The Potency of Cinnamomum Zeylanicum to Prevent Diseases: a Review

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1. Introduction

The use of cinnamon as a traditional herbal therapy or alternative complementary medicine has spread all over the world. Cinnamon was used traditionally as a remedy for arthritis, diarrhea, allergies and ulcers. Plant extracts are often used for treatment of various diseases because of their potentially beneficial bioactivities, such as antibacterial, antifungal, antiviral, antioxidant, anticancer, anti-diabetic, immunomodulatory, analgesic, and anti-inflammatory.1,2 Cinnamon is one of the potential plant medicines. Cinnamon is in the family of Lauraceae.2 The Latin names are Cinnamomum zeylanicum or Cinnamomum verum which is also known as "true cinnamon".3 Cinnamon has major bioactive compounds in every part of the tree including its bark, roots, leaves, and fruit.4 Three major bioactive compounds present in cinnamon bark essential oil are eugenol, trans-Cinnamaldehyde, and linalool. These compounds make up almost 85% of the total composition.5 Other bioactive compound found are cinnamaldehyde, β-caryophyllene, and eucalyptol.6 This herb is also one of the oldest in the herbal medicine pharmacopeia and was mentioned in Chinese Materia medica texts from more than 4,000 years ago.7 This literature review aimed to identify the bioactive compounds and bioactivity of cinnamon (Cinnamomum zeylanicum).

2. Methods
PubMed and Google Scholar were used as the searching engine in this study. The searching was conducted up to May 21, 2020 using the keywords "Cinnamomum zeylanicum" and "antioxidant" or "Cinnamomum zeylanicum" and "α-glucosidase". Articles selected were all published within the past ten years. Duplicate articles were excluded. From PubMed and Google Scholar, 125 and 41 results were obtained, respectively. Inclusion criteria for this review were: the relevant articles written in English related to Cinnamomum zeylanicum and the study of antioxidant and antidiabetic agents. There were 111 irrelevant titles excluded due to duplication and outside of the scope. As many as 55 full text articles were included in the review.

3. Results and discussion

Based on the results from the reviewed studies, we found that cinnamon extract (Cinnamomum zeylanicum) has several powerful bioactive compounds (Table 1).

Bioactive compounds from Cinnamomum zeylanicum

Cinnamaldehyde

Cinnamaldehyde (C9H8O) is a derivative compound of the volatile chemical, aldehyde that gives cinnamon its flavor and aroma. It is a natural flavonoid. As much as 90% of the total essential oil is cinnamaldehyde. This bioactive compound is commonly found in the bark of the cinnamon tree. 8 Kallel et al. and Behbahani et al. reported that the main bioactive compound in Cinnamomum zeylanicum essential oil is cinnamaldehyde with the content percentage around 71.5% - 77.34%. Meanwhile, Seroyi et al. also found cinnamaldehyde as much as 82.6% in the water extract. 9 It is also found in the methanol and ethanol extracts in lesser amounts. Cinnamaldehyde of the ethanolic and methanolic extracts are 14.63 ± 1.1 mg/g and 38.78 ± 0.78 mg/g, respectively.10-12

Babu et al. conducted translational research on antidiabetic compounds, especially cinnamaldehyde. In their study, diabetic rats were given cinnamaldehyde and glibenclamide. It found that cinnamaldehyde can be used as an antihyperglycemic, to reduce total cholesterol and triglyceride levels simultaneously, and increase high density lipoprotein (HDL) in diabetic rats. 13 A study also found that cinnamaldehyde increases the activity of glucose transporter 4 (GLUT 4) which transports blood glucose into cells to diminish the blood glucose levels. 14 Cinnamaldehyde also has antioxidant activity. 15

Eugenol

Eugenol (C10H12O) is a widely known and volatile component in clove extracts, but it is also found in cinnamon, especially in the leaves. 16,17 The study conducted by Rao et al. compared the bioactive compounds in the essential oil of cinnamon leaves and reported that eugenol compounds were found mostly on the top and larger leaves. Apart from the leaves, eugenol is also found in the bark of cinnamon. 17 Eugenol was also found in the essential oil of cinnamon bark between 4.6 % - 7.45 %, 6,18. The eugenol of essential oil of cinnamon leaves is as much as 58.10 %. 19

The methanolic extract of cinnamon bark contains as much as 10.97 % of eugenol. The eugenol has strong antioxidant activity, but also has cytotoxic effects when used in high doses. Further research is needed to confirm eugenol’s use as a safe pharmacological agent. 12 Eugenol is not found in the ethanolic extract.

