INTRODUCTION

Cinnamon an indigenous spice, belonging to the Lauracea family, is found in almost every household. Used mainly as a flavoring agent, it has been a major constituent of our food since a long time. For a long time, our ancestors have been using it as a remedy for respiratory and digestive ailments. However, less is known about its beneficial effect as an antioxidant, anti-inflammatory, antilipemic, antidiabetic, antimicrobial, and anticancer agent. This review highlights the diverse effects which can increase its use as an adjunct in complementary and alternative medicine.

Types of cinnamon

There are mainly four types of cinnamon:

- True cinnamon or Ceylon cinnamon or Mexican cinnamon (*Cinnamomum zeylanicum*)
- Indonesian cinnamon (*Cinnamomum burmanni*)
- Vietnamese cinnamon (*Cinnamomum loureiroi*)
- Cassia cinnamon or Chinese cinnamon (*Cinnamomum aromaticum*).

The following table depicts the main features of the different types of cinnamon [Table 1].

On the basis of the appearance of the quill, it is possible to differentiate Ceylon cinnamon from the others. It is softer and lighter in color and rolled in layers whereas the others are darker, hard, and hollow and rolled in only one layer. Even though very expensive, Ceylon cinnamon is preferred due to its ultra-low coumarin levels and the mild delicate taste. According to the European Food safe authority, cassia cinnamon has been the cause of exposure to coumarin which is highly hepatotoxic and carcinogenic.[1] Another recently available low coumarin containing cinnamon substitute has been found which is obtained from the leaves of *Cinnamomum osmophloeum* from Taiwan.[2]

BOTANY AND CHEMICAL COMPOSITION

Cinnamon is exported as cinnamon quills from four main countries: Indonesia, China, Vietnam and Sri Lanka. The quills are made by pealing the bark and then rolling it into pipes.

Different oils obtained from this interesting plant yield different constituents: Cinnamaldehyde (in the bark oil), eugenol (in the leaf oil), and camphor (in the root-bark oil).[3] The fruits and flowers are a rich source of trans-cinnamyl acetate.[4]
language. It was a component of the anointing oil used by Moses for the purpose of anointment (to make a person holy) as mentioned in the Bible. The Romans used it for its medicinal properties for ailment of the digestive and respiratory tract. It was also used in Roman funerals in order to fend off the odor of dead bodies. It was used in Egypt for embalming of mummies as well as for its fragrance and flavoring properties.

However being very expensive and highly treasured, the quest for cinnamon led to a world exploration in the 15th century. It was the motivation behind Christopher Columbus’s voyage which led to the discovery of the new world and for Vasco da Gama’s exploration of South India and Sri Lanka. The native of true cinnamon or Ceylon cinnamon was then found to be in Sri Lanka (also known as Ceylon). Thus it became evident, that any country which could hold that area captive, had a control over the world trade of cinnamon and would ultimately reap immense profits. Thus over years, initially the Portuguese ruled, who were later overpowered by the Dutch, followed by the British in 1815. Now it’s cultivated in Sri Lanka along the coastal belt from Negombo to Matara.

Following picture illustrates the many pleiotropic effects of this wonderful spice [Figure 1].

**CINNAMON IN DIABETES**

Management of the glycemic index in a diabetic is one of the foremost challenges confronted by the physicians in daily practice. Various known studies have demonstrated that a meticulous control with intensified insulin treatment and sulphonylureas (UK Prospective Diabetes Study Trial) can result in a decrease in microvascular complications as well as the hospitalization costs.[5-7] Furthermore, a precise control of not only the blood glucose levels, but also the lipid profile and blood pressure (BP) play an eminent role in preventing complications in a diabetic.[8] Along with that, the lack of compliance due to various patient centered factors[9] such as decrease effect of medicine over time[10] and development of dependence[11] with the allopathic medications due to the fear of a lifelong intake further adds on to the existing problem.

