990; Kim et al., 2006b; Kreydiyyeh et al., 2000; Lee, 2002; Roffey et al., 2006; Taher et al., 2004; Talpur et al., 2005) and *in vivo* studies (Kannappan et al., 2006; Kim et al., 2006a; 2006b; Onderoglu et al., 1999; Qin et al., 2003; 2004; Subash Babu et al., 2007; Verspohl et al., 2005) on the effects of cinnamon on insulin resistance and glucose metabolism have been published. Clinical trials investigating the effects of cinnamon in healthy subjects (Hlebowitz et al., 2007; Solomon and Blannin, 2007) as well as the efficacy of cinnamon in the treatment of diabetes mellitus type 1 and 2 (Altschuler et al., 2007; Blevins et al., 2007; Khan et al., 2003; Mang et al., 2006; Suppapitiporn et al., 2006; Vanschoonbeek et al., 2006) or insulin resistance (Wang et al., 2007) have also been published (see below).

In Vitro Studies

In vitro studies conducted with extracts or constituents of *Cinnamomum zeylanicum* or *C. cassia* have demonstrated that cinnamon may act as an insulin mimetic, to potentiate insulin activity or to stimulate cellular glucose metabolism.

The causes and control of type 2 diabetes mellitus are not clear, but there is strong evidence that dietary factors are involved in its regulation and prevention. Anderson et al. (2004) isolated water-soluble polyphenol polymers from cinnamon that increase insulin-dependent *in vitro* glucose metabolism roughly 20-fold and display antioxidant activity.

Insulin resistance and type 2 diabetes mellitus are rapidly increasing throughout the world. Various combinations of essential oils including cinnamon, cumin, fenugreek, and oregano have been shown to enhance insulin sensitivity in *in vitro* experiments. Talpur et al. (2005) found that the ability to alter systolic blood pressure in rat models was the most sensitive early index of insulin sensitivity. The combined essential oils lowered circulating glucose concentrations and systolic blood pressure in both Zucker fatty rats (a model of obesity and insulin resistance) and SHR (a model of genetic hypertension), suggesting that these natural products are capable of enhancing insulin sensitivity. However, it is not possible to make specific conclusions regarding the essential oil of cinnamon because only combinations of essential oils were used in this study.

Kim et al. (2006b) looked for a new anti-diabetic compound using derivatives of hydroxycinnamic acids purified from cinnamon. A naphthalenemethyl ester of 3,4-dihydroxyhydrocinnamic acid (DHH105) showed the highest glucose transport activity *in vitro*. According to the results received from *in vivo* trials with diabetic C57BL/6 mice and spontaneously diabetic ob/ob mice the authors conclude that DHH105 lowers blood glucose levels through the enhancement of glucose transport, mediated by an increase in insulin-receptor signaling.

Roffey et al. (2006) examined the effects of an aqueous extract of *C. zeylanicum* on glucose uptake and adiponectin secretion in 3T3-LI adipocytes in the presence or absence of insulin. The results indicate that although aqueous cinnamon extract has insulin-mimetic action in 3T3-LI adipocytes in terms of glucose uptake, secretion of the antidiabetic hormone adiponectin is adversely affected.

Jarvill-Taylor et al. (2001) investigated the ability of a hydroxychalcone from cinnamon to function as an insulin mimetic in 3T3-LI adipocytes. Comparative experiments were performed with the cinnamon methylhydroxychalcone polymer (MHCP) and insulin with regard to glucose uptake, glycogen synthesis, phosphatidylinositol-3-kinase dependency, glycogen synthase activation, and glycogen synthase kinase-3beta activity, as well as the phosphorylation state of the insulin receptor. MHCP seems to be an effective mimetic of insulin and may be useful in the treatment of insulin resistance.

Cao et al. (2007) showed that water-soluble cinnamon extract and HPLC-purified cinnamon polyphenols with doubly-linked procyanidin type-A polymers displayed insulin-like activity. The effects of cinnamon on the protein and mRNA levels of insulin receptor, glucose transporter 4, and tristetraprolin were investigated in mouse 3T3-LI adipocytes. The results suggest that cinnamon exhibits the potential to increase the amount of proteins involved in insulin signaling, glucose transport, and the anti-inflammatory/anti-angiogenesis response.