Cinnamic acid

Cinnamic acid (C9H8O2) is a compound found in cinnamon bark, derived from phenylalanine deamination. 20 Cinnamic acid has low toxicity and a broad spectrum of biological activity. 21 Generally, it is used as an antimicrobial agent. 22 Cinnamic acid is found in the cinnamon water extracts as much as 1.0 mg/g. 23 The methanolic and ethanolic extracts contain 0.68 ± 0.01 mg/g and 8.99 ± 0.5 mg/g, respectively. 10-12 Cinnamic acid derivates have phenolic hydroxyl groups, so they are often associated with antioxidants. Cinnamic acid has been reported as an
antioxidant, antibacterial, antiviral, and anti-fungal agent.\textsuperscript{12}

**Linalool**

*Linalool* (C\textsubscript{10}H\textsubscript{18}O) is the main bioactive compound in cinnamon essential oil.\textsuperscript{18,24} The concentration of linalool in the essential oil of the leaves is around 85.7%).\textsuperscript{19,25,26} Linalool in the essential oil of the bark is 7%.\textsuperscript{6} The presence of a higher linalool content will give the essential oil more flavor and aroma.\textsuperscript{27}

**β- Caryophyllene**

*β-Caryophyllene* (C\textsubscript{15}H\textsubscript{24}) is found in various essential oils, especially cloves.\textsuperscript{28} Many studies have proven that this compound is also present in cinnamon. *β-Caryophyllene* has a content around 2.8% - 6.4%\textsuperscript{6,18,24} *β-Caryophyllene* has been reported as an anti-inflammatory, antibiotic, antioxidant, and anti-carcinogenic.\textsuperscript{29}

**Coumarin**

*Coumarin* is found in aqueous and methanolic extracts of cinnamon. The methanolic extract contains 4.4 ± 0.10 mg/g of *coumarin* and the water extract contains as much as 4.8 mg/g of *coumarin*.\textsuperscript{11,23}

**Trans-cinnamyl acetate**

*Cinnamyl acetate* (C\textsubscript{11}H\textsubscript{12}O\textsubscript{2}) is an acetate ester produced by the condensation of *cinnamyl alcohol* and acetic acid. This compound is found in cinnamon leaf oil. This compound has the potential as a fragrance, metabolite, and insecticide.\textsuperscript{30} The cinnamon essential oil of leaves and bark contain *cinnamyl acetate* as much as 23.7% and 4.98%, respectively.\textsuperscript{1,31}

**1.8-cineole**

1.8 *cineole* (C\textsubscript{10}H\textsubscript{18}O) or often called eucalyptol is a natural constituent in some aromatic plants.\textsuperscript{32} This compound can be found in essential oils of the fruit, roots, bark, and leaves of cinnamon. 1.8 *cineole* has different content percentages: in the root, it is 6.39%, while in the bark, it is around 3.19% - 5.4%.\textsuperscript{1,6,33} The water extract also contains 1.8 *cineole* as much as 3.4%.\textsuperscript{9}

**Pharmacological activities of Cinnamomum zeylanicum**

**Anti-cancer activity**

There is strong relationship between antioxidant activity and antiproliferative activity. Cinnamon essential oil has potential as an antiproliferative agent against HeLa cells (cervical cancer epithelium) and Raji cells (cells from Burkitt lymphoma), due to the antioxidant compounds.\textsuperscript{1} The IC\textsubscript{50} of the cytotoxicity is <30μg/mL. It is also considered as an anti-tumorigenesis agent that prevents the development of certain cancers. Cinnamaldehyde and hydrocinnamic acid can be used to prevent oxidative damage.\textsuperscript{34} Antiproliferative action could occur through various mechanisms such as diminished integrity of cell membranes, depolarization, increasing permeability, decreased activity of membrane-bound enzymes, or inducing apoptosis.\textsuperscript{6} Some of its compounds have anticancer activities and cytotoxic activities, especially carvacrol, linalool, and cinnamaldehyde.\textsuperscript{35}

