



THE CEYLON MEDICAL JOURNAL

Established 1887

The Official Publication of the
Sri Lanka Medical Association
Volume 61, No.1, March 2016
Quarterly ISSN 0009-0875

Editors Emeritus

Chris G Urugoda MD, FRCP
Colvin Goonaratna FRCP, PhD
Janaka de Silva DPhil, FRCP

Editors

Anuruddha Abeygunasekera MS, FRCS
Varuni De Silva MBBS, MD

Section Editors

A Pathmeswaran MBBS, MD
B J C Perera MD, FRCPCH
Shalini Sri Ranganathan MD, PhD

Assistant Editors

Carukshi Arambepola MBBS, MD
Samath Dharmaratne MSc, MD
Tiran Dias MD, MRCOG
Ranil Fernando FRCS, PhD
Malik Goonewardene MS, FRCOG
Renuka Jayatissa MD, MSc
Prasad Katulanda MD, Dphil
Sarath Lekamwasam MD, PhD
Senaka Rajapakse MD, FRCP
Udaya K Ranawaka MD, FRCP
Chandu de Silva MBBS, MD
Sisira Siribaddana MD, FRCP

International Advisory Board

S Arulkumaran FRCOG, PhD
London, UK
Zulfiqar Ahmed Bhutta FRCPCH, PhD
Karachi, Pakistan
Andrew Dawson FRACF
Sydney, Australia
Barbara Gastel MD, MPH
Texas, USA
Kalle Hoppu MD, PhD
Helsinki, Finland
David Lallo MD, FRCP
Liverpool, UK
Ian Pearce BMBS, FRCS
Manchester, UK
Peush Sahni MS, PhD
New Delhi, India
Anita KM Zaidi MMBS, SM
Karachi, Pakistan

Online Manager

Rikaz Sheriff MBBS MSc

Health benefits of Ceylon cinnamon (*Cinnamomum zeylanicum*): a summary of the current evidence

Introduction

Cinnamon is obtained from the inner bark of trees from the genus *Cinnamomum*. There are two main varieties of cinnamon; *Cinnamomum zeylanicum* (CZ) and Cinnamon cassia (CC). CC is also known as *Cinnamomum aromaticum*/Chinese cinnamon. In addition to its culinary uses, in Ayurvedic medicine cinnamon is considered a remedy for respiratory, digestive and gynaecological ailments. Different parts of the plant (bark, leaves and root) possess the same array of hydrocarbons in varying proportions. The primary constituents being cinnamaldehyde (bark), eugenol (leaf) and camphor (root) [1].

CZ, also known as Ceylon cinnamon or 'true cinnamon' is indigenous to Sri Lanka and southern parts of India [2]. One important difference between CC and CZ is their coumarin content [3]. Coumarins are plant compounds that possess strong anticoagulant, carcinogenic and hepato-toxic properties. The levels of coumarins in CC appear to be very high and could pose health risks if consumed regularly in higher quantities, whereas CZ contains hardly any coumarin [4]. Hence, although CC has also demonstrated health benefits, numerous health agencies have advocated against the regular use of CC. However, regular use of CZ has not shown to carry such risks.

In vitro and in vivo studies in animals and humans from different parts of the world have demonstrated numerous beneficial health effects of CZ, such as anti-inflammatory properties, anti-microbial activity, reducing cardiovascular disease, boosting cognitive function and reducing risk of colonic cancer [5]. The current level of evidence is summarised in Table 1 and described further in the following sections.

In vitro and in vivo effects on blood pressure, glycaemic control and lipids

Two systematic reviews in the effects of CZ extracts on diabetes demonstrate numerous beneficial effects in animal models [6, 7]. In vitro CZ has demonstrated potential for; reducing post-prandial intestinal glucose absorption by inhibiting the activity of pancreatic α -amylase and α -glucosidase, stimulating cellular glucose uptake by membrane translocation of GLUT-4, stimulating glucose metabolism and glycogen synthesis, inhibiting gluconeogenesis by effects on key regulatory enzymes and stimulating insulin release and potentiating insulin receptor activity [6]. Cinnamtannin B1 has been identified as the potential active compound

