REVIEW

Diverse pharmacological properties of *Cinnamomum cassia*: A review

Syed Faisal Zaidi[1,2*], Muhammad Aziz[3], Jibran Sualeh Muhammad[4] and Makoto Kadowaki[1]

[1]Division of Gastrointestinal Pathophysiology, Institute of Natural Medicine, University of Toyama, Sugitani, Toyama, Japan
[2]Department of Basic Medical Sciences, College of Medicine, King Saud bin Abdulaziz University of Health Sciences, Jeddah, Kingdom of Saudi Arabia
[3]Medical student, Faculty of Health Sciences, Aga Khan University, Karachi, Pakistan
[4]Department of Gastroenterology and Hematology, University of Toyama, Sugitani, Toyama, Japan

Abstract: *Cinnamomum cassia* is widely utilized as a spice in different cookeries worldwide, especially in Asian cuisines. This herb is also being used in different forms of traditional medicine (Unani, Ayurvedic, Japanese and Chinese) for managing conditions like dyspepsia, peptic ulcer disease and ischemic brain injury. Recent studies have shown the scientific evidence for the medicinal use of this particular herb in several diseases like *H. pylori* infection, diabetes, brain ischemia and cancers. This article reviews the literature on potential benefits of the herb published within the last 10 years. The authors used Medical Subject Headings (MeSH) terms "*Cinnamomum"* with *"cassia"* or *"arromaticum"* to filter the PubMed database. To date, no systemic review focusing on medicinal use of *C. cassia* was found in the literature. Various research articles elucidating diverse pharmacological properties of *C. cassia* were identified. The standardised extract of *C. cassia* or the active compounds extracted from the herb might prove to be a novel candidate for early prevention and complimentary management of conditions like diabetes mellitus or *H. pylori*-associated disorders.

Keywords: *Cinnamomum cassia;* anti-inflammatory; anti-microbial; anti-*H. pylori*; anti-melanin; anti-cancer; anti-diabetic.

INTRODUCTION

Cinnamomum cassia (also known as *Cinnamomum arromaticum,* Chinese cinnamon or Chinese cassia) belongs to Laurel (*Lauraceae*) family of plant kingdom. It is harvested from the bark of its tree and is used as a flavouring agent in various Asian cuisines. Common cultivating countries are India, China, Uganda, Vietnam, Bangladesh and Pakistan. The herb is intensely aromatic and has a sweet taste with a tinge of bitterness. The herb is also used in different forms of traditional medicine. Recently, various studies have reported the medicinal use of this herb in different diseased conditions such as diabetes mellitus, peptic ulcer diseases, and various cancers (Gernot, 2012).

To generate a comprehensive and up-to-date evidence-base for the pharmacological and medicinal use of this herb, studies published within last ten years (2002-2012), including a study from our group, were reviewed and summarised. MeSH terms "*Cinnamomum"* with *"cassia"* or *"arromaticum"* were employed to explore the PubMed and Google Scholar databases. All the studies exploring the effect of this herb were included regardless of outcome of drug on the effect. This study outlines the published uses of this herb to treat diseases along with underlying mechanism if available.

**Corresponding author:* e-mail: sfaisalhz@gmail.com

Active constituents

Major active constituents of *C. cassia* are cinnamaldehyde (75-90%), coumarin (7%) and essential oil (4%) (Ng and Wu, 2011). The other constituents present in trace amount include eugenol, benzoic acid, cinnamic acid, salicylic acid, cinnamyl alcohol and the corresponding esters and aldehydes (Ng and Wu, 2011) (fig. 1). The average daily intake (ADI) of cinnamaldehyde permitted by Food and Drug Administration and World Health Organization (FDA/WHO) for an adult male is 1.25mg/kg (Ng and Wu, 2011)

Properties

The active chemicals in *C. cassia* has been reported to have anti-inflammatory, anti-oxidant, anti-cancer, anti-fungal, anti-pyretic, antimicrobial, anti-angiogenic and larvicidal activity (Lee *et al.,* 2007; Ng and Wu, 2011). Anti-hepatoma activities of *C. cassia* are also reported and the proposed mechanism may include induction of signalling factors within hepatic cells (Lee *et al.,* 2007). Studies have also examined whether *C. cassia* improves glycemic index, insulin resistance, and glucose tolerance in diabetics. Although various studies have supported the anti-diabetic claim by showing various molecular mechanisms (discussed below), only few have used clinical trials to support this claim (Rafehi *et al.,* 2011; Markey *et al.,* 2011; Mohamed *et al.*, 2011; Lee, 2002, Kwon *et al.*, 2006; Vanschoonbeek *et al.*, 2006).

