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Review Article

Cinnamon- A Natural Replacement for Synthetic Drugs: A Review

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Abstract

India is a country of spices, taste, flavor etc. Spices which are commonly used in India have lots of medicinal properties and are used from very ancient time for the treatment of diabetes, diarrhea, cardiovascular disorders, gastro-intestinal problems, nausea and many more. Charaka samhita along with Sushruta samhita are the two early texts on Ayurveda (Indian tradition medicine) in which medical use of herbs and spices used in India are given. In this review article, the medical use of *Cinnamomum zeylanicum* (cinnamon; daalchini) is discussed. Cinnamon is beneficial in oxidative stress, insulin resistance, glucose transport, inflammation, cancer, Alzheimer's disease etc. These are the medical conditions which are necessary to be treated for the survival. But their treatment, therapy and medicine are not in an affordable price to all the people. Hence cinnamon can be used as an alternative to these expensive treatments.

Keywords

Alzheimer's disease

Cancer

Cinnamon

Insulin resistance

Oxidative stress

Introduction

Nature bestowed us with a variety of foods and herbal products, which are considered to be less toxic and free from side effects than synthetic ones (Valiathan, 1998). India is rich in flavors, taste, herbal spices etc. In India herbs and spices which were added in different types of food for flavor or as preservative, many of them have antioxidant activity (Shahidi and Wanasundara, 1992; Schwarz et al., 2001; Tanabe et al., 2002). Plants product improves glucose metabolism and diabetes not only by hypoglycemic effect but also by improving lipid metabolism and antioxidant status (Bailey et al., 1989). Aromatic plants and their essential oil have antimicrobial (Mansoub and Myandoab, 2011) and antioxidant effects (Botsoglou et al., 2002). Number of herbs contains a variety of phenolic acids, triterpenes, phytosterols, saponins, carotenoids, flavonoids and anthocyanin's, which shows to exert cancer chemo-preventive and antioxidant properties (Agrawal et al., 2010).

Essential oil from aromatic plants provides antioxidative defense mechanism by activating antioxidant enzyme activity (Hsu et al., 2011). Hence researchers ware taking keen interest to find natural antioxidant from plant materials in order to replace

synthetic antioxidant (Chanwitheesuk et al., 2005). Cinnamon is among the world's oldest spice, it is a spice which is potentially used in naturopathic medicine from ancient times, cited in Chinese books 4000 years ago and it is also traditionally used in Ayurveda and Chinese medicine to treat diabetes (Qin et al., 2003; Modak et al., 2007). Cinnamon is popular flavoring ingredient and this made cinnamon to be widely used in food products. *Cinnamomum zeylanicum* bark is the outer skin of an evergreen tall tree which belongs to Lauraceae family (Kwon et al., 2009).

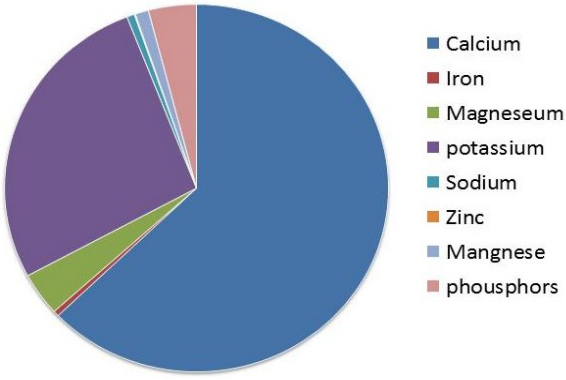
Chemical composition of cinnamon

Cinnamon is herb which is used as a spice in almost all the food preparations. Chemical constituent of cinnamon make it rich in many health beneficial properties like anti-oxidative, antimicrobial, insulin sensitivity, anti-ulcer, anti-diabetic, anti-inflammatory etc. Cinnamon bark contains essential oils, resinous compounds, cinnamate, cinnamic acid and cinnamaldehyde. Tung et al., 2008 reported trans-cinnamaldehyde, L- borenol, L- bornyl acetate, caryophyllene oxide, eugenol, b- caryophyllene, E-nerolidol and cinnamyle acetate. Chemically cinnamon bark also contains terpinolene, α- terpinol, α- cubebene and α- thujene (Tung et al., 2008). Cinnamaldehyde present in cinnamon absorbes oxygen at its ages which make cinnamon pungent in taste and responsible for its scent. Dark color of cinnamon is due to the presence of resinous compounds (Singh et al., 2007).Chemical composition of cinnamon is given in Table 1 and in Fig. 1 showing the amount of minerals present in cinnamon.

Table 1. Chemical composition and properties of cinnamon.

Chemical Components	Micronutrients	Vitamins	Antioxidants	Properties
Cinnamic acid	Calcium	Folates	Carotenes	Anti-oxidative Antimicrobial Anti-inflammatory Anti-diabetic Antitumor Antiseptic Local anesthetic Carminative Anti-clotting Gastrointestinal Weight reducer
Cinnamyl aldehyde	Copper	Niacin	Zea-xanthin	
Tannin	Iron	Pantothenic acid	Lutein	
Eugenol	Magnesium	Pyridoxine	Cryptoxanthin	
Coumarin	Manganese	Riboflavin	Vitamin C	
Ethyle-cinnamate	Phosphorous	Thiamin	Vitamin E	
Linalool	Zinc	Vitamin A	Oleoresins	

Fig. 1: Minerals present in cinnamon.