At this point, introduction of cinnamon, as a natural product has revived the interest of many scientists due to its abundant pleiotropic effects. Role of cinnamon in regulating the glucose levels in the body has been implied in numerous small randomized control trials. However, the results have either been conflicting or not significant enough. A meta-analysis by Allen et al. done for 10 randomized controlled trials including 543 patients has established that cinnamon, when taken in a dose of 120 mg/day to 6 g/day for approximately 4 months leads to a statistical decrease in levels of fasting plasma glucose along with an improvement in the lipid profile.[12]

Various hypothesis regarding its mechanism of action in diabetes have been put forth. Cinnamon has been said to have an insulin mimetic and insulin sensitizing action.[13] *Cinnamon cassia* plays a significant role in phosphorylation of signaling proteins and enhancement of expression of insulin sensitive glucose transporters which results in mitigation of the insulin resistance.[14] It has been demonstrated that following the exposure to cinnamon water extracts, there is an increase expression of peroxisome proliferator activated
The cinnamonaldehyde component of cinnamon is responsible for its anti-microbial activity. It can inhibit the growth of Listeria and *Escherichia coli* in food products thereby potentiating their shelf life. In one of the studies, the effect of cinnamon was studied against various organisms like bacteria such as *Staphylococcus aureus*, fungus like *Aspergillus flavus* , *Mucor plumbeus* and yeast species such as *Candida lipolytica*. Its combination along with clove oil has been effective against *A. flavus*. The cinnamon oil possesses antimicrobial action in the range 10-150 μg ml⁻¹. One of the studies investigated the antimicrobial activity of *C. zeylanicum* against fluconazole resistant Candida. They went ahead and experimented the effect of commercially available preparations in five HIV patients suffering from oral candidiasis. It was concluded that there was no improvement in these patients, highlighting the need of further research on this aspect.

Another interesting fact about cinnamon is its role in altering the expression of a gene icaA which plays a role in the formation of biofilms. *Staphylococcus epidermidis* is one of the leading causes of biofilms which is why it has emerged as a notorious nosocomial pathogens. The literature on the effect of cinnamon on viruses is limited. However, it is said to inhibit protein synthesis which is responsible for is ability to improve survival in mice following infection with influenza A/PR/8 virus.

**ANTIOXIDANT PROPERTY**

Lipid oxidation is a major challenge during the food processing in the food industry. A natural antioxidant is hereby the need of the hour. The methanol extract is said to have maximum anti-oxidant property as compared to the ethanolic and water extract. The antioxidant property is due to the eugenol component which inhibited peroxynitrite-induced nitration and lipid peroxidation in *in vitro* models. The oil is said to form a phosphomolybdenum complex which is responsible for its antioxidant activity.

This anti-oxidant effect has been recently extended to its application in liver disorders. The ethanolic extract has demonstrated to decrease the carbon tetrachloride induced lipid peroxidation resulting in a fall markers of oxidative stress such as MDA.

**ANTI-INFLAMMATORY EFFECT**

The multifaceted nature of cinnamon has incited researchers to look further into its likely uses. Cinnamon water extract possesses anti-inflammatory effect *in vitro* ascribed to fall in levels of tumor necrosis factor α and Interleukin 6. Twigs of *C. osmophloeum* contain compounds such as trans-cinnamaldehyde, caryophyllene oxide, eugenol, L-borneol which possess anti-inflammatory activity.

**CINNAMON AND HEART DISEASES**

An animal study on Sprague Dawley rats evaluated the effect of *C. cassia* on Ischemic Heart Disease. The active components cinnamaldehyde and cinnamic acid are said to be cardio protective due to their ability to produce nitric oxide as well as the associated anti-inflammatory property. Its vasorelaxation effect has also been attributed the cinnamaldehyde component which inhibits the L type calcium channel.

