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Research Paper

Phyto-chemical and Pharmacological Activities Review on *Cinnamoum zeylanicum* Blume

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ABSTRACT:
This review paper combines ethanomedicinal applications and a pharmacological assessment of Cinnamoum zeylanicum Blume (family: Lauraceae). In-vitro, in-vivo studies from different parts of the world have demonstrated numerous beneficial medicinal effects of C. zeylanicum Blumeto treatment of a number of diseases around the world, due its potential proanthocyanidins give it anti-oxidant, anti-bacterial, anti-cancer, anti-diabetic, anti-inflammatory, anti-tyrosinase, anti-mutagenic, and cardiovascular qualities that lower cholesterol levels and have immunomodulatory qualities.In traditional medicine, cinnamon is regarded a treatment for respiratory, digestive, and gynecological ailments. C. zeylanicum may enhance insulin levels and has a low coumarin content.Cinnamon is regarded as useful and vital in the realm of medicine due to its radical scavenging and reducing qualitiesand shows astringent, carminative, Antispasmodic and Anti-septic activity.The essential oil of this plant contains high quantities of phenolic and bioactive components that can scavenge free radicals and prevent β-carotine oxidation.Many volatile oils mostly cinnamaldehyde,cinnamic acid and cinnamate are abundant in the plant.Other than essential oil components this plant also consists a rich source of phytochemical compounds, bioactive phenolic compounds, flavonoids, terpenoids, glycosides etc

Key Words*: Cinnamoum zeylanicum Blume, Lauraceae, essential oil, chemical constituents, pharmacological activities.*

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I. Introduction

Cinnamomum zeylanicum Blume (Fig. 1) also known as *Ceylon cinnamon*belongs to the Family Lauracae. The main part of its tree which is used for the spice purpose is its bark. This is one of the oldest and most important spice crops used for culinary purposes in Sri Lanka for centuries. With the exception of *C. zeylanicum*, Cassia, Saigon and Korintje Cinnamon are also classified under the *C. zeylanicum* category because they are very similar to each other with only slight variations in color, taste, shape and Coumarin content. All Cassia type Cinnamon are hard and have high levels of Coumarin a substance known to cause liver damage, while Ceylon Cinnamon is the only soft and brittle Cinnamon with ultra-low Coumarin levels[1].

1.1. Taxonomical Classification

Kingdom	:	Plantae
Division	:	Tracheophyta
Class	:	Magnoliopsida
Order	:	Laurales
Family	:	Lauraceae
Genus	:	***Cinnamomum***
Species	:	***Zylanicum*****Blume**

Figure 1:*Cinnamomum zeylanicum* Blume leaf and bark

1.2. Vernacular Names

Language	:	Vernacular Name	Language	:	Vernacular Name
Telugu	**:**	Dalchina Chekka	**Urdhu**	**:**	Darchini
Kannada	**:**	Dalchinni	**Sanskrit**	**:**	Darusita
Tamil	**:**	Karuva/ Ilavangam	**Sinhala**	**:**	Kurundu
Hindi	**:**	Darchini			

1.3. Plant synonyms

This plant is mostly known by three names as *Ceylon cinnamon, True cinnamon*and*Mexican cinnamon.*

1.4. Geographical Distribution

Cinnamon is found widely in Sri Lanka but also grows in Malabar, Cochin-China, Sumatra and in Eastern Islands too. Besides India, it is also cultivated in Brazil, Mauritius, India, Jamaica and in other countries also.

1.5.Botanical Description

C. zeylanicum Blume), a moderate sized or large tree with a rather thick, reddish bark, glabrous young parts and finely silky buds.[2]