Potential therapeutic applications of cinnamon

Antioxidant

Free radicals are the molecules which have unpaired electron in their outer orbit (Uttara et al., 2009). Molecules which give rise to fee radical are the group of oxidants which is collectively known as reactive oxygen species (ROS), and when they increase in the body they cause oxidative stress (Kunwar et al., 2011). To maintain the normal physiological functions, balance between formation and removal of reactive oxygen molecules is must (Pari and Amudha, 2011).

In human body → ROS generation = ROS removal by antioxidants

Antioxidant are the molecules which are able to prevent or slow down the oxidation of other molecules by free radicals, hence protect cell and tissue from the damage through free radicals (Lim and Lee, 2013). Process by which antioxidants prevent oxidative stress and its other properties are given in Fig. 2.

The use of synthetic antioxidants in cosmetics, pharmaceutical and food products has been in common practice, butylated 4-hydroxytoluene (BHT) and butylated 4-hydroxyanisole (BHA) are commonly used

synthetic antioxidants in food industry (Chung, 1999). Use of synthetic antioxidants has been questioned because of their potential health risks and toxicity (Kalt et al., 1999). It was observed that synthetic antioxidants are dangerous for human health (Gupta and Sharma, 2006). Indian spices having antioxidants and their antioxidant capacities according to the ORCA value is given in Fig. 3.

Fig. 2: Mechanisms and other properties of cinnamon.

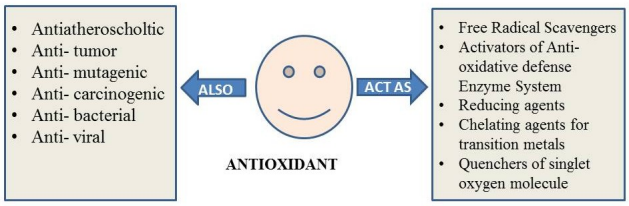
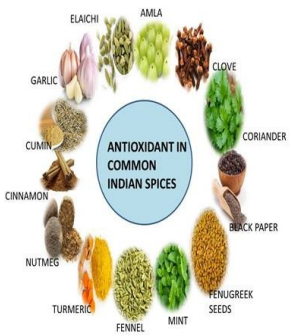
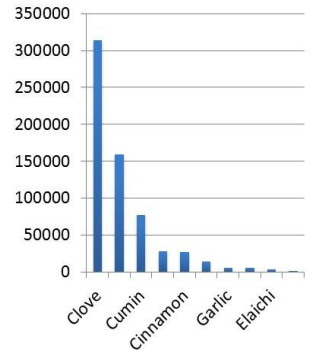


Fig. 3: Common Indian spices having antioxidant and their antioxidant capacities according to ORCA value.



Common Indian spices with Anti-oxidative properties



Anti-oxidative capacity of common Indian spices according to ORCA value

Fruit of cinnamon which is an underutilized and unconventional part has good amount of phenolic antioxidant and it may even protect against mutagenesis (Doughari, 2012). Cinnamon oil is an important endogenous antioxidant and also used as a protective agent against tissue damage (Rao and Gan, 2014). Cinnamon is a natural product which is safe in all respect, is rich in polyphenolic compound that shows antioxidant activity in-vitro (Shobana and Naidu, 2000).

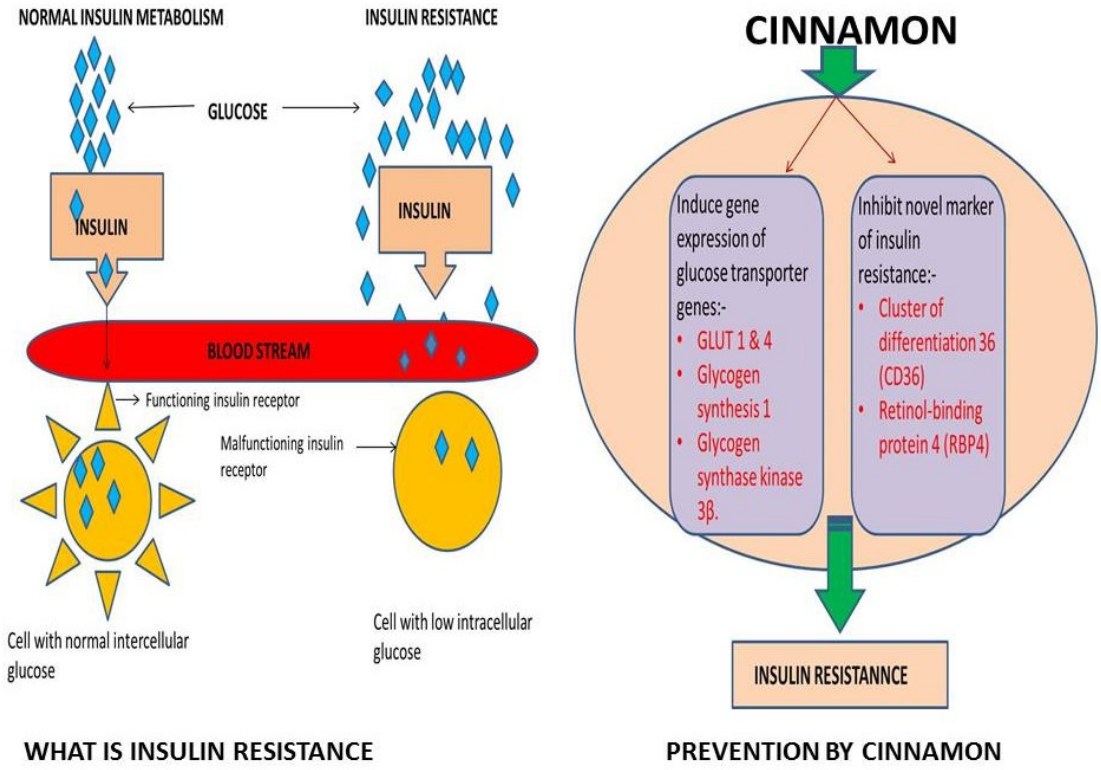
Aqueous extract of cinnamon decreased fasting blood glucose, decreased systolic blood pressure, increased lean mass and decreased body fat (Ziegenfuss et al., 2006). There exists a positive correlation between plasma glucose levels and plasma malondyaldehyde (MDA), a measure of lipid peroxidation. In people with metabolic syndrome, cinnamon improves impaired fasting glucose by its antioxidant effects and thus regulate of cinnamon supplementation assessed by plasma MDA levels (Roussel et al., 2009). Aqueous extract of cinnamon reduced plasma MDA levels in metabolic syndrome, which results in decreased lipid peroxidation, increased plasma sulfhydryl groups which indicate a protection of antioxidant sulfhydryl groups against oxidation (Hayden and Tyagi, 2004).