Table 1. Summary of current evidence

Effects on blood glucose	In vitro	Reducing intestinal glucose absorption and stimulating cellular glucose uptake Stimulating glycolysis and glycogenesis, and inhibiting gluconeogenesis Stimulating insulin release and potentiating insulin receptor activity
	In vivo (animals)	Reducing FBG and HbA1c, and increasing insulin levels
Effects on cholesterol	In vivo (animals)	Reducing LDL cholesterol and increasing HDL cholesterol
Effects on blood pressure	In vivo (animals)	Reduction in blood pressure
Anti-oxidant properties	In vitro	Reduced oxidative stress and free radical scavenging activity
	In vivo (humans)	Reduced oxidative stress and lipid peroxidation
Activity against micro-organisms	In vitro	Bactericidal and fungicidal Anti-bacterial activity (<i>Salmonella enteritidis</i> , oral cavity anaerobic bacteria)
	In vivo	Anti-fungal activity (<i>Candida</i>) Anti-parasitic activity (<i>Cryptosporidium parvum</i>)
Others	In vitro	Inhibiting tau aggregation and filament formation (Alzheimer's disease) Stimulation of collagen synthesis in dermal fibroblasts (anti-ageing skin treatment) Inhibition of osteoclastogenesis (osteoporosis)
	In vivo (animals)	Reducing nephropathy and neuropathy (diabetes) Reduced acid secretion and increased mucus secretion of stomach (peptic ulcer disease) Anti-inflammatory, analgesic and wound healing activity Hepato-protective activity

responsible for these effects [6]. The beneficial effects of CZ observed with in vivo animal models include; attenuation of weight loss associated with diabetes, reduction of fasting blood glucose (FBG), reducing LDL and increasing HDL cholesterol, reducing HbA1c and increasing circulating insulin levels [6]. In addition CZ also showed beneficial effects against diabetic neuropathy and nephropathy in animal models [6].

Effects of CZ extracts (CZA) on mean arterial blood pressure (BP) of normotensive rats (NR), salt-loaded hypertensive rats (SLHR), L-NAME hypertensive rats (LNHR) and spontaneously hypertensive rats (SHR) have been studied [8]. Immediately after intravenous administration, a significant drop in BP was shown in NTR, SLHR and LNHR in a dose dependent manner and the drop in BP was not dose dependent in SHR [8]. These observations indicate that CZ could have potential health benefits in diseases such as diabetes mellitus and hypertension.

In-vitro and in-vivo anti-oxidant properties

The volatile oils of CZ have 55.9% and 66.9% antioxidant activity at 100 and 200 ppm concentration, respectively [9]. The dried fruit extracts of CZ with ethyl acetate, acetone, methanol and water exhibited antioxidant activity in the order of water > methanol > acetone > ethyl acetate [10]. The etheric (0.69 mg),

methanolic (0.88 mg) and aqueous (0.44 mg) cinnamon extracts, inhibited the oxidative process in 68%, 95.5% and 87.5% respectively [11]. CZ bark extracts were found to be potent in free radical scavenging activity especially against DPPH (2,2-diphenyl-1-picrylhydrazyl) radicals and ABTS (2,2'-azino-bis-3-ethylbenzthiazoline-6-sulphonic acid) radical cations, while the hydroxyl and superoxide radicals were also scavenged by the tested compounds [12]. Similarly CZ has 65.3% of anti-oxidant activity and strong free radical scavenging activity [13].

Operating room personnel who consumed tea with CZ (100 mg/ 300 ml) daily for 10 days had their blood samples analysed for biomarkers of oxidative stress including lipid peroxidation level (LPO), total antioxidant power (TAP) and total thiol molecules (TTM). Consumption of cinnamon induced a significant reduction in plasma LPO [14]. Treatment of 54 healthy volunteers with CZ 100 mg/30ml of tea daily was significantly effective in the reduction of lipid peroxidation and increasing TAP and TTM in comparison with controls [15]. The extent of increase in plasma TBARS (thiobarbituric acid reactive substances) and TAP in the CZ group was significantly higher than in those given only regular tea [15]. Hence, CZ has the potential of reducing the oxidative stress associated with diseases such as diabetes, and the potential to reduce oxidative stress associated complications of these diseases.