- **Leaves:**Simple, opposite or sub-opposite without stipules, variable in size, 7.5-25cm long, oval or lanceolate-oval, subacute at base, slightly acuminate, obtuse, glabrous, stiffy coriaceous, strong, 3 or 5-nerved.with fine, reticulate venation, shining above, slightly paler beneath, bright pink when young, petioles 1.2-2.5 cm long, stout, flattened above.
- **Flowers**: Regular, bisexual or monoecious, pale yellow, small, numerous on rather long, slightly pubescent pedicels in subterminal panicles longer than leaves, lax peduncles often clustered, glabrous or pubescent, bracts absent; perianth about 0.6 cm long, silky, tube short-campanulate, segments 6, oblong-lanceolate, acute or obtuse, usually persistent, imbricated in two rows; stamens 9 in three rows, perigynous, anthers 4-celled, filaments of the first and second rows without glands and filaments of the third row with glands, staminodes 3, sagittate forming the fourth row; ovary superior, unilocular with a solitary ovule pendulous from the top, style shorter than stamens, stigma bilobed.
- **Fruit:**Fruit about 1.2 cm long, oblong-ovoid, surrounded by much enlarged perianth, dry or fleshy, dark purple, seed without endosperm.
- **Bark:**Inside filled with thin concentric layers composed of multiple layers rolled like cigar-quill with Golden brown color.

1.5. Ethno-Botanical Uses

- *Ceylon cinnamon* is considered as an alternative treatment for diabetes mellitus. In one study, Ceylon cinnamon brought insulin levels in diabetic rats to close to normal levels. Other studiesTrusted Source support the idea that *C. cinnamon* is useful for diabetes treatment.
- It enhanced antioxidant enzyme activity. This means it may prevent or treat certain types of cancer.
- Acording to Unani System of Medicine Darchini (Cinnamon) shows following properties

- ❖ Antiseptic
- ❖ Absorbent
- ❖ Stimulant
- ❖ Demulscent
- ❖ Deobstruent
- ❖ Emmenagogue
- ❖ Exhilarant
- ❖ Aphrodisiac
- ❖ Stomachic
- ❖ Liver Toni
- ❖ Tonic for Principal organs
- ❖ Diuretic

II. Phyto-chemicals from C. cinnamon

The plant *C. zeylanicum* is a rich source of essential oil and phytochemical compounds, bioactive phenolic compounds, flavonoids, and polymers that are constituted a therapeutic chemical composition.

2.1. Behrooz Alizadeh Behbahaniet al., 2020[3]extracted the essential oils from leaves and examines the chemical constituents, antioxidant potential, antibacterial mechanism, and antiproliferative activity of *C. zeylanicum* bark. The compositions of the oil were analyzed by GC-MS, and the major constituents were found to be (*E*)-cinnamaldehyde (71.50%), linalool (7.00%), *β*-caryophyllene (6.40%), eucalyptol (5.40%), and eugenol (4.60%). *C. zeylanicum* essential oil contained remarkable levels of phenolic and bioactive compounds with outstanding ability to scavenge free radicals and inhibit *β*-carotene oxidation. The growth of pathogenic and spoilage bacteria, especially Gram-positive ones (i.e. *Listeria innocua*, *Staphylococcus aureus*, and *Bacillus cereus*), was highly inhibited by the oil, compared to the Gram-negative pairs (i.e. *Escherichia coli*, *Pseudomonas aeruginosa*, and *Salmonella typhi*). The cells of *L. innocua* and *E. coli* (as the most sensitive and resistant strains to the oil, respectively) treated with *C. zeylanicum* essential oil were observed by scanning electron microscopy to unravel structural changes. This study indicated that *C. zeylanicum* essential oil with remarkable antioxidant and antimicrobial properties could be applied to develop novel natural preservatives for food and medicinal purposes.(Figure 2).