Cinnamon possesses antioxidant activity in rat fed with high fat diet (Dhuley, 1999). Cinnamon's essential oil has antioxidant properties (Case et al., 1995; Lee et al., 2001; Yu et al., 2002; Lee et al., 2007). According to Mathew and Abraham (2006), methanolic extract of Cinnamon have large number of antioxidant compounds; which can effectively scavenge reactive oxygen species along with superoxide anions and hydroxyl radicals as well as other free radicals under in vitro condition cinnamon extracts also said to be reduce lipid peroxidation in the β-carotene-linoleic acid system (Mancini-Filho et al., 1998). Cinnamon extracts also known to have protective capacity against irradiation induced lipid peroxidation in liposomes, and quenched hydroxyl radicals and hydrogen peroxide (Peschel et al., 2006).

Cinnamon, insulin sensitivity and glucose transport

GLUT4 is a Glucose transporter which transports glucose across plasma membranes into skeletal muscle and adipocytes. Study done by Qin et al. (2010a) shows that cinnamon extract increases glucose uptake and GLUT4 expression in 3T3-L1 adipose cells. Water extract of cinnamon reduced blood glucose, plasma insulin and soluble cluster of differentiation 36 (CD36) (Qin et al., 2010b). Soluble cluster of differentiation 36 (CD36) is known to be a novel marker of insulin resistance (Handberg et al., 2006). Retinol-binding protein 4 (RBP4), a novel adipokine which is also responsible for insulin resistance in plasma and adipose tissues is also inhibited by cinnamon extract (Yang et al., 2007). In insulin-resistant in humans and rodents, retinol-binding protein 4 is increased in the serum which leads to insulin resistance in muscle and increases glucose production in liver (Graham et al., 2006; Polonsky, 2006). Plasma RBP4 levels are inversely related to the expression of GLUT4 in adipose tissue (Graham et al., 2006; Polonsky, 2006). Glut1, Glut4, glycogen synthesis 1, and glycogen synthase kinase 3β are the genes which regulate glucose uptake; consumption of cinnamon extract also appears to regulate their mRNA expression in adipose tissue (Qin et al., 2010b). Fig. 4 shows, what is insulin resistance and its prevention by cinnamon.

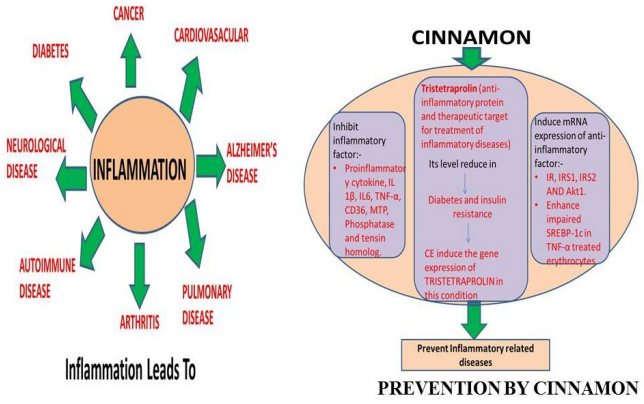
Fig. 4: What is insulin resistance? and it's prevention by cinnamon.