Taher et al. (2004) investigated the ability of cinnamon (*C. zeylanicum*) extracts to stimulate preadipocytes of the cell line 3T3-L1 and studied the effect of cinnamon extracts as an alternative to insulin in 3T3-LI adipocytes using the oil red O staining method. Cinnamtannin B1 and water extracts of cinnamon induced adipocyte differentiation of 3T3-L1 cells. The authors concluded that cinnamtannin B1 or cinnamon water extracts can promote adipogenesis similar to insulin.

Cinnamon was highly active in the insulin-dependent utilization of glucose using a rat epididymal adipocyte assay and may therefore play a role in improving glucose and insulin metabolism (Broadhurst et al., 2000). Cinnamon extracts have furthermore been shown to potentiate the action of insulin in isolated rat epididymal adipocytes (Berrio et al., 1992). Increased activity of the insulin-stimulated utilization of glucose by the extract in the absence of added insulin was observed.

Khan et al. (1990) investigated an unidentified factor that potentiates the action of insulin in glucose metabolism in selected foods and spices in the rat epididymal fat cell assay. Cinnamon potentiated insulin activity by a factor of 4.3. These results were confirmed by Imparl-Radosevic et al. (1998). Bioactive compounds extracted from cinnamon potentiate insulin activity, as measured by glucose oxidation in the rat epididymal fat cell assay. Enzyme studies done *in vitro* suggest that certain cinnamon compounds, like insulin, affect protein phosphorylation-dephosphorylation reactions in the intact adipocyte.

Aldose reductase is an enzyme in carbohydrate metabolism that converts glucose to its sugar alcohol form, sorbitol, using NADPH as the reducing agent. Lee (2002) prepared aldose reductase from lenses of Sprague-Dawley male rat eyes. Cinnamaldehyde effectively inhibited aldose reductase. Cinnamyl

alcohol, transcinnamic acid, and eugenol exhibited only weak inhibition against aldose reductase. In comparison, quercitrin (a glycoside formed from the flavonoid quercetin and the deoxy sugar rhamnose) was 6 times more potent than cinnamaldehyde.

Finally, the aqueous extracts of cinnamon significantly lowered the absorption of alanine from the rat intestine. Alanine is an important amino acid for gluconeogenesis; it is converted back to pyruvate within the liver and used as a gluconeogenic substrate (Kreydiyyeh et al., 2000).

Animal Studies

Verspohl et al. (2005) evaluated the *in vivo* effect of extracts from *C. cassia* and *C. zeylanicum* on blood glucose and plasma insulin concentrations in rats under various conditions. *C. cassia* extract was superior to *C. zeylanicum* extract in this regard. A decrease in blood glucose concentrations was observed in a glucose tolerance test, whereas no such difference occurred in rats that were not challenged by a glucose load. The elevation in plasma insulin was direct since a stimulatory *in vitro* effect of insulin release from INS-1 cells (an insulin secreting cell line) was observed. Thus these data suggest that the *C. cassia* extract has a direct antidiabetic potency.

Onderoglu et al. (1999) investigated the *in vivo* effects of cinnamon bark on streptozotocin-induced tissue injury, and on a variety of biochemical and haematological parameters in rats. Streptozotocin is a naturally occurring chemical that is particularly toxic to the insulin-producing beta cells of the pancreas in mammals. This compound is used in medical research to produce an animal model for type 1 diabetes. The effects on glycaemia were also evaluated in this series of experiments. Long-term administration of cinnamon caused improvement in tissue injury induced by streptozotocin treatment; however, no effects on blood glucose concentrations were detected. These data indicate that long-term use of cinnamon bark may possibly provide benefit against diabetic conditions.

Treatment of streptozotocin-induced diabetic C57BL/6 mice and spontaneously diabetic ob/ob mice with a naphthalenemethyl ester of 3,4-dihydroxyhydrocinnamic acid (DHH105) decreased blood glucose concentrations to near normal (Kim et al., 2006b). Cinnamaldehyde was administered for 45 days to streptozotocin-induced male diabetic Wistar rats in order to isolate and identify the putative antidiabetic compounds of *C. zeylanicum*. Plasma glucose concentration was significantly ($p < 0.05$) decreased in a dose-dependent manner compared to the control. In addition, oral administration of cinnamaldehyde significantly decreased glycosylated hemoglobin (HbA1C), a marker of mid-term glucose homeostasis, and at the same time markedly increased plasma insulin and hepatic glycogen concentrations (Subash Babu et al., 2007). Cinnamaldehyde also restored altered plasma enzyme concentrations (aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, alkaline phosphatase, and acid phosphatase) to near normal levels.