*Eugenol* and *cinnamaldehyde* have the ability to inhibit proliferation of breast (T47D) and lung (NCI-H322) cancer cell lines.\textsuperscript{15} *Cinnamaldehyde* inhibits cyclin-dependent kinases (CDKs) that are involved in the regulation of the cell cycle.\textsuperscript{36} Figure 2 shows the mechanisms of flavonoids as an anti-cancer phytochemical. The mechanisms are inactivation of carcinogens, triggering termination of the cell cycle, triggering apoptosis, and inhibition of angiogenesis.\textsuperscript{37}

Flavonoids inhibit the proliferation of tumor cells through inhibition of reactive oxygen species (ROS) formation and suppression of 5-LOX, COX-2, and xanthine oxidase, which are the main catalysts for tumor development and promotion. Many types of cancer are related to CDK hyperactivation, due to mutations in the CDK inhibitor gene or CD gene. Flavonoids cause the cessation of cell cycle checkpoints in the G1/S and G2/M by inhibiting CDK inhibition in human melanoma cells and breast cancer.\textsuperscript{38}
Inhibition of lipid oxidation

Lipid oxidation that occurs in food causes reduced shelf life and quality of the foods. Lipid oxidation is also involved in the pathogenesis of diseases.39 Cinnamon ethanolic extract is associated with inhibition of lipid oxidation and has strong antioxidant activity, so it can be used as a substitute for synthetic antioxidants in processed food. This extract improves nutrition and health by decreasing harmful oxidative derivatives and free fatty acids (FFA).2 Cinnamon essential oil also has vigorous antioxidant activity and can potentially suppress lipid oxidation.6 Eugenol, cinnamaldehyde, and linalool have powerful antioxidant activity. They reduce nitrotyrosine formation by reducing peroxynitrite which promotes lipid oxidation.2

Anti-arrhythmia

Ventricular arrhythmias occur mostly due to damage, which can be caused by surgery or myocardial infarction. Cinnamon has been used in traditional herbal medicines to treat various health conditions including heart failure.40 The cinnamon ethanolic extract has high antioxidant activity. Antioxidant compounds have the potential to protect the heart against arrhythmias caused by ischemia. Further research is needed to develop cinnamon extracts into new anti-arrhythmic drugs. Cinnamon extract is able to reduce the QT interval. The decreasing of the amplitude of the R waves indicate the reduction of the cardiac contractility. Cinnamon ethanolic extract can be used as a negative inotropic agent because it reduces contractility. It also significantly reduces markers of heart damage, such as cTnI and LDH. cTnI is a significant marker of myocardial infarction.10

Anti-inflammatory

Cinnamon has strong antioxidant and anti-inflammatory activities.23 Its antioxidants contribute to the anti-inflammatory activity.41 Cinnamon inhibits the synthesis of COX-2 and prostaglandins.41,42 Cinnamaldehyde and linalool play an important role as anti-inflammatory agents. Cinnamon essential oil prevents systemic inflammation in endotoxin-induced mice. The protective effect was confirmed by the proinflammatory cytokines that were significantly reduced. Cinnamaldehyde demonstrated its inhibitory activity against Interleukin-1 beta (IL-1β) and tumor necrosis factor-alpha (TNF-α) production. Cinnamaldehyde and linalool can be used as prophylactic agents against inflammation caused by overactivity of TLR4 and or NLRP3 signaling pathways.43

Anti-diabetic

Antioxidant compounds of the cinnamon extract improve oxidative stress and reduces blood glucose levels in diabetic-induced mice.44 Figure 3 shows the potential of antioxidants in the type 2 diabetes mellitus pathway induced by oxidative stress. The existing ROS and reactive nitrogen species (RNS) causes oxidative stress in diabetes which leads to insulin resistance, endothelial and β cell dysfunction. It occurs by exposure to prolonged high glucose or FFA levels, or a combination of both, and lower secretion of insulin and dysfunction of mitochondrial products.45 Cinnamon reduces blood glucose level by reducing insulin resistance and increasing liver glycogenesis.46,47 Phenolic acid in cinnamon is also proposed as an active compound in the modulation of insulin signals. Cinnamaldehyde has antihyperglycemic and antihyperlipidemic activity in diabetic animals. Cinnamon extract can be used to be a potential antidiabetic agent, but the molecular target of this solvent from cinnamon or cinnamaldehyde is still unclear.13,48 α-glucosidase inhibitors have an important role as antidiabetic agents. The α-glucosidase inhibitor activity found in cinnamon extract is reversible, so this enzyme will still remain intact post inhibition. Cinnamon extract suppresses postprandial hyperglycemia associated with disaccharides.49 Cinnamon extract significantly inhibits the enzymatic activity of pancreatic α-amylase and
intestinal α-glucosidase. It contributes to the lowering of the level of HbA1c in diabetic patients and decreases the incidence of vascular chronic complications, both macrovascular and microvascular. As well-known in translational research, acarbose has already been studied clinically in type 2 diabetes mellitus.