Cinnamon and inflammation

Inflammation and type 2 diabetes mellitus are strongly related because elevated inflammatory cytokines contribute to insulin resistance (Qin et al., 2010a). Since tristetraprolin is an anti-inflammatory protein which makes it a potential therapeutic target for the treatment of inflammation related diseases. In obese population with metabolic syndrome, tristetraprolin gene expression is reduced in the adipose tissue (Duncan et al., 2003). Tristetraprolin is also known to offer a partial protection against the development of insulin resistance and diabetes (Cao et al., 2008). Study done by Cao et al., (2008) concluded that in obese insulin resistance people cinnamon extract induces the expression of tristetraprolin mRNA levels in 3T3-L1 adipocytes. Tumor necrosis factor (TNF)-α is a proinflammatory cytokine, which is a related to obesity, insulin resistance, and metabolic syndrome, induces the overproduction of intestinal apolipoprotein B48 (apoB48) - containing lipoproteins (Cao et al., 2007; Bouchard et al., 2007). mRNA expression of the inflammatory factors [interleukin (IL) 1β, IL6, and TNF-α] is reduced by Cinnamon extract treatment; and improvement of the mRNA expression of IR, IRS1, IRS2, PI3K, and Akt1; inhibits CD36, microsomal triglyceride transfer protein (MTP), and phosphatase and tensin homolog; and enhances impaired sterol regulatory element-binding protein (SREBP)-1c expression in TNF-α- treated erythrocytes (Qin et al., 2007). Cinnamon extract reduces inflammation-related dyslipidemia and decreases risk factors associated with cardiovascular diseases (Qin et al., 2010a). Adverse effects of inflammation and its prevention by cinnamon is summarized in Fig. 5.

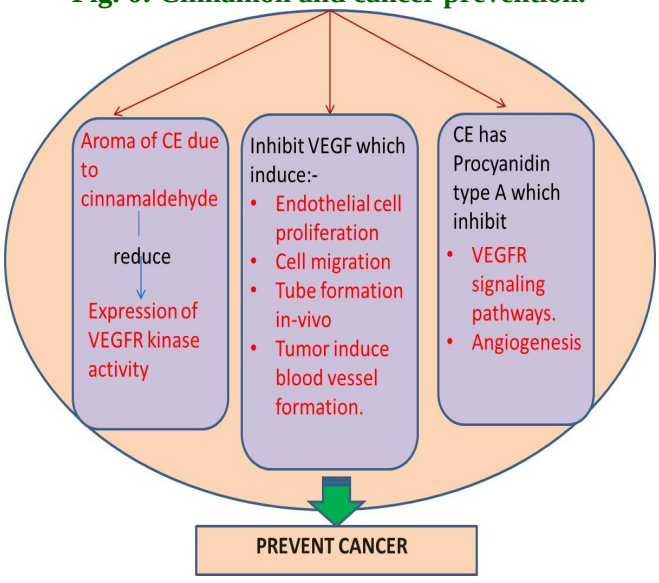
Fig. 5: Adverse effects of inflammation and its prevention by cinnamon.



Cinnamon, vascular endothelial growth factor (VEGF) and cancer

Vascular endothelial growth factor is a mitogenic and angiogenic factor which causes tumor progression, collateral vessel formation in ischemic tissues, inflammation, development of diabetic retinopathy (Ferrara, 2004). Vascular endothelial growth factor is also a novel mediator of adipogenesis in obesity and insulin resistance condition (Nishimura et al., 2007). Vascular endothelial growth factor is the most critical factors that activate angiogenesis, which make it an attractive target for antiangiogenics treatment. Many of the anti-VEGF agents cause side effects and therefore not recommended for long-term use. Naturally occurring VEGF inhibitors identification from foods is an alternative approach to control with an advantage of anticipated safety. Extract of Cinnamon is known to inhibit VEGF-induced endothelial cell proliferation, cell migration, and tumor-induced blood vessel formation *in vivo* (Lu et al., 2010). Aroma of cinnamaldehyde in cinnamon extract, has minute effect on VEGF receptor (VEGFR) kinase activity, procyanidin type A trimer (MW 864) and a tetramer (MW 1152) in cinnamon extract, inhibit the kinase activity of purified VEGFR and VEGFR signaling pathways (Qin et al., 2010b). Cinnamon is identified as a natural inhibitor of VEGF signaling that could potentially be useful in cancer prevention and/or treatment (Lu et al., 2010). Fig. 6 shows the mechanism by which cinnamon proves beneficial in cancer.

Fig. 6: Cinnamon and cancer prevention.



Cinnamon and Alzheimer's disease

Extracellular plaques of β-amyloid and intracellular neurofibrillary tangles of tau are the trademarks of Alzheimer's disease (Ferrari et al., 2003). Insulin resistance increased the incidence of Alzheimer's disease; it is now also referred to as type 3 diabetes (De la Monte and Wands, 2008). Study done by Blurton-Jones and LaFerla, (2006) shows that the tangles of tau are followed by events of amyloid formation, which results in the central pathology of this neurodegenerative process. Thus, preventing tau aggregation may be key step for the Alzheimer's disease therapies. Aqueous extract of cinnamon is found to inhibit tau aggregation and its filament formation, and a complete disassembly of recombinant tau filaments in the brain of a person who died of Alzheimer's disease (Peterson et al., 2009).

A-linked proanthocyanidin trimer molecule and cinnamaldehyde in cinnamon extract contain a significant proportion of inhibitory activity. Cinnamon extract also blocked cell swelling in an in vitro model of ischemic stroke (Panickar et al., 2009). Hence the compounds present in cinnamon may be beneficial to Alzheimer's disease and/or stroke and may lead to the discovery of other potential therapeutics. Fig. 7 shows the formation of amyloid plaques and tangles of tau in Alzheimer's disease and how cinnamon prevents them.

Cinnamon and blood

Red blood cells (RBCs) require a robust antioxidant system to neutralize the significant oxidative load encountered during circulatory transit; this is particularly true during physiological stress (Rogers et al., 2009).