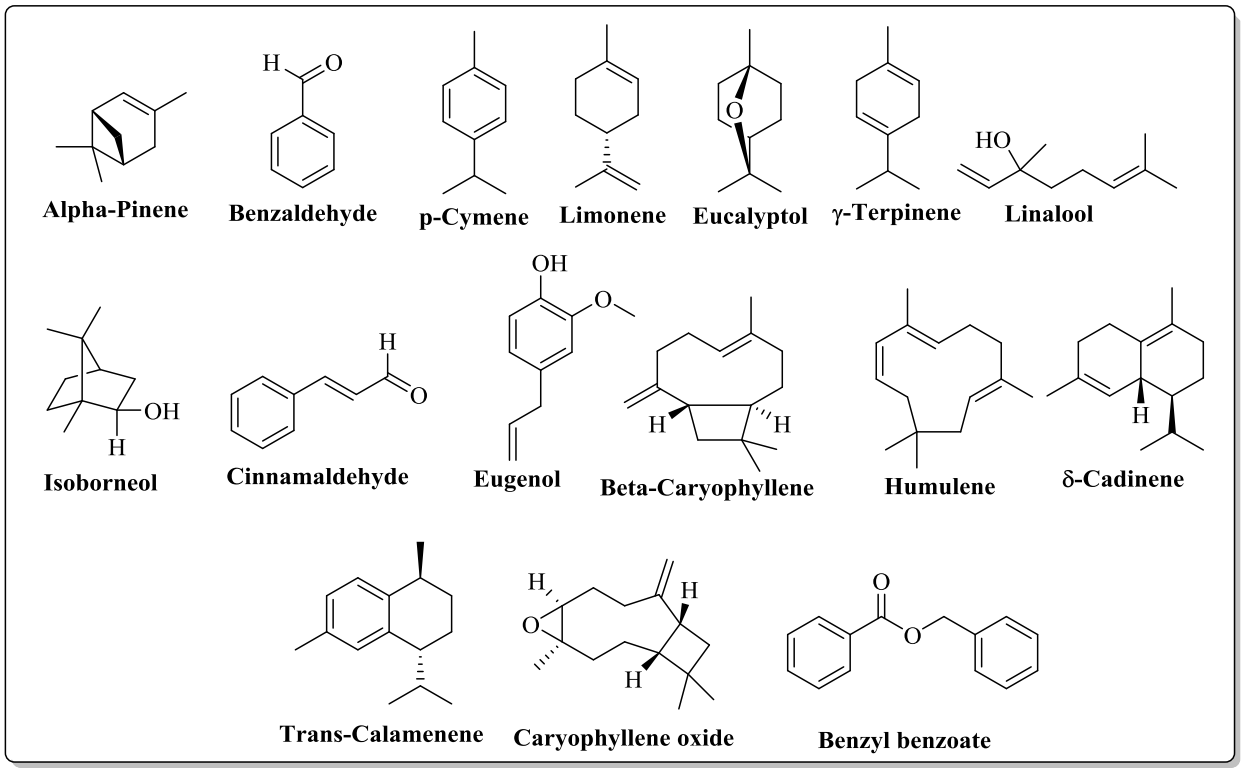

Figure 2. Essential oil components from *C. zeylanicum*

2.2. G. K. Jayaprakashaet al., 2006[4]defatted cinnamon fruit powder was successively extracted with benzene ethyl acetate, acetone, MeOH, and water. The concentrated water extract contained the maximum amount of phenolics and showed the highest antioxidant activities. Hence, it was fractionated by Diaion HP-20SS, Diaion HP-20, and Sephadex LH-20 column chromatographies. It gave five purified compounds, the purities of which were analyzed by HPLC. Compounds were identified as 3,4-dihydroxybenzoic acid (protocatechuic acid), epicatechin-(2β→*O*-7,4β→8)-epicatechin-(4β→8)-epicatechin (cinnamtannin B-1), 4-[2,3-dihydro-3-

(hydroxymethyl)-5-(3-hydroxypropyl)-7-(methoxy)benzofuranyl]-2-methoxyphenyl β-D-glucopyranoside (urolignoside), quercetin-3-*O*-(6-*O*-α-L-rhamnopyranosyl)-β-D-glucopyranoside (rutin), and quercetin-3-*O*-α-L-rhamnopyranoside by using extensive spectral studies. The antioxidant activities of purified compounds were screened for their antioxidative potential using β-carotene−linoleate and 1,1-diphenyl-2-picrylhydrazyl model systems. All of the compounds showed antioxidant and radical scavenging activities. This is the first report of the isolation and identification of nonvolatile constituents and as well as antioxidant activities from cinnamon fruits.(Figure 3).