Cinnamic acid, a constituent of *C. cassia* might act as a depigmenting agent by its effect on melanin synthesis pathway (Kong *et al.*, 2008). *C. cassia* and cinnamon oil has potent nematicidal activity against *Bursaphelenchus xylophilus* (Kong *et al.*, 2007). *Guizhi-Fuling*-Capsules (GZFLC), a traditional Chinese formulation containing *C. cassia*, has shown to be protective against brain ischemic damage (Li *et al*., 2007). Also, synergistic effects of *C. cassia* together with several other herbs have been suggested for a polyherbal mixture as a potent anti-oxidant (fig. 2).

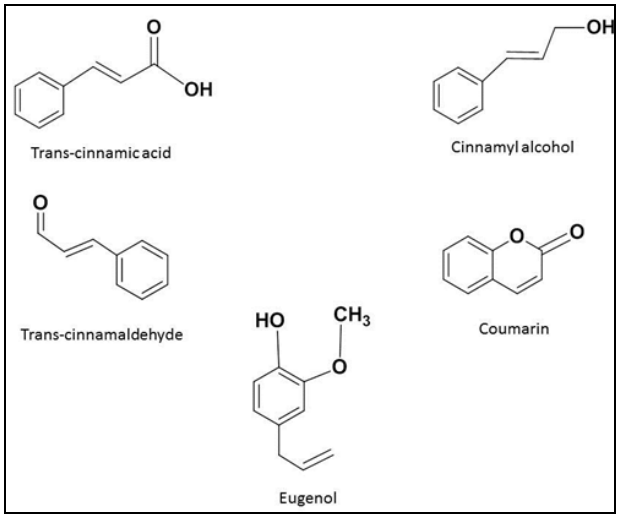

Fig. 1: Chemical structures of various constituents of *Cinnamomum cassia*.

Mechanism of action

Anti-bacterial

C. cassia has been shown to have anti-microbial properties against various pathogens. Ethanol extract of *C. cassia* has shown to have strong activity against *Pseudomonas aeruginosa*. Disc diffusion method was employed to demonstrate this effect (Sharma *et al*., 2009). Agar dilution method was utilized to reveal that pure cinnamaldehyde and its oil extracts are effective against *Staphylococcus aureus, Escherichia coli, Enterobacter aerogenes, Proteus vulgaris, Pseudomonas aeruginosa, Vibrio cholerae, Vibrio parahaemolyticus* and *Salmonella typhymurium*. The minimum inhibitory concentration (MIC) of cinnamaldehyde was reported to be 75 microg/ml to 600 microg/ml (Ooi *et al.,* 2006).

Anti-fungal

Cinnamon has demonstrated to have anti-fungal activity against four species of Candida; *Candida albicans, Candida tropicalis, Candida glabrata,* and *Candida krusei* (MIC: 100 microg/ml to 450 microg/ml), four isolates of molds; three Aspergillus spp. and one Fusarium sp. (MIC: 75 microg/ml to 150 microg/ml) and three isolates of dermatophytes; Microsporum gypseum, Trichophyton rubrum and T. mentagraphytes (MIC: 18.8 microg/ml to 37.5 microg/ml). The MIC was stated after utilizing agar dilution method (Ooi *et al,* 2006). Another study used mice models and *in vitro* assay to exhibit the anti-proliferative activity of *C. cassia* on oral candidiasis (*C. albicans*) with cinnamaldehyde as the major compound producing the effect (Taguchi *et al.*, 2010).