**CINNAMON AND LIPID PROFILE**

Cinnamon is also known to have a lipid lowering effect. An *in vitro* study prove *C. zeylanicum* extract (0.75 g/kg bark powder) to be as effective as simvastatin (0.6 mg/ kg body weight). However, whether this effect is significant or not in humans remains to be elucidated. According to another study, the effect of cinnamon on cholesterol level becomes insignificant in rats even after increasing the intake to up to 5 times the normal. One of the studies which studied the effect of cinnamon on gastric emptying as well postprandial glycemic and lipemic responses did not find any change in the nine individuals enrolled in the study.
CINNAMON AND CANCER

The pathogenesis of cancers have been multimodal and various treatment medications aim at various steps in order to inhibit the process. One of the main etiologies of gastric carcinoma is the gram-negative bacilli *Helicobacter pylori* (*H. pylori*). It is also known to be responsible for conditions such as atrophic gastritis, duodenal ulcer, and gastric lymphomas. In a pilot study of fifteen patients, *H. pylori* levels were checked by radiolabelled urea breath test before and after administration of cinnamon alcoholic extract. Though it was not completely effective in eradicating the *H. pylori*, it did decrease the colonization to some extent. Thus, it was suggested that in a concentration of 80 mg/day, it may be valuable with further research.[38] Since its discovery, nuclear factor kappa B (NFkB), an inducible transcription factor, has become a significant target for treatment of various diseases and malignancies.[39] Substances acting on pathways involved in its activation has given a new dimension to cancer therapy.[40] One animal study suggested that *C. cassia* can inhibit the survival, viability and proliferation of tumor cells *in vitro* without having a significant effect on the normal cells. On further detailed analysis, it was found that such an effect could be attributed to the ability of the extract to induce apoptosis in tumor cells and also by inhibiting the activity of NFkB.[41] Two derivatives: 2′-hydroxycinnamaldehyde (2HCA) and 2′-benzoyl-oxyxcinamaldehyde also induce mechanism by escalating the levels of reactive oxygen species.[42] 2HCA also has an additional mechanism whereby it causes apoptosis by stalling the activity of proteasome, thereby making the cell more susceptible to oxidative stress.[43]

Extensive research has been done to see the effect of cinnamon on melanoma cells. It has been found to impede the activity of pro angiogenic factors which is a major prerequisite for the tumor cells to proliferate and simultaneously increase the activity of CD8(+) T cells.[44] The polyphenol component of cinnamon extract is a potent inhibitor of Vascular Endothelial growth factor, an eminent factor involved in the growth of endothelial cells, and migration during angiogenesis.[45]

CINNAMON AND BLOOD PRESSURE

Though the effect of cinnamon has been extensively researched with respect to diabetes, little work has been done regarding its role in maintenance of BP. It causes peripheral vasodilation, resulting in the fall in BP in dogs and guinea pigs.[46] A systemic review done of three studies have suggested that cinnamon can cause a significant fall in systolic as well as diastolic BP though the precise mechanism remains to be ascertained.[47] Another study done on 59 subjects, suggests that the dietary supplementation with cinnamon can lead to significant fall in systolic BP.[48] The vasorelaxant property of cinnamon due to the production of nitric oxide has said to be the sole cause of this effect. However, an *in vivo* trial hypothesized its effect on KATP channels in the vascular smooth muscles resulting in the fall in BP.[49,50]

POSSIBLE INTERACTIONS WITH CINNAMON

Cassia cinnamon contains high levels of coumarins, which can prove to be toxic in high doses. A daily intake of more than 0.1 mg/kg body weight can lead to conspicuous effect on the blood coagulation profile if the patient is simultaneously on drugs such as warfarin. However, these results are very contradictory. Coumarin is also a highly hepatotoxic toxin and its addition into food products is prohibited. However, due to the lack of awareness regarding the standard limits of cinnamon in these products, it is advisable for patients of hepatic disorders to avoid cinnamon.

CONCLUSION

The above review highlights the significance of this regularly consumed spice with respect to the cardiovascular system, hematological system, central nervous system, etc., Given its broad spectrum of applicability, this particular palatable spice can be used as an adjunct to the regular medications in most of the patients. However, despite all these pleiotropic effects, further research is mandated in order to substantiate the clinical effects of the drug in the dose in which it is being consumed.