**Anti-atherosclerosis**

Antioxidant activity of the cinnamon water extracts suppresses the incidence of atherosclerosis. *Cinnamaldehyde* and *eugenol* inhibit the activity of the cholesteryl ester transfer protein (CETP). The activity of CETP involves promoting the development of atherosclerosis by decreasing the HDL level. The inhibition of CETP promotes the production of HDL and prevents the development of atherosclerosis.

**Anti-cholinesterase**

Antioxidants of cinnamon extract and the essential oil are related to the anticholinesterase activity. This cholinesterase inhibition is linked to neurodegenerative diseases such as Alzheimer’s. The cinnamon bark and leaves show an acetylcholinesterase inhibitory activity, so it is useful for managing Alzheimer’s. Alzheimer’s disease is characterized by inadequate production of acetylcholine in the brain. This cholinergic system plays a vital role in memory. The loss of cholinergic neurons from Meynert’s basal is an important factor in memory deficits in people with Alzheimer’s.

| Extract  | Bioactive compounds                                      | Bioactivity                                      | Literature                        |
|----------|--------------------------------------------------------|-------------------------------------------------|-----------------------------------|
| Aquadest | Cinnamaldehyde, trans-cinnamyl acetate, 1.8 cineole,   | Antioxidant, antiproliferative, antimicrobial,   | Kallel I et.al [1], Behbahani BA et.al [6], Seroyi J et.al [9], Kachaniova M et.al [18], Mahomodally F et.al [19], Durak A et.al [23], Loizzo M et.al [24], Baker I et.al [41] |
|          | linalool, β-caryophyllene, eugenol, cinnamic acid,     | antidiabetic, antinflammatory                    |                                   |
|          | coumarin, eugenol acetate                              |                                                 |                                   |
| Ethanol  | Cinnamaldehyde, methyl-eugenol, cinamic acid           | Antioxidant, cardioprotective, anti cholinesterase | Shahid MZ et.al [2] Sedighi M et.al [10] |
| Methanol | Cinnamaldehyde, coumarin, cinnamic acid, cinnamyl      | Antioxidant                                      | Khuwijitjaru P et.al [11], Abdeen A et.al [12] |
|          | alcohol, eugenol, oleic acid                           |                                                 |                                   |
Figure 1. Journal selection process

Figure 2. Role of flavonoids in cancer

Figure 3. Antioxidants in the treatment of type 2 DM
4. Conclusion

Bioactive compounds of cinnamon extract are cinnamaldehyde, eugenol, cinnamic acid, linalool, β-caryophyllene, coumarin, trans-cinnamyl, and 1,8 cineole. Each compound has its own powerful bioactivity potential, such as anticancer, lipid oxidation inhibitor, anti-arrhythmia, anti-inflammatory, antidiabetic, anti-atherosclerosis, and anticholinesterase.

5. Future recommendations

Further phytochemical studies of cinnamon's bioactive compounds are still needed. Information in this medicinal plant's phytochemical profile is still limited. Translational research concerning the bioactivities of the active compounds related to the development of specific diseases especially needs to be continued.