In vitro and in vivo anti-microbial properties

CZ has shown potential for in-vitro anti-microbial action against a wide variety of gram positive (*Staphylococcus aureus*, *Streptococcus pneumoniae* and *Streptococcus pyogenes*), gram negative (*Escherichia coli*, *Haemophilus Influenzae*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Salmonella typhi*) and anaerobic bacteria (*Clostridium difficile* and *Clostridium perfringens*) [6]. It has also demonstrated in-vitro anti-microbial activity against *Mycobacterium tuberculosis*. In addition there seems to be activity against numerous fungi of *Aspergillus spp.* and *Candida spp.* CZ has demonstrated activity against the human rotavirus too [6].

Administration of CZ oil is beneficial in protecting susceptible hosts against opportunistic zoonotic parasites such as *Cryptosporidium parvum* [16]. Two infants who were chronic carriers of *Salmonella enteritidis* and received short term (10 days) administration of grounded CZ bark had consistently negative stool cultures with neither clinical nor microbiological relapses [17,18]. Activity of CZ against fluconazole resistant and susceptible *Candida* were studied in HIV infected patients having pseudo-membranous candidiasis, where three patients out of five showed improvements in oral candidiasis [19]. The effects of sugared chewing gum containing cinnamic aldehyde and natural flavours from CZ on the short-term germ-killing effect on total and hydrogen sulphide (H₂S)-producing salivary anaerobes has been investigated [20]. Significant reductions in total salivary anaerobes and H₂S-producing salivary anaerobes were observed 20 minutes after participants chewed the gum.

Other in vitro effects

An aqueous extract of CZ is known to inhibit tau aggregation and filament formation in the brain, which are hallmarks of Alzheimer's disease [21]. The extract also promotes complete disassembly of recombinant tau filaments and cause substantial alteration of the morphology of paired-helical filaments isolated from brains of those with Alzheimer's disease, although it was not deleterious to the normal cellular function of tau. An A-linked proanthocyanidin trimer molecule isolated from the CZ extract has shown to contain a significant proportion of this inhibitory activity [21]. CZ extracts facilitate collagen biosynthesis in human dermal fibroblasts [22]. CZ extract up-regulated both mRNA and protein expression levels of type I collagen without cytotoxicity, cinnamaldehyde was the major active component promoting the expression of collagen by HPLC and NMR analysis. This suggests that CZ extracts might be useful in anti-aging treatment of skin [22]. CZ extracts have also exhibited strong inhibitory effects on osteoclastogenesis [23]. CZ dose-dependently inhibited osteoclast-like cell formation at concentrations of 12.5-50 µg/ml without

affecting cell viability. This finding raises prospects for the development of a novel approach in the treatment of osteopenic diseases [23].

Other in vivo effects in animals

CZ is known to have anti-secretagogue and anti-gastric ulcer effects [24]. CZ suspension pre-treatment decreased the basal gastric acid secretion in pylorus ligated rats and effectively inhibited gastric haemorrhagic lesions induced by 80% ethanol, 0.2M NaOH, and 25% NaCl. It also showed anti-ulcer activity against indomethacin. CZ treatment replenished the gastric wall mucus secretion reduced by ethanol [24]. CZ extracts at 100 and 200 mg/kg doses significantly reduced the extent of the diarrhoea (71.7% and 80.4%) in test animals [25].

In a study using two animal models for the investigation of the anti-nociceptive and anti-inflammatory effects of CZ and selected plants, CZ induced a dose-dependent analgesic protective effect against both thermal stimuli. Furthermore, CZ showed an anti-inflammatory effect against chronic inflammation of cotton pellet granulomata [26]. These effects have been confirmed by other authors [27]. CZ has wound healing properties. Topical CZ containing ointments accelerated the wound healing process and specifically increased epithelialisation [28]. Oral CZ increased the wound breaking strength, granulation tissue breaking strength and hydroxyproline content in wister rats [29].