REFERENCES

1. Abraham K, Wöhrlin F, Lindtner O, Heinemeyer G, Lampen A. Toxicology and risk assessment of coumarin: Focus on human data. Mol Nutr Food Res 2010;54:228-39.
2. Yeh TF, Lin CY, Chang ST. A potential low-coumarin cinnamon substitute: *Cinnamomum osmophloeum* leaves. J Agric Food Chem 2014;62:1706-12.
3. Wijesekera RO. Historical overview of the cinnamon industry. CRC Crit Rev Food Sci Nutr 1978;10:1-30.
4. Jayaprakasha GK, Rao LJ. Chemistry, biogenesis, and biological activities of *Cinnamomum zeylanicum*. Crit Rev Food Sci Nutr 2011;51:547-62.
5. Reichard P, Nilsson BY, Rosenqvist U. The effect of long-term intensified insulin treatment on the development of microvascular complications of diabetes mellitus. N Engl J Med 1993;329:304-9.
6. Intensive blood-glucose control with sulphonylureas or insulin compared with conventional treatment and risk of complications in patients with type 2 diabetes (UKPDS 33). UK Prospective Diabetes Study (UKPDS) Group. Lancet 1998;352:837-53.
7. Menzin J, Korn JR, Cohen J, Lobo F, Zhang B, Friedman M, et al.
Relationship between glycemic control and diabetes-related hospital costs in patients with type 1 or type 2 diabetes mellitus. J Manag Care Pharm 2010;16:264-75.

8. Skyler JS. Effects of glycemic control on diabetes complications and on the prevention of diabetes. Clin Diabetes 2004;22:162-6.

9. Jin J, Sklar GE, Min Sen Oh V, Chuen Li S. Factors affecting therapeutic compliance: A review from the patient’s perspective. Ther Clin Risk Manag 2008;4:269-86.

10. Bender BG, Bender SE. Patient-identified barriers to asthma treatment adherence: Responses to interviews, focus groups, and questionnaires. Immunol Allergy Clin North Am 2005;25:107-30.

11. Apter AJ, Boston RC, George M,Norfleet AL, Tenhave T, Coyne JC, et al. Modifiable barriers to adherence to inhaled steroids among adults with asthma: It’s not just black and white. J Allergy Clin Immunol 2003;111:1219-26.

12. Allen RW, Schwartzman E, Baker WL, Coleman CI, Phung OJ. Cinnamon use in type 2 diabetes: An updated systematic review and meta-analysis. Ann Fam Med 2013;11:452-9.

13. Howard ME, White ND. Potential benefits of cinnamon in type 2 diabetes. Am J Lifestyle Med 2012;7:23-6.

14. Jitomir J, Willoughby DS. Cassia cinnamon for the attenuation of glucose intolerance and insulin resistance resulting from sleep loss. J Med Food 2009;12:467-72.

15. Sheng X, Zhang Y, Gong Z, Huang C, Zang YQ. Improved insulin resistance and lipid metabolism by cinnamon extract through activation of peroxisome proliferator-activated receptors. PPAR Res 2008;2008:581348.

16. Rafehi H, Ververis K, Karagiannis TC. Controversies surrounding the clinical potential of cinnamon for the management of diabetes. Diabetes Obes Metab 2012;14:493-9.

17. Malik J, Munjal K, Deshmukh R. Attenuating effect of standardized lyophilized Cinnamomum zeylanicum bark extract against streptozotocin-induced experimental dementia of Alzheimer’s type. J Basic Clin Physiol Pharmacol 2014. [Epub ahead of print].

18. Jain S, Sangma T, Shukla SK, Mediratta PK. Effect of Cinnamomum zeylanicum bark extract on scopalamine-induced cognitive impairment and oxidative stress in rats. Nutr Neurosci 2014.