6. Abbreviation

CDK : Cyclin-dependent kinase
5 LOX : Arachidonate 5-lipoxygenase
COX 2 : Cyclooxygenase-2
IL-1β : Interleukin-1-Beta
TNF-α : Tumor Necrosis Factor-Alfa
TLR4 : Toll-like Receptor-4
NLRP3 : NLR Family Pyrin Domain Containing 3
ROS : Reactive oxygen species
RNS : Reactive nitrogen species
HbA1c : Hemoglobin A1C
CETP : Cholesteryl Ester Transfer Protein

7. References

1. Kallel I, Hadrich B, Gargouri B, Chaabane A, Lassoued S, Gdoura R, et al. Optimization of cinnamon (Cinnamomum zeylanicum Blume) essential oil extraction: evaluation of antioxidant and antiproliferative effects. Evid Based Complement Alternat Med. 2019; 6498347.
2. Shahid MZ, Saima H, Yasmin A, Nadeem MT, Imran M, Afzaal M. Antioxidant capacity of cinnamon extract for palm oil stability. Lipids Health Dis. 2018; (1):116. 5-8.
3. Pasiecznik N. 2019. Cinnamomum verum (cinnamon). Wallingford, UK: CABI.
4. Jayaprakasha GK, Rao LJ. Chemistry, biogenesis, and biological activities of Cinnamomum zeylanicum. Crit Rev Food Sci Nutr. 2011; (6):547–62.
5. Kumar V, Marković T, Emerald M, Dey A. Herbs: composition and dietary importance. Encycl Food Heal. 2015; 332–7.
6. Behbahani BA, Falah F, Arab FL, Vasee M, Yazdi FT. Chemical composition and antioxidant, antimicrobial, and antiproliferative activities of cinnamomum zeylanicum bark essential oil. Evid Based Complement Alternat Med. 2020; 190603.
7. Qin B, Nagasaki M, Ren M, Bajotto G, Oshida Y, Sato Y: Cinnamon extract (traditional herb) potentiate in vivo insulin-regulated glucose utilization via enhancing insulin signaling in rats. Diabetes Res Clin Pract. 2003; (62):139-48.
8. National Center for Biotechnology Information. Cinnamaldehyde. 2020 [accessed on august 13 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Cinnamaldehyde
9. Jin S, Cho K-H. Water extracts of cinnamon and clove exhibits potent inhibition of protein glycation and anti-atherosclerotic activity in vitro and in vivo hypolipidemic activity in zebrafish. Food Chem Toxicol: an Int J Publ Br Ind Biol Res Assoc. 2011; 49(7):1521–9.
10. Sedighi M, Nazari A, Faghihi M, Rafieian-Kopaei M, Karimi A, Moghimian M, et al. Protective effects of cinnamon bark extract against ischemia-reperfusion injury and...
arrhythmias in rat. Phytother Res. 2018; 32(10):1983–91.

11. Khuwijitjaru P, Sayputikasikorn N, Samuhasaneetoo S, Penroj P, Siriwongwilachat P, Adachi S. Subcritical water extraction of flavoring and phenolic compounds from cinnamon bark (Cinnamomum zeylanicum). J Oleo Sci. 2012;61(6):349–55.

12. Abdeen A, Abdelkader A, Abdo M, Wareth G, Aboubakr M, Aleya L, et al. Protective effect of cinnamon against acetaminophen-mediated cellular damage and apoptosis in renal tissue. Environ Sci Pollut Res Int. 2019; 26(1):240–9.

13. Babu PS, Prabuseenivasan S, Ignacimuthu S. Cinnamaldehyde: a potential antidiabetic agent. Phytomedicine. 2007;14(1):15–22.

14. Nikzamir A, Palangi A, Kheirollaha A, et al. Expression of glucose transporter 4 (GLUT4) is increased by cinnamaldehyde in C2C12 mouse muscle cells. Iran Red Crescent Med J. 2014; 16:1-5.

15. Sharma UK, Sharma AK, Pandey AK. Medicinal attributes of major phenylpropanoids present in cinnamon. BMC Complement Altern Med. 2016; 16:156.

16. National Center for Biotechnology Information [Internet]. Eugenol. 2020 [accessed on August 13 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Eugenol

17. Rao BRR, Rajput DK, Sastry KP, Kothari SK, Bhattacharya AK. Leaf essential oil profiles of cinnamomum zeylanicum Blume. Indian Perfumer. 2006; 50:44-6.

18. Kacaniova M, Terentjeva M, Vukovic N, Puchalski C, Roychoudhury S, Kunova S, et al. The antioxidant and antimicrobial activity of essential oils against Pseudomonas spp. isolated from fish. Saudi Pharm J. 2017; 25(8):1108-16.