Anti-diabetic

There is an on-going debate whether *C. cassia* possesses anti-diabetic effect (Rafehi *et al,* 2011). A clinical trial evaluated *C. cassia* to observe improvement in fasting serum glucose, insulin sensitivity and lipid profile in post-menopausal diabetics (type II) (Vanschoonbeek *et al.*, 2006). The difference compared with a placebo was statistically not significant as cinnamon supplementation did not improve postprandial response to glucose (7.2±0.2 HBA_{1c} for placebo vs.7.5±0.3 for *C. cassia, P*>0.05) and lipids (2.77±0.24 LDL-cholesterol in placebo vs. 2.85 ±0.16 for *C. cassia, P*>0.05) and neither affected appetite (Vanschoonbeek *et al.*, 2006).

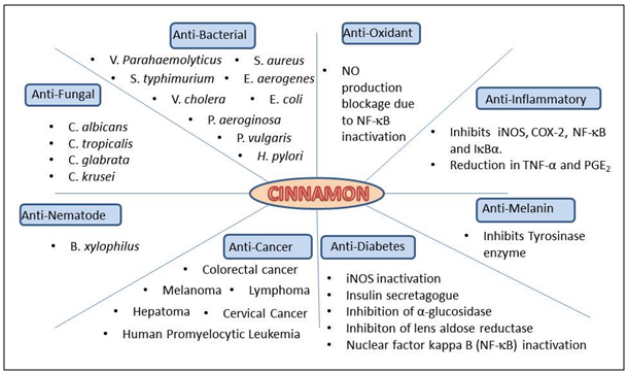

Fig. 2: Various pharmacological properties of *Cinnamomum cassia.*

Studies supporting the anti-diabetic claim have proposed several mechanisms. One study used cinnamaldehyde derived from *C. cassia* to show inhibition of lens aldose reductase, which mediates the polyol pathway on rat model (Lee, 2002). In a non-diabetic individual glucose is not catabolised to sorbitol because of low enzyme affinity. With higher blood glucose levels, the delivery of glucose to tissues such as lens and nerves is increased and is converted by aldose reductase to sorbitol. Sorbitol is not readily diffusible across the membrane and thus accumulates leading to formation of cataract. Inhibition of this enzyme in diabetes can lead to decreased formation of cataracts as the study demonstrates. The author extracted the lens aldose reductase from the mice models and revealed the final results with spectrofluoro-photometer (Lee 2002).

Additional model exhibits the reversible competitive inhibition of α-glucosidase in streptozotocin (STZ) nourished mice. Dialysis experiment was implemented to ascertain the nature of this inhibition (Mohamed *et al.,* 2011). Carbohydrate metabolism can be impaired with α-glucosidase inhibitors such as acarbose. This study

compared *C. cassia* with acarbose as a potential inhibitor of α-glucosidase (control). Cinnamon reduced maltose induced post-prandial glucose spike by 86.3% (600mg) as compared to control 54.2% (5mg) (P<0.001 vs. control) The reduction for sucrose induced post-prandial glucose spike was also significant with a reduction of 67.58% for cinnamon (600mg) against 70.71% for control (5mg) (p<0.01 vs. control).

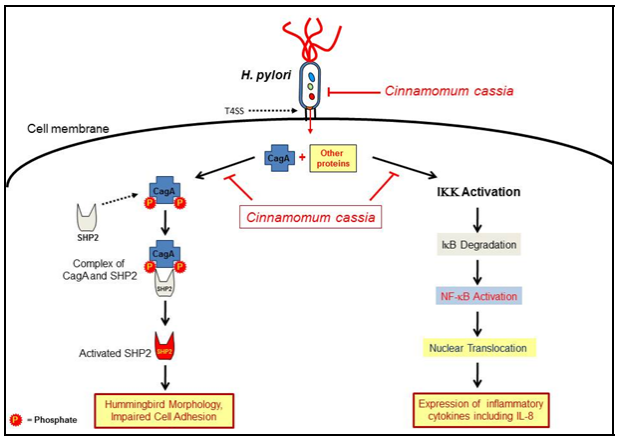

Fig. 3: Multiple actions of *Cinnamomum cassia* against *H. pylori* associated pathogenesis. (T4SS: Type IV secretion system, CagA: Cytotoxin associated gene-A, IKK: IκB Kinase, IκB: Inhibitor of Kappa-B, NF-κB: Nuclear Factor Kappa-B, IL-8: Interleukin-8, SHP-2: Src homology phosphatase-2)