Kim et al. (2006a) studied the anti-diabetic effect of *Cinnamomum cassia* extract in a type 2 diabetic animal model (C57BIKsj db/db). Within 6 weeks of administration, blood glucose concentration was significantly decreased in a dose-dependent manner ($p < 0.001$). In addition, serum insulin concentrations were significantly higher ($p < 0.01$) and intestinal alpha-glycosidase activity was significantly lower, after 6 weeks of administration. These results suggest that cinnamon extract has a regulatory role in blood glucose homeostasis and may also exert a blood glucose-suppressing effect by improving insulin sensitivity or slowing the absorption of carbohydrates.

Qin et al. (2003) evaluated the effect of cinnamon extract on insulin action in male Wistar rats utilizing the "hyperinsulinemic euglycemic clamp," a technique measuring the amount of glucose necessary to compensate for an increased insulin level without causing hypoglycemia. Possible changes in insulin signaling which occurred in skeletal muscle were further analyzed. The results suggest that the cinnamon extract improves insulin action via increasing glucose uptake *in vivo*, possibly by enhancing the insulin-signaling pathway in skeletal muscle.

Qin et al. (2004) fed normal male Wistar rats a high-fructose diet (HFD) for three weeks with or without cinnamon extract added to the drinking water in order to determine whether cinnamon extract would improve glucose utilization. *In vivo* glucose utilization was again measured by the euglycemic clamp technique. Early administration of cinnamon extract to HFD-fed rats seems to prevent the development of insulin resistance at least in part by enhancing insulin signaling and possibly via the NO pathway in skeletal muscle.

Kannappan et al. (2006) divided adult male albino rats into five groups and fed either control or high fructose diets and cinnamon bark extract for 60 days. The levels of glucose, insulin, and protein-bound sugars were higher and activities of enzymes of glucose metabolism were altered in high fructose rats as compared to control animals. The levels were brought back to near-normal when administered with cinnamon bark extract. These findings indicate that cinnamon can improve glucose metabolism *in vivo* in fructose-fed rats.

HEALTHY SUBJECTS

As discussed above, *in vivo* studies in animals show that cinnamon may have beneficial effects on glucose homeostasis; therefore the aim of a study by Solomon and Blannin (2007) was to further investigate this phenomenon in humans. Seven lean healthy adult male volunteers underwent three oral glucose tolerance tests supplemented with a single dose of either a placebo or 5 g of cinnamon using a randomized-crossover design. Cinnamon ingestion reduced total plasma glucose responses to oral glucose ingestion (–13% and –10% for cinnamon, $p < 0.05$), as well as improving insulin sensitivity as assessed by insulin sensitivity index measures based on Matsuda's model ($p < 0.05$)

compared with control. These data illustrate that cinnamon supplementation may be important to *in vivo* glycaemic control and insulin sensitivity in humans.

Hlebowitz et al. (2007) measured the effect of cinnamon on gastric emptying rate (GER) in 14 healthy subjects in a crossover experiment using standardized real-time ultrasonography. The subjects were examined after an 8 h fast if they had normal fasting blood glucose concentrations. GER was calculated 15–90 min after ingestion of 300 g rice pudding (GER1) or 300 g rice pudding and 6 g cinnamon (GER2). The addition of cinnamon to the rice pudding significantly delayed gastric emptying and lowered postprandial glucose response ($p < 0.05$ for both). The effect of cinnamon on satiety was not significant. This study shows that the intake of 6 g cinnamon with rice pudding can reduce postprandial blood glucose and delay gastric emptying without affecting satiety. The inclusion of cinnamon in the diet may lower postprandial glucose response; a change that is at least partially explained by a delayed GER.

CLINICAL TRIALS

Seven clinical studies investigating the effect of cinnamon on insulin resistance as well as type 1 and type 2 diabetes have been published to date (see Table 1). Four did not report statistically significant beneficial effects (Altschuler et al., 2007; Blevins et al., 2007; Suppapitiporn et al., 2006; Vanschoonbeek et al., 2006) while the remaining three studies found such effects (Khan et al., 2003; Mang et al., 2006; Wang et al., 2007).