Erythropoietin (Epo), is a hormone released during hypoxia in the kidneys, it enhances red blood cell (RBC) production i.e. (erythropoiesis) by stimulating the proliferation of erythroid progenitors and precursors in the bone marrow (Krants, 1991; Fandrey et al., 1994). Vitamin A supplementation also increases erythropoietin and hemoglobin concentrations in children with poor vitamin A status (Mwanri et al., 2000; Zimmerman et al., 2006).

Antioxidant supplementation was associated with the increase in bone marrow cell counts after irradiation (Wambi et al., 2008). Pretreatment of animals with

antioxidants leads to the significant increase in the total white blood cell and neutrophil counts in peripheral blood at 4 and 24 h (Wambi et al., 2008). Cinnamon extracts have anti-cancer effect which is associated with the modulation of angiogenesis and effector function of CD8+ T cells (Kwon et al., 2010). Having black cumin seeds, thyme, cinnamon barks or their mixture as biological feed additives leads to the significant increase in RBC count (Demir et al., 2008).

All the stimulatory and inhibitory factors which are responsible for the preventions of discussed disease and are controlled by pharmaceutical properties of cinnamon are summarized in Table 2.

Fig. 7: Alzheimer's disease and its prevention by cinnamon.

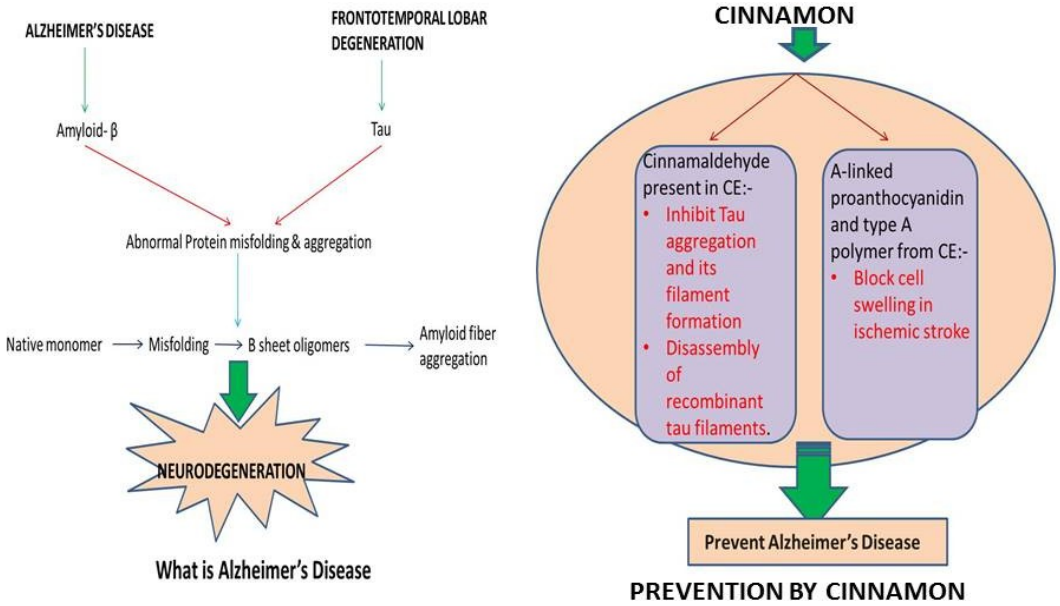


Table 2. Prevention of diseases by cinnamon.

Cinnamon		
Stimulate	**Inhibit**	**Prevent**
Gene expression of glucose transporter genes:- • GLUT 1 & 4 • Glycogen synthesis 1 • Glycogen synthase kinase 3β	Novel marker of insulin resistance:- • Cluster of differentiation 36 (CD 36) • Retinol-binding protein 4 (RBP 4)	Insulin resistance
mRNA expression of anti- inflammatory factors:- • IR, IRS 1, IRS 2 & Akt 1 • Impaired regulatory SREBP-1c expression in TNF-α treated erythrocyte. • mRNA expression of tristetraprolin	Inflammatory factors:- • Pro-inflammatory cytokine interleukin (IL) 1β, IL6. • TNF-α • Microsomal triglyceride transfer protein (MTP) • Phosphatase • Tensin homolog	Inflammation
	• Tau aggregation and its filament formation. • Disassembly of recombinant tau filaments.	Alzheimer's disease
	• Cell swelling	Ischemic stroke
	• VEGF-induced endothelial cell proliferation. • Tumor-induced blood vessel formation in vivo. • VEGF receptor (VEGFR) kinase activity. • VEGFR signaling pathways.	Cancer
• Increase Sulfhydryl group	• Reduce MDA level. • Decrease fasting blood glucose. • Decrease lipid peroxidation.	Oxidative Stress

Conclusion

Cinnamon is one of the most common Indian spice which is used in almost all the food preparations as flavoring agent, as preservative, for fragrance etc. Cinnamon is in use for the treatment of many medical conditions from very ancient times. Above literature shows that cinnamon and its components are beneficially related to metabolic syndrome *i.e.* insulin sensitivity, glucose, lipids, antioxidant, blood, inflammation and body weight. Cinnamon also improves the factors related to Alzheimer's disease, stroke and cancer in vitro studies. Considering all these health beneficial properties, cinnamon is a boom in Indian spices. Cinnamon may be used as an alternative therapeutic drug for the expensive treatment of cancer, inflammation, cardiovascular disease, diabetes, insulin sensitivity etc.