Insulin dependent diabetes mellitus (IDDM type I) is characterized by destruction of pancreatic β-cells in the islets. The inflammatory mechanisms involved include inducible nitric oxide synthase (iNOS) and nuclear factor kappa B (NF-κB) expression, nitric oxide (NO) and interleukin production which ultimately results in β-cell dysfunction. One study showed that 1mg/ml *C. cassia* extract (CCE) can completely block iNOS expression and NF-κB activation at mRNA level in streptozotocin nourished mice. iNOS expression was manifested using RT-PCR and western blotting and NF-κB was assayed by using gel mobility shift assays of nuclear extracts. Hence, a protective effect of cinnamon against diabetes is anticipated in humans (Kwon *et al.,* 2006).

Other studies have shown that cinnamon has insulin secretagogue and insulin sensitizing properties. Insulin signalling pathways are up regulated in skeletal muscles leading to increased glucose uptake. This was illustrated by showing increased expression of insulin dependent substrates i.e. IRS-1/PI 3-kinase on mice models (Qin *et al.,* 2003).

Another study demonstrated altered body composition in association with improved insulin sensitivity. In this study, high fat/high fructose (HF/HF) diet was fed to rats and then divided into groups with one receiving cinnamon. Pancreatic weight was reduced in HF/HF diet as compared to HF/HF + cinnamon diet (p-value <0.01). Also Cinnamon increased glucose infusion in HF/HF as compared to rats that were only given HF/HF diet without cinnamon (Jain *et al.,* 2011).

Anti-oxidant

C. cassia ethanol extract has significant anti-oxidant properties (Boga *et al*., 2011). The underlying mechanism probably includes inhibition of NO production, a potent free radical, via inhibition of NF-κB by cinnamaldehyde. NO activity was assayed *in vitro* using Griess reagent, western blotting and gel electrophoresis (Lee *et al.,* 2005). Cinnamon is used along with several herbs to formulate an herbal tea preparation to lower nitric oxide and oxygen derived free radicals preventing cardiovascular diseases, cancers, arthritis etc. The authors used DPPH free radical scavenging activity, NO scavenging activity and superoxide radical scavenging activity (Jain *et al.,* 2011).

Anti-cancer

Cinnamon has been extensively studied for its anti-neoplastic activity. It has anti-proliferative and apoptotic activity affecting variety of cancers including colorectal cancer, human promyelocytic leukemia, hepatoma, cervical cancer, lymphoma and melanoma through several pathways as exemplified using *in vitro* experiments (Lee *et al.,* 2007; Ng and Wu, 2011, Ka *et al.,* 2003). In most cases the most toxic factor for cancer growth was found out to be cinnamaldehyde (Ka *et al.,* 2003).

In vitro analysis revealed that CD95 (APO-1/CD95) and p53 pathway is affected by cinnamaldehyde in hepatoma cells. p53 is the guardian of genome as it identifies DNA damage and stops replication cycle allowing the cell to repair its damaged content. If the condition is irreversible, p53 directs the cell to undergo apoptosis by increasing Bax (pro-apoptotic) expression while inhibiting Bcl-xl (anti-apoptotic) expression. p53 is induced by cinnamomum thus increasing apoptosis of hepatoma cells (Ng and Wu, 2011). Cinnamaldehyde induces oxygen radicals to cause disruption of mitochondrial membrane and leakage of cytochrome-c, which prompts program cell death in human promyelocytic leukemia cells (Ka *et al.,* 2003). Her-2 gene is down regulated by *C. cassia* in cervical cancer along with mitochondrial membrane disruption, which results in cell death (Koppikar *et al.,* 2010). Anti-melanoma effects of cinnamon extract are produced by NF-κB and AP-1 inactivation, stimulation of pro-apoptotic factors, and modulation of angiogenesis and cytotoxic T lymphocytes. Anti-apoptotic factors including Bcl-2 and Bcl-xl were found to be suppressed by cinnamaldehyde in the mice-melanoma model (Kwon *et al.,* 2010). The activation of Nrf-2 (nuclear factor-E2-related factor 2) dependent anti-oxidant pathway by cinnamon extract in colon cells has been implicated as chemo-preventive activity for colorectal cancers (Wondrak *et al.,* 2010). Cinnamaldehyde further, inactivated AP-1 transcription factor in colon cancer cells,

which is a source for potential oncogenes (Lee *et al.,* 2007).