19. Mahomoodally F, Aumeeruddy-Elalfi Z, Venugopala KN, Hosenally M. Antiglycation, comparative antioxidant potential, phenolic content and yield variation of essential oils from 19 exotic and endemic medicinal plants. Saudi J Biol Sci. 2019; 26(7):1779–88.

20. Khalil RA, Absy RB, Doumit S, Bitar J, Nasser R, Khoury E. Cinnamaldehyde and cinnamic acid from cinnamon bark (Cinnamomum verum) increase the binding of glucose to human albumin. Biochimica clinica. 2018; 42(2):112-8.

21. Sova M. Antioxidant and Antimicrobial Activities of Cinnamic Acid Derivatives. Mini-Reviews Med Chem. 2012;12(8):749–67.

22. Kuchi VS, Ilahy R, Siddiqui MW. Commercial Disinfectants in Skirmishing Postharvest Diseases. Postharvest Disinfection of Fruits and Vegetables. Elsevier Inc. 2018; 273–292 p.

23. Durak A, Gawlik-Dziki U, Pecio L. Coffee with cinnamon - impact of phytochemicals interactions on antioxidant and anti-inflammatory in vitro activity. Food Chem. 2014; 162:81–8.

24. Loizzo MR, Tundis R, Menichini F, Duthie G. Anti-rancidity effect of essential oils, application in the lipid stability of cooked turkey meat patties and potential implications for health. Int J Food Sci Nutr. 2015; 66(1):50–7.

25. National Center for Biotechnology Information [Internet]. Linalool. 2020 [accessed on august 14 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Linalool

26. Jirovetz, L., Buchbauer, G., Ruzicka, J., Shafi, M. P., & Rosamma, M. K. Analysis of Cinnamomum zeylanicum Blume leaf oil from South India. J Essent Oil Res. 2001; 13(6):442-3.

27. Raina VK, Srivastava SK, Aggarwal KK, Ramesh S, Kumar S. Essential oil composition of Cinnamomum zeylanicum Blume leaves from Little Andaman, India. Flavour Fragr J. 2001; 16(5):374-6.
28. National Center for Biotechnology Information [Internet]. Beta-Caryophyllene. 2020 [accessed on 14 agustus 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/beta-Caryophyllene

29. Liyanage T, Madhujith T, Wijesinghe KGG. Comparative study on major chemical constituents in volatile oil of true cinnamon (Cinnamomum verum Presl. syn. C. zeylanicum Blum.) and five wild cinnamon species grown in Sri Lanka. Trop Agric Res. 2017; 28(3):270.

30. National Center for Biotechnology Information. Cinnamyl-acetate. 2020 [accessed on august 14 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Cinnamyl-acetate

31. Boniface Y, Philippe S, Lima HRD, Pierre NJ, Alitonou G, Fatiou T, et al. Chemical composition and antimicrobial activities of Cinnamomum zeylanicum Blume dry leaves essential oil against food-borne pathogens and adulterated microorganisms. Int Res J Biol Sci. 2012; 1(6):18-25.

32. National Center for Biotechnology Information [Internet]. Eucalyptol. 2020 [accessed on august 15 2020]. Available at: https://pubchem.ncbi.nlm.nih.gov/compound/Eucalyptol

33. Paranagama PA, Wimalasena S, Jayatilake GS, Jayawardena AL, Senanayake UM, et al. Analysis of volatile oil in the leaves of murraya koenigii. J Trop Med Plants. 2002; 3(2):187-9.

34. N. K. Leela. Cinnamon and cassia in Parthasarathy VA, Chempakam B, Zachariah TJ Ed. Chemistry of Spices. Cambridge: International Cabi. 2008; 124–144

35. Bouyahya A, Abrini J, Bakri Y, Dakka N. Essential oils as anticancer agents: news on mode of action. Phytothérapie. 2016; 1–14.

36. Jeong HW, Kim MR, Son KH, Han MY, Ha JH, Garnier M, et al. Cinnamaldehydes inhibit cyclin dependent kinase 4/cyclin D1. Bioorg Med Chem Lett. 2000; 10:1819-22.

37. Ginwala R, Bhavsar R, Chigbu DGI, Jain P, Khan ZK. Potential role of flavonoids in treating chronic inflammatory diseases with a special focus on the anti-inflammatory activity of apigenin. Antioxidants. 2019; 8(2):1-28.