19. Anderson RA, Qin B, Canini F, Poulet L, Roussel AM. Cinnamon counteracts the negative effects of a high fat/high fructose diet on behavior, brain insulin signaling and Alzheimer-associated changes. PLOS One 2013;8:e83243.

20. Muthuswamy S, Rupasinghe HP, Stratton GW. Antimicrobial activity of cinnamon bark extract on Escherichia coli O157:H7, listeria innocua and fresh-cut apple slices. J Food Saf 2008;28:534-49.

21. Hong JW, Yang GE, Kim YB, Eom SH, Lew JH, Kang H. Anti-inflammatory activity of cinnamon water extract in vivo and in vitro LPS-induced models. BMC Complement Altern Med 2012;12:237.

22. Tung YT, Chua MT, Wang SY, Chang ST. Anti-inflammation activities of essential oil and its constituents from indigenous cinnamon (Cinnamomum osmophloeum) twigs. Bioresearch Technol 2008;99:3908-13.

23. Moral J, Li H, Sun J, Wang S. Protective effects of cinnamic acid and cinnamaldehyde on isoproterenol-induced acute myocardial ischemia in rats. J Ethnopharmacol 2013;150:125-30.

24. Alvarez-Collazo J, Alonso-Carbajo L, López-Medina AI, Alpizar YA, Tajada S, Nilius B, et al. Cinnamonaldehyde inhibits L-type calcium channels in mouse ventricular cardiomyocytes and vascular smooth muscle cells. Pflugers Arch 2014;466:2089-99.

25. Javed I, Faisal I, Rahman Z, Khan MZ, Muhammad F, Aslam B, et al. Lipid lowering effect of Cinnamomum zeylanicum in hyperlipidaemic albino rabbits. Pak J Pharm Sci 2012;25:141-7.

26. Hayashi K, Imanishi N, Kashiwayama Y, Kawano A, Terasawa K, Shimada Y, et al. Inhibitory effect of cinnamaldehyde, derived from Cinnamomi cortex, on the growth of influenza A/PR/8 virus in vitro and in vivo. Antiviral Res 2007;74:1-8.

27. Mancini-Filho J, Van-Koijj A, Mancini DA, Cozzolino FF, Torres RP. Antioxidant activity of cinnamon (Cinnamomum zeylanicum, Brenyne) extracts. Boll Chim Farm 1998;137:443-7.

28. Chericoni S, Prieto JM, Jacopini P, Cioni P, Morelli I. In vitro activity of the essential oil of Cinnamomum zeylanicum and eugenol in peroxynitrite-induced oxidative processes. J Agric Food Chem 2005;53:4762-5.

29. Jayaprakashaka GK, Jagan Mohan Rao L, Sarkariah KK. Volatile constituents from Cinnamomum zeylanicum fruit stalks and their antioxidant activities. J Agric Food Chem 2003;51:4344-8.

30. Moselhy SS, Ali HK. Hepatoprotective effect of cinnamon extracts against carbon tetrachloride induced oxidative stress and liver injury in rats. Biol Res 2009;42:93-8.

31. Hong JW, Yang GE, Kim YB, Eom SH, Lew JH, Kang H. Anti-inflammatory activity of cinnamon water extract in vivo and in vitro LPS-induced models. BMC Complement Altern Med 2012;12:237.

32. Tung YT, Chua MT, Wang SY, Chang ST. Anti-inflammation activities of essential oil and its constituents from indigenous cinnamon (Cinnamomum osmophloeum) twigs. Bioresearch Technol 2008;99:3908-13.

33. Song F, Li H, Sun J, Wang S. Protective effects of cinnamic acid and cinnamaldehyde on isoproterenol-induced acute myocardial ischemia in rats. J Ethnopharmacol 2013;150:125-30.

34. Alviraz-Collazo J, Alonso-Carbajo L, López-Medina AI, Alpizar YA, Tajada S, Nilius B, et al. Cinnamonaldehyde inhibits L-type calcium channels in mouse ventricular cardiomyocytes and vascular smooth muscle cells. Pflugers Arch 2014;466:2089-99.