CZ has hepato-protective effects in a study where liver injury was induced in rats by carbon tetrachloride (CCl₄) [30]. Administration of CZ extracts (0.01, 0.05 and 0.1 g/kg) for 28 days significantly reduced the serum levels of liver enzymes. In addition, treatment with CZ increased the levels of superoxide dismutase and catalase enzymes in rats [30]. Water-based extract from CZ was a potent inhibitor of VEGFR2 kinase (vascular endothelial growth factor receptor) activity which is involved in angiogenesis [31]. As a result, CZ inhibited VEGF-induced endothelial cell proliferation, migration and tube formation in vitro, sprout formation from aortic ring ex vivo and tumour-induced blood vessel formation in vivo [31].

In conclusion, the available *in-vitro* and *in-vivo* evidence suggests that CZ has anti-microbial, anti-parasitic, anti-oxidant, free radical scavenging and wound healing properties. In addition, CZ may lower blood glucose, serum cholesterol and blood pressure, suggesting beneficial cardiovascular and metabolic effects. However, most studies have been conducted using animal models. Future studies are necessary to determine whether these effects are reproducible in humans, their public health implications and their safety.

Conflicts of interests

There are no conflicts of interest.

References

- Gruenwald J, Freder J, Armbruester N. Cinnamon and health. *Crit Rev Food Sci Nutr* 2010; **50**: 822-34.
- Paranagama PA, Wimalasena S, Jayatilake GS, *et al.* A comparison of essential oil constituents of bark, leaf root and fruit of cinnamon (*Cinnamomum zeylanicum* Blum), grown in Sri Lanka. *J Nat Sci Foundation* 2010; **29**: 147-53.
- Archer A. Determination of cinnamaldehyde, coumarin and cinnamyl alcohol in cinnamon and cassia by high-performance liquid chromatography. *J Chromatogr* 1988; **447**: 272-6.
- Bundesinstitut für Risikobewertung: High daily intakes of cinnamon: Health risk cannot be ruled out. In: *BfR Health Assessment No 044/2006*. Edited by Federal Institute for Risk Assessment. Germany; 2006.
- Jayaprakasha GK, Rao LJ. Chemistry, biogenesis, and biological activities of *Cinnamomum zeylanicum*. *Crit Rev Food Sci Nutr* 2011; **51**: 547-62.
- Ranasinghe P, Jayawardana R, Galappaththy P, *et al.* Efficacy and safety of 'true' cinnamon (*Cinnamomum zeylanicum*) as a pharmaceutical agent in diabetes: A systematic review and meta-analysis. *Diabetic Medicine* 2012; **29**: 1480-92.
- Bandara T, Uluwaduge I, Jansz ER. Bioactivity of cinnamon with special emphasis on diabetes mellitus: A review. *Int J Food Sci Nutr* 2012; **63**: 380-86.
- Nyadjeu P, Dongmo A, Nguefack TB, Kamanyi A. Antihypertensive and vasorelaxant effects of *Cinnamomum zeylanicum* stem bark aqueous extract in rats. *J Complement Integr Med* 2011; **8**.
- Jayaprakasha GK, Jagan Mohan Rao L, Sakariah KK. Volatile constituents from *Cinnamomum zeylanicum* fruit stalks and their antioxidant activities. *J Agric Food Chem* 2003; **51**: 4344-8.
- Jayaprakasha GK, Negi PS, Jena BS, Rao LJM. Antioxidant and antimutagenic activities of *Cinnamomum zeylanicum* fruit extracts. *J Food Compos Anal* 2007; **20**: 330-6.
- Mancini-Filho J, Van-Koijij A, Mancini DA, Cozzolino FF, Torres RP. Antioxidant activity of cinnamon (*Cinnamomum Zeylanicum*, Breyne) extracts. *Bollettino Chimico Farmaceutico* 1998; **137**: 443-7.
- Mathew S, Abraham TE. Studies on the antioxidant activities of cinnamon (*Cinnamomum verum*) bark extracts, through various in vitro models. *Food Chem* 2004; **94**: 520-8.