Anti-H. pylori and gastro protective

Under the traditional Unani medicinal system of Pakistan, the herb has been consumed for curing gastric complaints of diarrhoea, flatulence and vomiting (Zaidi *et al.,* 2009). *H. pylori is* one of the common causes of dyspepsia and various other gastric aliments (Muhammad *et al.*, 2012). Although *H. pylorus is* a non-invasive organism, it stimulates a robust inflammatory and immune response. Bacterial colonization, persistence and virulence, and resulting innate and adaptive host immune responses are all important in the pathogenesis of *H. pylori* related diseases (Muhammad *et al.*, 2013).

An *in vitro* study performed revealed that ethanol extract of Cinnamon has weak anti-*H. pylori* activity by blocking the enzyme urease which is involved in the pathogenesis of *H. pylori* infection of the gut, however, methylene chloride extracts displays a strong anti-*H. pylori* activity, the mechanism of which was not mentioned (Tabak *et al.,* 1999). Human gastric epithelial cells infected with *H. pylori* exhibits reduced IL-8 secretion when treated with *C. cassia*. The concentrations of 50µg/ml and 100µg/ml show the most potent effect and almost totally block the *H. pylori* induced IL-8 secretion. Furthermore, the similar anti-inflammatory effect is also shown in TNF-α (tumour necrosis factor-alpha) stimulated cells, which represent non-infectious inflammatory factors (Zaidi *et al.,* 2012). Furthermore, we also found the inhibition of hummingbird morphology, a characteristic feature of *H. pylori*-infected cells, by *C. cassia* and its major constituent, Cinnamaldehyde, in AGS gastric epithelial cells (data not published) (fig. 3).

Anti-nematodes

To the best of our knowledge, only one study has reported nematicidal use of cinnamon extracts against *Bursaphelenchus xylophilus,* which infects pine trees and causes pine wilts. Cinnamaldehyde was found to be the most potent chemical derived from Cinnamon (Kong *et al.,* 2007). More studies performed on animal models or human trials with different nematodes are required to extrapolate and support the nematicidal effect.

Anti-ischemic and neuroprotective

Guizhi-Fuling-Capsules (GZFLC) is one of the traditional Chinese medicines composed of five different herbs including c*innamomum cassia.* In an *in vivo* rat model experiment, this formulation has been shown to have anti-ischemic effect preventing brain infarction. IL-1β (interleukin-1β) and TNF-α, potent inflammatory mediators, are suppressed whereas IL-10 and IL-10 related inflammation negating cytokines are expressed considerably (Li *et al.,* 2007). Further, research could be carried to find out which herb has the best possible aforementioned effect. Experiments carried out on rat model have shown that cinnamon avoids neuronal cell loss tempted by glutamate by hindering of Ca^{++} influx mechanism (Shimada *et al.,* 2000).

Anti-inflammatory

Mous emacrophages were treated with lip-opolysaccharide (LPS) endotoxin obtained from *E. coli* to cause inflammation. As a result NO levels were increased in these macrophages which are drastically reduced when macrophages are treated with LPS and cinnamaldehyde with a dose dependent response. The underlying mechanism of this suppression is directly related to inhibition of iNOS, COX-2 (cyclooxygenase-2), IκBα (NF-kappa-B inhibitor alpha), and NF-κB. LPS also induces TNF-α, which in turn lead to increased expression of IL-1β and interleukin-6 (IL-6). Cinnamaldehyde also blocked TNF-α and Prostaglandin E_2 (PGE_2) (Liao *et al.,* 2012).