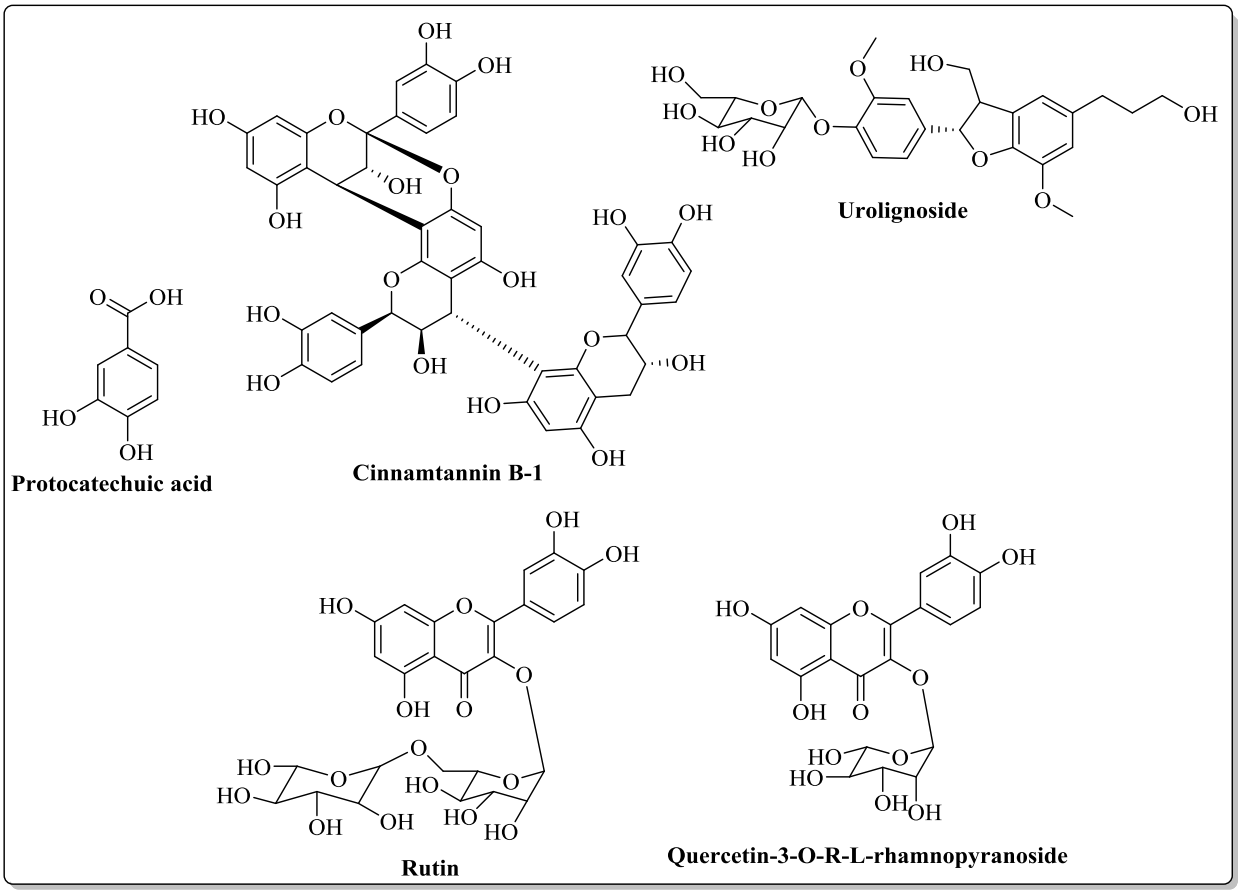

Figure 3. Phenolic Constituents in the Fruits of *C. zeylanicum*

2.3. K. Nagendra Prasadet al., 2009[5]were extracted and analysis of the high-performance liquid chromatography coupled to diode array detector (HPLC-DAD) of *C. zeylanicum*, three flavonoid compounds namely quercetin, kaempferol and quercetrin were identified and quantified. This study suggested that *Cinnamomum* leaf can be used potentially as a readily accessible source of natural antioxidants.(Figure 4).