38. Chahar MK, Sharma N, Dobhal MP, Joshi YC. Flavonoids: a versatile source of anticancer drugs. Pharmacogn. Rev. 2011; 5:1-12.

39. Wasowicz E, Gramza A, Hes M, Jelen HH, Korczak J, Malecka M, et al. Oxidation of lipids in food. Pol J Food Nutr Sci. 2004; 54(1a):87-100.

40. Zarshenas, M. M., Zargaran, A, Abolhassanzadeh, Z, & Vessal, K. Jorjani (1042-1137). J Neurol. 2012; 1-2:6637-9.

41. Baker I, Chohan M, Opara EI. Impact of cooking and digestion, in vitro, on the antioxidant capacity and anti-inflammatory activity of cinnamon, clove and nutmeg. Plant Foods Hum Nutr. 2013; 68(4):364–9.

42. Guo JY, Huo HR, Zhao BS, Liu HB, Li LF, Ma YY, et al. Cinnamaldehyde reduces IL-1β-induced cyclooxygenase-2 activity in rat cerebral microvascular endothelial cells. Eur J Pharmacol. 2006; 537(1-3):174-180.

43. Lee SC, Wang SY, Li CC, Liu CT. Anti-inflammatory effect of cinnamaldehyde and linalool from the leaf essential oil of Cinnamomum osmophloeum Kanehira in endotoxin-induced mice. J Food Drug Anal. 2018; 26(1):211–20.

44. Krishnakumar IM, Issac A, Johannah NM, Eapen N, Balu M, Ramadassan K. Effects of the polyphenol content on the anti-diabetic activity of Cinnamomum zeylanicum extracts. Food Funct. 2014; 5(9):2208–20.

45. Unuofin JO, Lebelo SL. Antioxidant effects and mechanisms of medicinal plants and their bioactive compounds for the prevention and treatment of type 2 diabetes: an updated review. Oxid Med Cell Longev. 2020; 2020.

46. Qin B, Panicar KS, Anderson RA. Cinnamon: potential role in the prevention of insulin resistance, metabolic syndrome, and type 2
47. Couturier K, Qin B, Batandier C. Cinnamon increases liver glycogen in an animal model of insulin resistance. Metabolism. 2011; 60(11):1590-7.

48. Li J, Liu T, Wang L. Antihyperglycemic and antihyperlipidemic action of cinnamaldehyde in C57BLKS/J db/db mice. J Tradit Chin Med. 2012; 32(3):446-52.

49. Shihabudeen HMS, Priscilla DH, Thirumurugan K. Cinnamon extract inhibits α-glucosidase activity and dampens postprandial glucose excursion in diabetic rats. Nutr Metab (Lond). 2011; 8(1):46.

50. Adisakwattana S, Lerdsuwankij O, Poputtachai U, Minipun A, Suparpprom C. Inhibitory activity of cinnamon bark species and their combination effect with acarbose against intestinal α-glucosidase and pancreatic α-amylase. Plant Foods Hum Nutr. 2011; 66(2):143–8.

51. Baron AD. Postprandial hyperglycaemia and α-glucosidase inhibitors. Diabetes Res Clin Pract. 1998; 40(SUPPL.):S1–5.

52. Dalai MK, Bhadra S, Chaudhary SK, Chanda J, Bandyopadhyay A, Mukherjee PK. Anticholinesterase activity of Cinnamomum zeylanicum L. leaf extract. TANG [Humanitas Medicine]. 2014; 4(2):11.1-6.

53. Kumar P, Singh VK, Singh DK. Kinetics of enzyme inhibition by active molluscicidal agents ferulic acid, umbelliferone, eugenol and limonene in the nervous tissue of snail Lymnaea acuminate. Phytother Res. 2009; 23:172-7.

54. Arachchige SPG, Abeysekara WPKM, Ratnasooriya WD. Antiamylase, anticholinesterases, antiglycation, and glycation reversing potential of bark and leaf of ceylon cinnamon (Cinnamomum zeylanicum Blume) in vitro. Evid Based Complement Alternat Med. 2017; 5076029.

55. Vieira THF, Guimaraes IM, Silva FR, Ribeiro FM. Alzheimer's disease: targeting the cholinergic system. Curr Neuropharmacol. 2016; 14(1):101–15.