- Prakash D, Suri S, Upadhyay G, Singh BN. Total phenol, antioxidant and free radical scavenging activities of some medicinal plants. *Int J Food Sci Nutr* 2007; **58**: 18-28.
- Ranjbar A, Ghasmeinezhad S, Zamani H, *et al.* Antioxidative stress potential of *Cinnamomum zeylanicum* in humans: A comparative cross-sectional clinical study. *Therapy* 2006; **3**: 113-7.
- Ranjbar A, Ghaseminejhad S, Takalu H, *et al.* Anti oxidative stress potential of cinnamon (*Cinnamomum zeylanicum*) in operating room personnel; a before/after cross sectional clinical trial. *Int J Pharmacol* 2007; **3**: 482-6.
- Abu El Ezz NMT, Khalil FAM, Shaapan RM. Therapeutic effect of onion (*Allium cepa*) and cinnamon (*Cinnamomum zeylanicum*) oils on cryptosporidiosis in experimentally infected mice. *Global Veterinaria* 2011; **7**: 179-83.
- Rosti L, Gastaldi G. Chronic salmonellosis and cinnamon. *Pediatrics* 2005; **116**: 1057.
- Rosti L, Gastaldi G, Frigiola A. Cinnamon and bacterial enteric infections. *Indian J Pediatr* 2008; **75**: 529-30.
- Quale JM, Landman D, Zaman MM, Burney S, Sathe SS. In vitro activity of *Cinnamomum zeylanicum* against azole resistant and sensitive *Candida* species and a pilot study of cinnamon for oral candidiasis. *Am J Chin Med* 1996; **24**: 103-9.
- Zhu M, Carvalho R, Scher A, Wu CD. Short-term germ-killing effect of sugar-sweetened cinnamon chewing gum on salivary anaerobes associated with halitosis. *J Clin Dent* 2011; **22**: 23-6.
- Peterson DW, George RC, Scaramozzino F, *et al.* Cinnamon extract inhibits tau aggregation associated with Alzheimer's disease in vitro. *J Alzheimer's Dis* 2009; **17**: 585-97.
- Takasao N, Tsuji-Naito K, Ishikura S, Tamura A, Akagawa M. Cinnamon extract promotes type I collagen biosynthesis via activation of IGF-I signaling in human dermal fibroblasts. *J Agric Food Chem* 2012; **60**: 1193-200.
- Tsuji-Naito K. Aldehydic components of Cinnamon bark extract suppresses RANKL-induced osteoclastogenesis through NFATc1 downregulation. *Bioorganic and Med Chem* 2008; **16**: 9176-83.
- Alqasoumi S. Anti-secretagogue and antiulcer effects of 'cinnamon' *Cinnamomum zeylanicum* in rats. *J Pharmacognosy Phytother* 2012; **4**: 53-61.
- Rao HJ, Lakshmi. Anti-diarrhoeal activity of the aqueous extract of the bark of *Cinnamomum zeylanicum* Linn in mice. *J Clin Diag Res* 2012; **6**: 215-9.
- Atta AH, Alkofahi A. Anti-nociceptive and anti-inflammatory effects of some Jordanian medicinal plant extracts. *J Ethnopharmacol* 1998; **60**: 117-24.
- Ganapaty S, Beknal AK. Anti-inflammatory and analgesic activity of *Cinnamomum zeylanicum* leaf oil. *Indian Drugs* 2005; **42**: 824-5.
- Farahpour MR, Habibi M. Evaluation of the wound healing activity of an ethanolic extract of Ceylon cinnamon in mice. *Veterinari Medicina* 2012; **57**: 53-7.

29. Kamath JV, Rana AC, Chowdhury AR. Pro-healing effect of *Cinnamomum zeylanicum* bark. *Phytother Res* 2003; **17**: 970-2.
30. Eidi A, Mortazavi P, Bazargan M, Zaringhalam J. Hepatoprotective activity of cinnamon ethanolic extract against CCL 4-induced liver injury in rats. *EXCLI Journal* 2012; **11**: 495-507.
31. Lu J, Zhang K, Nam S, *et al.* Novel angiogenesis inhibitory activity in cinnamon extract blocks VEGFR2 kinase and downstream signaling. *Carcinogenesis* 2010; **31**: 481-8.

P Ranasinghe and **P Galappaththy**, *Department of Pharmacology, Faculty of Medicine, University of Colombo, Sri Lanka.*

Correspondence: e-mail: priyanga.ranasinghe@gmail.com.