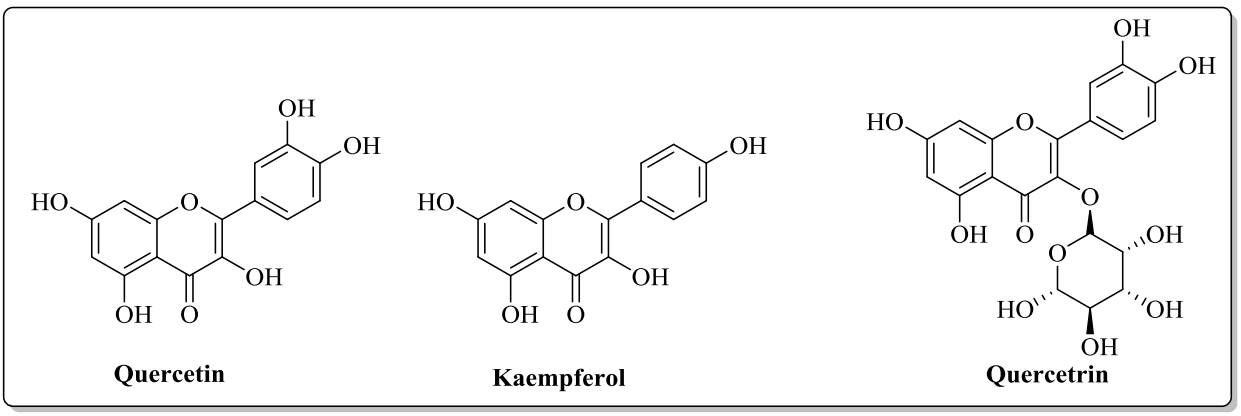

Figure 4. Flavanoids from *C. zeylanicum*

2.4. T. Sivapriya and Sheila John, 2019[6] study the purify, identification, isolation and elucidattion the molecular structure of bio active compounds presents in enriched fraction of methyl hydroxyl chalcone polymer (MHCP) in *C. zelaynicum*. The bioactive compounds identified were Ellagic acid 3-O-pentoside, Afzelechin 3-O-glucopyranoside, gallocatechin 3-O-pentosid (Figure 5).

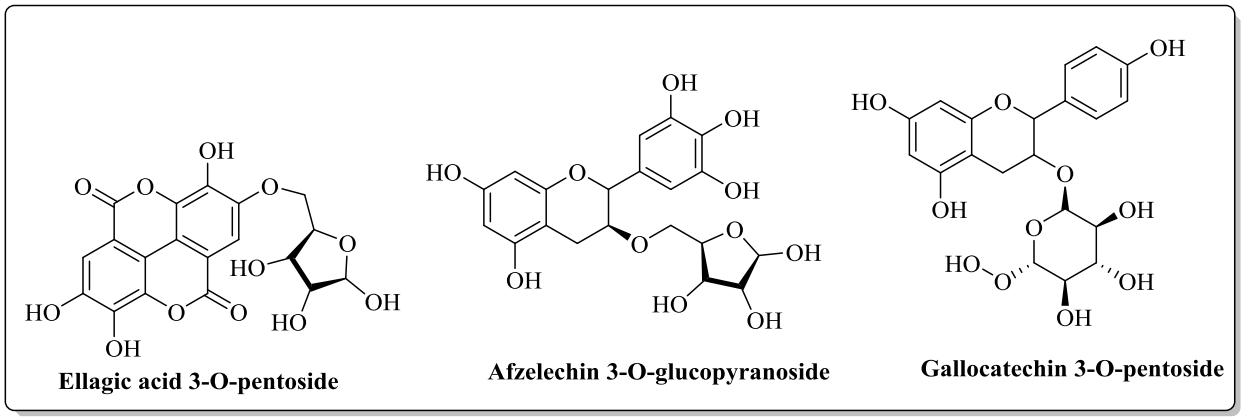

Figure 5. Methyl hydroxyl chalcone polymer from *C. zeylanicum*

III. Pharmacological Activities of C. zeylanicum

C. zeylanicum has large range of bioactivity profile. Reported activity studies are listed below

3.1. In-vitro and in-vivo anti-microbial properties

Abu El Ezz NMet al 2011[7]investigated the effect of administration of onion (*Allium cepa*) and cinnamon (*C. zeylanicum*) oils on the development and progression of the experimental cryptosporidiosis in mice. The results showed that the two oils were effective against experimental infection of mice with Cryptosporidium parvum. *A. cepa* oil showed more potent than *C. zeylanicum*. It was concluded that administration of onion or cinnamon oils was beneficial in protecting susceptible hosts against opportunistic zoonotic parasites such as *Cryptosporidium parvum*.