35. Javed I, Faisal I, Rahman Z, Khan MZ, Muhammad F, Aslam B, et al. Lipid lowering effect of Cinnamomum zeylanicum in hyperlipidaemic albino rabbits. Pak J Pharm Sci 2012;25:141-7.

36. Sambaiah K, Srinivasan K. Effect of cumin, cinnamon, ginger, mustard and tamarind in induced hypercholesterolemic rats. Nahrung 1991;35:47-51.

37. Markey O, McClean CM, Medlow P, Davison GW, Trinick TR, Wilmott BL. Effect of cinnamon on gastric emptying, arterial stiffness, postprandial lipemia, glycemia, and appetite responses to high-fat breakfast. Cardiovasc Diabetol 2011;10:78.

38. Nir Y, Potasman I, Stermer E, Tabak M, Neeman I. Controlled trial of the effect of cinnamon extract on Helicobacter pylori. Helicobacter 2000;5:94-7.

39. Garg A, Aggarwal BB. Nuclear transcription factor-kappaB as a target for cancer drug development. Leukemia 2002;16:1053-68.

40. Karin M, Cao Y, Greten FR, Li ZW. NF-kappaB in cancer: From innocent bystander to major culprit. Nat Rev Cancer 2002;2:301-10.

41. Kwon HK, Hwang JS, So JS, Lee CG, Sahoo A, Ryu JH, et al. Cinnamon extract induces tumor cell death through inhibition of NFkappaB and AP1. BMC Cancer 2010;10:392.

42. Han DC, Lee MY, Shin KD, Jeon SB, Kim JM, Son KH, et al. 2-benzoyloxycinnamaldehyde induces apoptosis in human carcinoma via reactive oxygen species. J Biol Chem 2004;279:6911-20.

43. Hong SH, Kim J, Kim JM, Lee SY, Shin DS, Son KH, et al. Apoptosis induction of 2-hydroxycinnamaldehyde as a proteasome inhibitor is associated with ER stress and mitochondrial perturbation in cancer cells. Biochem Pharmacol 2007;74:557-65.

44. Kwon HK, Jeon WK, Hwang JS, Lee CG, So JS, Park JA, et al. Cinnamon extract suppresses tumor progression by modulating...
angiogenesis and the effector function of CD8+ T cells. Cancer Lett 2009;278:174-82.

45. Lu J, Zhang K, Nam S, Anderson RA, Jove R, Wen W. Novel angiogenesis inhibitory activity in cinnamon extract blocks VEGFR2 kinase and downstream signaling. Carcinogenesis 2010;31:481-8.

46. Harada M, Yano S. Pharmacological studies on Chinese cinnamon. II. Effects of cinnamaldehyde on the cardiovascular and digestive systems. Chem Pharm Bull (Tokyo) 1975;23:941-7.

47. Akilen R, Pimlott Z, Tsiami A, Robinson N. Effect of short-term administration of cinnamon on blood pressure in patients with prediabetes and type 2 diabetes. Nutrition 2013;29:1192-6.

48. Wainstein J, Stern N, Heller S, Boaz M. Dietary cinnamon supplementation and changes in systolic blood pressure in subjects with type 2 diabetes. J Med Food 2011;14:1505-10.

49. Nyadjeu P, Dongmo A, Nguelefack TB, Kamanyi A. Anti hypertensive and vasorelaxant effects of Cinnamomum zeylanicum stem bark aqueous extract in rats. J Complement Integr Med 2011;8.

50. Nyadjeu P, Nguelefack-Mbuyo EP, Atsamo AD, Nguelefack TB, Dongmo AB, Kamanyi A. Acute and chronic antihypertensive effects of Cinnamomum zeylanicum stem bark methanol extract in L-NAME-induced hypertensive rats. BMC Complement Altern Med 2013;13:27.