Within the same study, carrageenan was introduced in mouse model to cause paw edema. The edema was shown to be limited by cinnamaldehyde infusion by suppressing NO, TNF-α, and PGE_2. This suppression by cinnamaldehyde is due to inhibition of iNOS, COX-2, and NF-κB. Moreover, cinnamic aldehyde also showed anti-oxidant properties by enhancing the enzymes including catalase, super oxide dismutase, and glutathione peroxidase activities (Liao *et al.,* 2012). The above mentioned study was also supported by another study which used the cinnamon extract to block NO, TNF-α and PGE_2 in LPS induced inflammation in murine macrophages. The study also reveals a direct blocking of Src (spleen tyrosine kinase) / Syk kinase action to mediate NF-κB action (Yu *et al.,* 2012).

Anti-melanin

Guinea pigs were exposed to ultraviolet-B radiation to increase pigmentation of their skin. Cinnamic acid was then applied topically to reduce the pigmentation. Results revealed that cinnamic acid when applied topically reduced skin melanin by 29% without any adverse reactions. Cinnamic acid blocks tyrosinase enzyme to mediate its action, but does not show appreciable activity against dopachrome tautomerase (Kong *et al.,* 2008). Therefore, Cinnamon might be used in cosmetics and beauty products to enhance skin whitening by its effect on melanin bio-synthetic pathway in skin cells. Studies are required to explore possible effect on alpha-melanocyte stimulating hormone and microphthalmia transcription factor (Mitf) expression for de-pigmenting pathway.

Anti-allergy

Allergic diseases related to mucosal mast cells, such as food allergies, are thought to be treated by cinnamaldehyde. Inhibitory effects of cinnamaldehyde on phospholipase C (PLC) signalling pathway in human

embryonic kidney cells have been shown (Kim *et al.,* 2008). Similar pathways are thought to play a major role in intracellular mobilization of Ca^{++} ions in mucosal mast cells. Yahara *et al.* confirms this by showing inhibition of mucosal mast cell activation via suppression of PLCγ1 signalling pathway (Yahara *et al.,* 2011).

Pregnancy and lactation

Although adverse reactions of cinnamon in pregnancy and lactation have not been reported, however, to the best of our knowledge, no study is available to establish a relationship between the herb and its safety and efficacy during pregnancy and lactation.

CONCLUSION

Cinnamon has been broadly studied for its anti-microbial, anti-inflammatory, anti-cancer, anti-diabetic, anti-melanin and anti-oxidant effects. Hereby we review these effects with the underlying pathophysiological mechanism and type of study involved. The anti-diabetic effects need to be explored and should be studied extensively as we believe that the data available in this regard is scarce. The emerging multiple mode of actions of cinnamon against *H. pylori*-related pathogenic pathways also demands for *in vivo* experiments and clinical trials. In view of all the pharmacological properties discussed above, the therapeutic applications of cinnamon are quite vast and the potential for unveiling more benefits is tremendous. Clinical trials on a large scale would provide a better insight and the true relationship between the molecular, chemical and physical properties.

REFERENCES

Boğa M, Hacıbekiroğlu I and Kolak U (2011). Antioxidant and anti-cholinesterase activities of eleven edible plants. *Pharm Biol.,* **49**(3): 290-295.

Couturier K, Batandier C, Awada M, Hininger-Favier I, Canini F, Anderson RA, Leverve X and Roussel AM (2010). Cinnamon improves insulin sensitivity and alters the body composition in an animal model of the metabolic syndrome. *Arch. Biochem. Biophys.,* **501**(1): 158-1561.

Gernot Katzer (2007). Cassia (*Cinnamomum cassia* (L.) Presl). *Gernot Katzer*. Web. 3 Apr 2012. <http://www.uni-graz.at/~katzer/engl/Cinn_cas.html>.

Jain DP, Pancholi SS and Patel R (2011). Synergistic antioxidant activity of green tea with some herbs. *J. Adv. Pharm. Technol. Res.,* **2**(3): 177-183.

Ka H, Park HJ, Jung HJ, Choi JW, Cho KS, Ha J and Lee KT (2003). Cinnamaldehyde induces apoptosis by ROS-mediated mitochondrial permeability transition in human promyelocytic leukemia HL-60 cells. *Cancer Lett.,* **196**(2): 143-152.

Kageyama-Yahara N, Wang X, Katagiri T, Wang P, Yamamoto T, Tominaga M and Kadowaki M (2011). Suppression of phospholipase Cg1 phosphorylation by cinnamaldehyde inhibits antigen-induced extra cellular calcium influx and degranulation in mucosal mast cells. *Biochem. Biophys. Res. Commun.,* **416**: 283-288.