3.2. In-vitro and in-vivo anti-parasitic effects

Samarasekera Ret al 2005[8]studied the mosquito control properties of essential oils of leaf and bark of Ceylon *C. zeylanicum* Blume and their eight compounds were investigated against *Culex quinquefasciatus, Anopheles tessellatus* and *Aedes aegypti*. *C. zeylanicum* bark oil showed good knock-down and mortality against *A. tessellatus* (LD_{50} 0.33 µg/mL) and *C. quinquefasciatus* (LD^{50} 0.66 µg/mL) than leaf oil (LD^{50} 1.03 and 2.1 µg/mL). Cinnamaldehyde was a major constituent of the bark oil and eugenol in the leaf oil. Cinnamaldehyde and eugenol both were more active against *C. quinquefasciatus, A. tessellatus* and *A. aegypti* than the bark and leaf oil. Mosquitocidal activity of cinnamyl acetate against three mosquito species was comptarable to that of the *Cinnamomum* bark oil, whereas eugenyl acetate was effective on *A. tessellatus* and *C. quinquefasciatus.* The other compounds showed less or no activity against mosquitoes tested.

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

Ranasinghe Pet al., 2012[9]studied the *in-vitroC. zeylanicum* demonstrated a potential for reducing post-prandial intestinal glucose absorption by inhibiting pancreatic α-amylase and α-glucosidase, stimulating cellular glucose uptake by membrane translocation of glucose transporter-4, stimulating glucose metabolism and glycogen synthesis, inhibiting gluconeogenesis and stimulating insulin release and potentiating insulin receptor activity. The beneficial effects of *C. zeylanicum* in animals include attenuation of diabetes associated weight loss, reduction of fasting blood glucose, LDL and HbA(1c) , increasing HDL cholesterol and increasing circulating insulin levels. *C. zeylanicum* also significantly improved metabolic derangements associated with insulin resistance. It also showed beneficial effects against diabetic neuropathy and nephropathy, with no significant toxic effects on liver and kidney and a significantly high therapeutic window.

3.4. In-vitro and in-vivo anti-oxidant properties

Chericoni S et al., 2005[10]were tested in two in vitro models of peroxynitrite-induced nitration and lipid peroxidation. The essential oil and eugenol showed very powerful activities, decreasing 3-nitrotyrosine formation with IC_{50} values of 18.4 microg/mL and 46.7 microM, respectively (reference compound, ascorbic acid, 71.3 microg/mL and 405.0 microM) and also inhibiting the peroxynitrite-induced lipid peroxidation

showing an IC_{50} of 2.0 microg/mL and 13.1 microM, respectively, against 59.0 microg/mL (235.5 microM) of the reference compound Trolox. On the contrary, (E)-cinnamaldehyde and linalool were completely inactive.