In conclusion, the available *in vitro* and *in vivo* studies strongly suggest that cinnamon has hypoglycemic properties. However, the available human data are less consistent and indicate that cinnamon may have modest effects on blood glucose in subjects with type 2 diabetes. Additional evidence is needed before the extent to which cinnamon can be used to prevent and/or treat diabetes in humans is fully understood.

Immunomodulatory Properties

A study by Shan et al. (1999) showed that the extract of *C. cassia* markedly stimulated human lymphocytes to proliferate *in vitro*. Kurokawa et al. (1998) characterized antipyretic compounds from *C. cassia*. The antipyretic activity was significantly correlated with interleukin-1alpha regulatory activity. Reddy et al. (2004) found that an extract from the stem bark of *C. cassia* had an inhibitory effect on LPS-induced activity of NF-kappaB, a transcription factor regulating the expression of inflammatory and immune genes. Trans-cinnamaldehyde and 2-methoxycinnamaldehyde were identified as the NF-kappaB inhibitors.

Nagai et al. (1982) studied the anti-allergic action of an aqueous extract of *C. cassia in vitro*. Their results suggest that the extract showed an anticomplement action and inhibited the complement dependent allergic reaction.

Koh et al. (1998) studied two kinds of cinnamaldehyde derivative, 2′-hydroxycinnamaldehyde (HCA) and 2′-benzoxycinnamaldehyde (BCA), for their immunomodulatory effects in a series of *in vitro* experiments. Treatment of mouse splenocyte cultures with these cinnamaldehydes induced suppression of lymphoproliferation following both concavalin A and lipopolysaccharide stimulation in a dose-dependent manner. The results in this study suggest both derivatives inhibit the lymphoproliferation and induce a T-cell differentiation through the blockade of early steps in the signaling pathway leading to cell growth.

Kanari et al. (1989) isolated a neutral polysaccharide, named cinnaman AX (L-arabinose : D-xylose = 4 : 3) from the dried bark of *C. cassia*. The polysaccharide showed reticuloendothelial system-potentiating activity in mice in a modified *in vivo* carbon clearance test using zymosan as positive control.

In conclusion, the available *in vitro* and *in vivo* data demonstrate that cinnamon has immunomodulatory properties. However, no human data are available to confirm this hypothesis in free-living individuals.

DISCUSSION

Historically, the medicinal uses of spices were often indistinguishable from their culinary uses. The value of phytochemicals in relation to human health has been recognized for centuries. The constituents of herbs and spices can have complimentary and overlapping actions, including reduction of inflammation, antioxidant effects, modulation of detoxification enzymes, modulation of the immune system, and antibacterial and antiviral effects. The available *in vitro* and animal *in vivo* trials on the properties of *Cinnamomum zeylanicum* and *C. cassia* suggest that this spice may have anti-inflammatory, antimicrobial, antioxidant, antitumor, cardioprotective, cholesterol-lowering, hypoglycemic, and immunomodulatory effects. On the other hand, there is little evidence that cinnamon has gastroprotective properties. The preponderance of available *in vitro* and *in vivo* data suggest that cinnamon has health benefits. However, controlled human studies will be necessary to determine whether these effects have public health implications.

Most human research on cinnamon has been conducted to establish whether this spice is suitable for the treatment of type 1 and/or type 2 diabetes mellitus. These results are conflicting, but some evidence does exist to support this hypothesis.

The *in vivo* and *in vitro* studies on the topic of insulin resistance and the insulin-mimetic actions of cinnamon, respectively, have yielded consistently positive results. In addition, four of the seven clinical studies published to date did not report statistically significant beneficial effects (Altschuler et al., 2007; Blevins et al., 2007; Suppapitiporn et al., 2006; Vanschoonbeek et al., 2006) while the remaining three studies found such effects (Khan et al., 2003; Mang et al., 2006; Wang et al., 2007). The negative studies employed 1–1.5 g of cinnamon as a daily dose, whereas the studies with statistically significant results utilized

up to 6 g. As no dose-ranging studies were conducted, it is possible to estimate from the available data that ≥3 g cinnamon daily may be effective. In addition, *C. zeylanicum* and *C. cassia* may demonstrate slight differences in their pharmacological effects so the source of cinnamon may be important. As noted by Pham et al. (2007), further well-designed studies are needed before recommendations can be made that cinnamon is effective as treatment for type 2 diabetes mellitus. The available data do not provide support for the hypothesis that cinnamon can be used to treat type 1 or type 2 diabetes or to reduce the risk of developing diabetes in healthy individuals.

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