Kim KY, Bang S, Han S, Nguyen YH, Kang TM, Kang KW and Hwang SW (2008). TRP-independent inhibition of the phospholipase C pathway by natural sensory ligands. *Biochem. Biophys. Res. Commun.,* **370**: 295-300.

Kong JO, Lee SM, Moon YS, Lee SG and Ahn YJ (2007). Nematicidal activity of cassia and cinnamon oil compounds and related rompounds toward bursa-phelenchus xylophilus (Nematoda: Parasitaphelen-chidae). *J. Nematol.,* **39**(1): 31-36.

Kong YH, Jo YO, Cho CW, Son D, Park S, Rho J and Choi SY (2008). Inhibitory effects of cinnamic acid on melanin biosynthesis in skin. *Biol. Pharm. Bull.,* **31**(5): 946-948.

Koppikar SJ, Choudhari AS, Suryavanshi SA, Kumari S, Chattopadhyay S and Kaul-Ghanekar R (2010). Aqueous cinnamon extract (ACE-c) from the bark of *Cinnamomum cassia* causes apoptosis in human cervical cancer cell line (SiHa) through loss of mitochondrial membrane potential. *BMC Cancer,* **10**: 210.

Kwon HK, Hwang JS, So JS, Lee CG, Sahoo A, Ryu JH, Jeon WK, Ko BS, Im CR, Lee SH, Park ZY and Im SH (2010) Cinnamon extract induces tumor cell death through inhibition of NFkappaB and AP1. *BMC Cancer,* **10**: 392.

Kwon KB, Kim EK, Jeong ES, Lee YH, Lee YR, Park JW, Ryu DG and Park BH (2006), Cortex cinnamomi extract prevents streptozotocin- and cytokine-induced beta-cell damage by inhibiting NF-kappaB. *World J. Gastroenterol.,* **12**(27): 4331-4337.

Lee CW, Lee SH, Lee JW, Ban JO, Lee SY, Yoo HS, Jung JK, Moon DC, Oh KW and Hong JT (2007). 2-Hydroxycinnamaldehyde Inhibits SW620 Colon Cancer Cell Growth through AP-1 Inactivation. *J. Pharmacol. Sci.,* **104**(1): 19-28.

Lee HS (2002). Inhibitory activity of *Cinnamomum cassia* bark-derived component against rat lens aldose reductase. *J. Pharm. Sci.,* **5**(3): 226-230.

Lee SH, Lee SY, Son DJ, Lee H, Yoo HS, Song S, Oh KW, Han DC, Kwon BM and Hong JT (2005). Inhibitory effect of 2'-hydroxycinnamaldehyde on nitric oxide production through inhibition of NF-kappa B activation in RAW 264.7 cells. *Biochem. Pharmacol.,* **69**(5): 791-799.

Li TJ, Qiu Y, Mao JQ, Yang PY, Rui YC and Chen WS (2007). Protective effects of guizhi-fuling-capsules on rat brain ischemia/reperfusion injury. *J. Pharmacol. Sci.,* **105**(1): 34-40.

Liao JC, Deng JS, Chiu CS, Hou WC, Huang SS, Shie PH and Huang GJ (2012). Anti-Inflammatory activities of *Cinnamomum cassia* constituents *in vitro* and *in vivo*. *Evid. Based Complement. Alternat. Med*. 429320.

Markey O, McClean CM, Medlow P, Davison GW, Trinick TR, Duly E and Shafat A (2011). Effect of cinnamon on gastric emptying, arterial stiffness, postprandial lipemia, glycemia and appetite responses to high-fat breakfast. *Cardiovasc. Diabetol.,* **10**: 78.

Mohamed Sham Shihabudeen H, Hansi Priscilla D and Thirumurugan K (2011). Cinnamon extract inhibits α-glucosidase activity and dampens postprandial glucose excursion in diabetic rats. *Nutr. Metab.* (Lond.), **8**(1): 46.

Muhammad JS, Zaidi SF and Sugiyama T (2012). Epidemiological ins and outs of *Helicobacter pylori*: A review. *J. Pak. Med. Assoc.,* **62**(9): 955-959.