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References

Agrawal, A.D., Bavaskar, S.R., Bagad, Y.M., Bhurat, M.R., 2010. Herbs and Human Health: A Review, Der. Pharmacia. Lettre 2(2), 338-345.

Bailey, C.J., Day, C., 1989. Traditional plant medicines as treatments for diabetes, Diabet. Care 12(8), 553-564.

Blurton-Jones, M., LaFerla, F.M., 2006. Pathways by which Abeta facilitates tau pathology, Curr. Alzheimer Res. 3(5), 437-448.

Botsoglou, N.A., Florou-Paner, P., Chiristaki, E., Fletouris, D.J., Spais, A.B., 2002. Effect of dietary oregano essential oil on performance of chickens and on iron-induced lipid oxidation of breast, thigh and abdominal fat tissue, Br. Poult. Sci. 43(2), 223-230.

Bouchard, L., Vohl, M.C., Deshaies, Y., Rheaume, C., Daris, M., Tchernof, A., 2007. Visceral adipose tissue zinc finger protein 36 mRNA levels are correlated with insulin, insulin resistance index, and adiponectinemia in women, Eur. J. Endocrinol. 157(4), 451-457.

Cao, H., Urban, J.F., Anderson, R.A., 2008. Cinnamon polyphenol extract affects immune responses by regulating anti- and proinflammatory and glucose transporter gene expression in mouse macrophages, J. Nutr. 138(5), 833-840.

Cao, H., Polansky, M.M., Anderson, R.A., 2007. Cinnamon extract and poly-phenols affect the expression of tristetraprolin, insulin receptor, and glucose transporter 4 in mouse 3T3-L1 adipocytes, Arch. Biochem. Biophys. 459(2), 214-222.

Case, G.L., He, L., Mo, H., Elson, C.E., 1995. Induction of geranly pyrophophate pyrophosphatase activity by cholesterol suppressive isoprenoids, Lipids 30(4), 357-359.

Chanwitheesuk, A., Teerawutgulrag, A., Rakariyatham, N., 2005. Screening of antioxidant activity and antioxidant compounds of some edible plants of Thailand. Food Chem. 92(3), 491-497.

Chung, J.G., 1999 Effects of butylated hydroxyanisole (BHA) and butylated hydroxytoluene (BHT) on the acetylation of 2-aminofluorene and DNA-2-aminofluorene adducts in the rat. Toxicol. Sci. 51, 202-210.

De la Monte, S.M., Wands, J.R., 2008. Alzheimer's disease is type 3 diabetes- -evidence reviewed. J. Diabet. Sci. Technol. 2(6), 1101-1113.

Demir, E., Kilinc, K., Yildirim, Y., Dincer, F., Eseceli, H., 2008. Comparative effects of mint, sage, thyme and flavomycin in wheat-based broiler diets. Arch. Zootechnica 11(3), 54-63.

Dhuley, J.N., 1999. Anti-oxidant effects of cinnamon (*Cinnamomum verum*) bark and greater cardamom (*Amomum subulatum*) seeds in rats fed high fat diet. Indian J. Exp. Biol. 37(3), 238-242.

Doughari, J.H., 2012. Phytochemicals: Extraction Methods, Basic Structures and Mode of Action as Potential Chemotherapeutic Agents. In: Phytochemicals - A Global Perspective of Their Role in Nutrition and Health (Ed.: Rao, V.). Intech. pp.1-32.

Duncan, B.B., Schmidt, M.I., Pankow, J.S., Ballantyne, C.M., Couper, D., Vigo, A., Hoogeveen, R., Folsom, A.R., Heiss, G., 2003. Atherosclerosis Risk in Communities Study. Low-grade systemic inflammation and the development of type 2 diabetes: the atherosclerosis risk in communities study. Diabet. 52(7), 1799-1805.

Fandrey, J., Frede, S., Jelkmann, W., 1994. Role of hydrogen peroxide in hypoxia-induced erythropoietin production. Biochem. J. 303, 507-510.

Ferrara, N., 2004. Vascular endothelial growth factor: basic science and clinical progress, Endocr. Rev. 25(4), 581-611.

Ferrari, A., Hoerndli, F., Baechi, T., Nitsch, R.M., Gotz, J., 2003. beta-Amyloid induces paired helical filament-like tau filaments in tissue culture, J. Biol. Chem. 278(41), 40162-40168.

Graham, T.E., Yang, Q., Blüher, M., Hammarstedt, A., Ciaraldi, T.P., Henry, R.R., Wason, C.J., Oberbach, A., Jansson, P.A., Smith, U., Kahn, B.B., 2006. Retinol-binding protein 4 and insulin resistance in lean, obese, and diabetic subjects. New Engl. J. Med. 354(24), 2552-2563.

Gupta, V.K., Sharma, S.K., 2006. Plants as natural antioxidants, Nat. prod. Radiance 5(4), 326-334.

Handberg, A., Levin, K., Hojlund, K., Beck-Nielsen, H., 2006. Identification of the oxidized low-density lipoprotein scavenger receptor CD36 in plasma: a novel marker of insulin resistance. Circulation 114(11), 1169-1176.

Hayden, M.R., Tyagi, S.C., 2004. Neural redox stress and remodeling in metabolic syndrome, type 2 diabetes mellitus, and diabetic neuropathy. Med. Sci. Monit. 10(12), RA291-307.

Hsu, D.Z., Li, Y.H., Chu, P.Y., Periasamy, S., Liu, M.Y., 2011. Sesame oil prevents acute kidney injury induced by the synergestic action of aminoglycoside and iodinate contrast rats. Antimicrob. Agents Chemother. 55(6), 2532-2536.

Kalt, W., Forney, C.F., Martin, A., Prior, R.L., 1999. Antioxidant capacity, vitamin C, phenolics, and anthocyanins after fresh storage of small fruits. J. Agri. Food Chem. 47(11), 4638-4644.

Krantz, S.B., 1991. Erythropoietin. Blood 77(3), 419-434.

Kunwar, A., Priyadarsini, K.I., 2011. Free radical, oxidative stress and importance of antioxidant in human health, J. Med. Allied Sci. 1(2), 53-60.

Kwon, H.K., Hwang, J.S., So, J.S., Lee, C.G., Sahoo, A., Ryu, J.H., Jeon, W.K., Ko, B.S., Im, C.R., Lee, S.H., Park, Z.Y., Im, S,H., 2010. Cinnamon extract induces tumor cell death through inhibition of NFB and AP1. BMC Cancer 10(392), 1-10.

Kwon, H.K., Jeon, W.K., Hwang, J.S., Lee, C.G., So, J.S., Park, J.A., Ko, B.S., Im, S.H., 2009. Cinnamon extract suppresses tumor progression by modulating angiogenesis and the effector function of CD8+ T cells. Cancer Lett. 278, 174-182.

Lee, J.S., Choi, M.S., Jeon, S.M., Jeong, T.S., Park, Y.B., Lee, M.K., Bok, S.H., 2001. Lipid-lowering and antioxidative activities of 3, 4-di (OH)-cinnamate and 3, 4-di (OH)-hydrocinnamate in cholesterol-fed rats. Clin. Chim. Acta. 314(1-2), 221-229.

Lee, M.K., Park, Y.B., Moon, S.S., Bok, S.H., Kim, D.J., Ha, T.Y., Jeong, T.S., Jeong, K.S., Choi, M.S., 2007. Hypocholesterolemic and antioxidant properties of 3-(4-hydroxyl) propanoic acid derivatives in high-cholesterol fed rats. Chem. Biol. Interact. 170(1), 9-19.

Lim, Y.S., Lee, S.T., 2013. *In vitro* antioxidant capacities of star fruit (*Averrhoa carambola*), an underutilised tropical fruit. J. Biol. 1(1), 21-24.

Lu, J., Zhang, K., Nam, S., Anderson, R.A., Jove, R., Wen, W., 2010. Novel angiogenesis inhibitory activity in cinnamon extract blocks VEGFR2 kinase and downstream signaling. Carcinogenesis 31(3), 481-488.

Mancini-Filho, J., Van-Koiij, A., Mancini, D.A., Cozzolino, F.F., Torres, R.P., 1998. Antioxidant activity of cinnamon (*Cinnamomum zeylanicum* Breyne) extracts. Boll Chim. Farm. 137(11), 443-447.

Mansoub, N.H., Myandoab, M.P., 2011. Influence of two herbal plants extract on performance and certain blood parameters of Japanese quails. Ann. Biol. Res. 2, 403-407.

Mathew, S., Abraham, T.E., 2006. In vitro antioxidant activity and scavenging effects of *Cinnamomum verum* leaf extract assayed by different methodologies. Food Chem. Toxicol. 44(2), 198-206.

Modak, M., Dixit, P., Londhe, J., Ghaskadbi, S., Devasagayam, T.P., 2007. Indian herbs and herbal drugs used for the treatment of diabetes. J. Clin. Biochem. Nutr. 40(3), 163-173.

Mwanri, L., Worsley, A., Ryan, P., Masika, J., 2000. Supplemental vitamin improves anemia and growth in anemic school children in Tanzania. J. Nutr. 130(11), 2691-2696.

Nishimura, S., Manabe, I., Nagasaki, M., Hosoya, Y., Yamashita, H., Fujita, H., Ohsugi, M., Tobe, K., Kadowaki, T., Nagai, R., Sugiura, S., 2007. Adipogenesis in obesity requires close interplay between differentiating adipocytes, stromal cells, and blood vessels. Diabet. 56 (6), 1517-1526.

Panickar, K.S., Polansky, M.M., Anderson, R.A., 2009. Cinnamon polyphenols attenuate cell swelling and mitochondrial dysfunction following oxygen-glucose deprivation in glial cells. Exp. Neurol. 216(2), 420-427.

Pari, L., Amudha, K., 2011. Antioxidant effect of naringin on nickel-induced toxicity in rats: an in vivo and in vitro study. Int. J. Pharm. Sci. Rev. Res. 2(1), 137-144.

Peschel, W., Sanchez-Rabaneda, F., Dickmann, W., Plesehen, A., Gartiza, I., Jimenez, D., Lamuela-Raventos, R., Buxaderas, S., Codina, C., 2006. An Industrial approach in the search of natural antioxidants from vegetables and fruit wastes. Food Chem. 97, 137-150.

Peterson, D.W., George, R.C., Scaramozzino, F., LaPointe, N.E., Anderson, R.A., Graves, D.J., Lew, J., 2009. Cinnamon extract inhibits tau aggregation associated with Alzheimer's disease *in vitro*. J. Alzheimers Dis. 17(3), 585-587.