Muhammad JS, Sugiyama T and Zaidi SF (2013). Gastric pathophysiological ins and outs of *Helicobacter pylori*: A review. *J. Pak. Med. Assoc.,* **63**(12): 1528-1533.

Ng LT and Wu SJ (2011). Antiproliferative activity of *Cinnamomum cassia* constituents and effects of pifithrin-alpha on their apoptotic signalling pathways in Hep G2 Cells. doi:10.1093/ecam/nep220.

Ooi LS, Li Y, Kam SL, Wang H, Wong EY and Ooi VE (2006). Anti-microbial activities of cinnamon oil and cinnamaldehyde from the Chinese medicinal herb *Cinnamomum cassia Blume. Am. J. Chin. Med.,* **34**(3): 511-522.

Qin B, Nagasaki M, Ren M, Bajotto G, Oshida Y and Sato Y (2003). Cinnamon extract (traditional herb) potentiates *in vivo* insulin-regulated glucose utilization via enhancing insulin signaling in rats. *Diabetes Res. Clin. Pract.,* **62**(3):139-148.

R&D Chemicals. N.p., n.d. Web. 9 Jun 2012. <http://www.rdchemicals.com/>.

Rafehi H, Ververis K and Karagiannis TC (2011). Controversies surrounding the clinical potential of cinnamon for the management of diabetes. *Diabetes Obes Metab.,* 2011 Nov 16. Doi: 10.1111/j.1463-1326.2011.01538.

Sharma A, Chandraker S, Patel VK and Ramteke P (2009). Antibacterial activity of medicinal plants against pathogens causing complicated urinary tract infections. *Indian J. Pharm. Sci.,* **71**(2): 136-139.

Shimada Y, Goto H, Kogure T, Kohta K, Shintani T, Itoh T and Terasawa K (2000). Extract prepared from the bark of *Cinnamomum cassia Blume* prevents glutamate-induced neuronal death in cultured cerebellar granule cells. *Phytother. Res.,* **14**(6): 466-468.

Tabak M, Armon R and Neeman I (1999). Cinnamon extracts' inhibitory effect on *Helicobacter pylori*. *J. Ethnopharmacol.,* **67**: 269-277.

Taguchi Y, Takizawa T, Ishibashi H, Sagawa T, Arai R, Inoue S, Yamaguchi H and Abe S (2010). Therapeutic effects on murine oral candidiasis by oral administration of cassia (*Cinnamomum cassia*) preparation. *Nihon Ishinkin Gakkai Zasshi.,* **51**(1): 13-21.

Vanschoonbeek K, Thomassen BJ, Senden JM, Wodzig WK and van Loon LJ (2006). Cinnamon supplementation does not improve glycemic control in postmenopausal type 2 diabetes patients. *J. Nutr.,* **136**(4): 977-980.

Wondrak GT, Villeneuve NF, Lamore SD, Bause AS, Jiang T and Zhang DD (2010). The cinnamon-derived dietary factor cinnamic aldehyde activates the Nrf2-dependent antioxidant response in human epithelial colon cells. *Molecules,* **15**(5): 3338-3355.

Yu T, Lee S, Yang WS, Jang HJ, Lee YJ, Kim TW, Kim SY, Lee J and Cho JY (2012). The ability of an ethanol extract of *Cinnamomum cassia* to inhibit Src and spleen tyrosine kinase activity contributes to its anti-inflammatory action. *J. Ethnopharmacol.,* **139**(2): 566-573.

Zaidi SF, Muhammad JS, Shahryar S, Usmanghani K, Gilani AH, Jafri W and Sugiyama T (2012). Anti-inflammatory and cytoprotective effects of selected Pakistani medicinal plants in *Helicobacter pylori*-infected gastric epithelial cells. *J. Ethnopharmacol.,* 141(1): 403-410.

Zaidi SF, Yamada K, Kadowaki M, Usmanghani K and Sugiyama T (2009). Bactericidal activity of medicinal plants, employed for the treatment of gastrointestinal ailments, against *Helicobacter pylori*. *J. Ethnopharmacol.,* **121**(2): 286-291.