Polonsky, K.S., 2006. Retinol-binding protein 4, insulin resistance, and type 2 diabetes, New Engl. J. Med. 354(24), 2596-2598.

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

Qin, B., Panickar, K.S., Anderson, R.A., 2010a. Cinnamon: Potential role in the prevention of insulin resistance, metabolic syndrome, and type 2 diabetes. J. Diabet. Sci. Technol. 4(3), 685-693.

Qin, B., Polansky, M.M., Anderson, R.A., 2010b. Cinnamon extract regulates plasma levels of adipose-derived factors and expression of multiple genes related to carbohydrate metabolism and lipogenesis in adipose tissue of fructose-fed rats. Horm. Metab. Res. 42(3), 187-193.

Qin, B., Qiu, W., Avramoglu, R.K., Adeli, K., 2007. Tumor necrosis factor-alpha induces intestinal insulin resistance and stimulates the overproduction of intestinal apolipoprotein B48-containing lipo-proteins. Diabet. 56(2), 450-461.

Rao, P.V., Gan, S.H., 2014. Cinnamon: A multifaceted medicinal plant. Evid. Based Complement. Alternat. Med. 2014, 1-12.

Rogers, S.C., Said, A., Corcuera, D., McLaughlin, D., Kell, P., Doctor, A., 2009. Hypoxia limits antioxidant capacity in red blood cells by altering glycolytic pathway dominance. FASEB J. 23(9), 3159-3170.

Roussel, A.M., Hininger, I., Benaraba, R., Ziegenfuss, T.N., Anderson, R.A., 2009. Antioxidant effects of a cinnamon extract in people with impaired fasting glucose that are overweight or obese. J. Am. Coll. Nutr. 28(1), 16-21.

Schwarz, K., Bertelsen, G., Nissen, L.R., Gardner, P.T., Heinonen, M.I., Hopia, A., Huynh-Ba, T., Lambelet, P., McPhail, D., Skibsted, L.H., Tijburg, L., 2001. Investigation of plant extracts for the protection of processed foods against lipid oxidation: Comparison of antioxidant assays based on radical scavenging, lipid oxidation and analysis of the principal antioxidant compounds. Eur. Food Res. Technol. 212 (3), 319-328.

Shahidi, F., Wanasundara, P.D., 1992. Phenolic antioxidants, Crit. Rev. Food Sci. Nutr. 32(1), 67-103.

Shobana, S., Naidu, K.A., 2000. Antioxidant activity of selected Indian spices. Prostaglandins Leukot. Essent. Fatty Acids 62(2), 107-110.

Singh, G., Maurya, S., Delampasona, M.P., Catalan C.A.N., 2007. A comparison of chemical, antioxidant and antimicrobial studies of cinnamon leaf and bark volatile oils, oleoresins and their constituents. Food Chem. Toxicol. 45, 1650-1661

Tanabe, H., Yoshida, M., Tomita, N., 2002. Comparison of the antioxidant activities of 22 commonly culinary herbs and spices on the lipid oxidation of pork meat. Anim. Sci. J. 73 (5), 389-393.

Tung, Y.T., Chua, M.T., Wang, S.Y., Chang, S.T., 2008. Anti-inflammation activities of essential oil and its constituents from indigenous cinnamon (*Cinnamomum osmophloeum*) twigs. Bioresour. Technol. 99(9), 3908-3913.

Uttara, B., Singh, A.V., Zamboni, P., Mahajan, R.T., 2009. Oxidative stress and neurodegenerative diseases: A review of upstream and downstream antioxidant therapeutic options. Curr. Neuropharmacol. 7(1), 65-74.

Valiathan, M.S., 1998. Healing plants, Curr. Sci. 75, 1122-1126.

Wambi, C., Sanzari, J., Wan, X.S., Nuth, M., Davis, J., Ko, Y.H., Sayers, C.M., Baran, M., Ware, J.H., Kennedy, A.R., 2008. Dietary antioxidants protect hematopoietic cells and improve animal survival after total-body irradiation, Radiat. Res. 169(4), 384-396.

Yang, Y., Zhou, L., Gu, Y., Zhang, Y., Tang, J., Li, F., Shang, W., Jiang, B., Yue, X., Chen, M., 2007. Dietary chickpeas reverse visceral adiposity, dyslipidaemia and insulin resistance in rats induced by a chronic high-fat diet. Br. J. Nutr. 98(4), 720-726.

Yu, L., Perret, J., Davy, B., Wilson, J., Melby, C.L., 2002. Antioxidant properties of cereal products. J. Food Sci. 67(7), 2600-2603.

Ziegenfuss, T.N., Hofheins, J.E., Mendel, R.W., Landis, J., Anderson, R.A., 2006. Effects of a water-soluble cinnamon extract on body composition and features of the metabolic syndrome in pre-diabetic men and women. J. Int. Soc. Sports Nutr. 3, 45-53.

Zimmermann, M.B., Biebinger, R., Rohner, F., Dib, A., Zeder, C., Hurrell, R.F., Chaouki, N., 2006. Vitamin A supplementation in children with poor vitamin A and iron status increases erythropoietin and hemoglobin concentrations without changing total body iron. Am. J. Clin. Nutr. 84(3), 580-586.