3.5. Toxic effects

Domaracký ***M et al., 2007***[11]evaluated the influence of five essential oils obtained from plant species which are known to have positive antimicrobial, antioxidative and anti-inflammatory effects--sage Essential Oils from *Salvia officinalis* L, oregano EO from *Origanum vulgare* L, thyme EO from *Thymus vulgaris* L, clove EO *from Syzygium aromaticum* L and cinnamon EO from *C. zeylanicum* on the growth and development of mouse preimplantation embryos in vivo. Essential oils were added to commercial diet at concentrations of 0.25% for sage EO, thyme EO, clove EO, cinnamon EO and 0.1% for oregano EO, and fed to ICR female mice for 2 weeks ad libitum. Females were then mated with males of the same strain. Embryos obtained on Day 4 of pregnancy at the blastocyst stage were stained by morphological triple staining (Hoechst, PI, Calcein-AM) and evaluated using fluorescent microscopy. The effects of essential oils were estimated by the viability of embryos, number of nuclei and distribution of embryos according to nucleus number. Cinnamon EO significantly decreased the number of nuclei and the distribution of embryos according to nucleus number was significantly altered. Sage EO negatively influenced the distribution of embryos according to nucleus number. Clove and oregano EOs induced a significantly increased rate of cell death. Only thyme EO had no detectable effects on embryo development. In conclusion, none of the essential oils had any positive effect on embryo development, but some of them reduced the number of cells and increased the incidence of cell death.

3.6.Anti-hyperglycemic activity

Zare Ret al., 2019[12]studied the Anti-hyperglycemic activityof *C. zeylanicum.* Cinnamon supplementation led to improvement of all anthropometric (BMI, body fat, and visceral fat), glycemic (FPG, 2hpp, Hb_{A1C}, Fasting Insulin, and Insulin Resistance), and lipids (Cholesterol Total, LDL-c and HDL-c) outcomes (except for triglycerides level). All observed changes (except for Cholesterol Total and LDL-c) were significantly more prominent in patients with higher baseline BMI (BMI $\geq$ 27). Based on the study findings, cinnamon may improve anthropometric parameters, glycemic indices and lipid profile of patients with type II diabetes. These benefits are significantly more prominent in patients with higher baseline BMI (BMI $\geq$ 27). The trial protocol was registered in Iranian Registry of Clinical Trials database.

3.7.Anti-hyperlipidemic activity

Tuzcu Zet al., 2017[13]evaluated the effects of cinnamon polyphenol extract on hepatic transcription factors expressions including SREBP-1c and LXR-α in rats fed high fat diet (HFD). Twenty-eight Wistar rats were allocated into four groups: (i) normal control: animals fed with normal chow; (ii) cinnamon: animals supplemented with cinnamon polyphenol; (iii) HFD: animals fed a high-fat diet; and (iv) HFD + cinnamon: animals fed a high-fat diet and treated with cinnamon polyphenol. Obesity was linked to hyperglycemia, hyperlipidemia, and oxidative stress as imitated by elevated serum glucose, lipid profile, and serum and liver malondialdehyde (MDA) concentrations. Cinnamon polyphenol decreased body weight, visceral fat, liver weight and serum glucose and insulin concentrations, liver antioxidant enzymes, and lipid profile ($P < 0.05$) and reduced serum and liver MDA concentration compared to HFD rats ($P < 0.05$). Cinnamon polyphenol also suppressed the hepatic SREBP-1c, LXR-α, ACLY, FAS, and NF-κB p65 expressions and enhanced the PPAR-α, IRS-1, Nrf2, and HO-1 expressions in the HFD rat livers ($P < 0.05$). In conclusion, cinnamon polyphenol reduces the hyperlipidemia, inflammation, and oxidative stress through activating transcription factors and antioxidative defense signaling pathway in HFD rat liver.

3.8.Anti-inflammatory activity

Han X and Parker TL2017[14]reported the effect of cinnamon (Cinnamomum zeylanicum) bark essential oil (CBEO) on human skin cells. First evaluated the impact of CBEO on 17 protein biomarkers that play critical roles in inflammation and tissue remodeling. The impact of CBEO on genome-wide gene expression was also evaluated. CBEO showed strong anti-proliferative effects on skin cells and significantly inhibited the production of several inflammatory biomarkers, including vascular cell adhesion molecule-1, intercellular cell adhesion molecule-1, monocyte chemoattractant protein-1, interferon gamma-induced protein 10, interferon-inducible T-cell alpha chemoattractant, and monokine induced by gamma interferon. In addition, CBEO significantly inhibited the production of several tissue remodeling molecules, including epidermal growth factor receptor, matrix metalloproteinase-1, and plasminogen activator inhibitor-1. Macrophage colony-stimulating factor, which is an immunomodulatory protein molecule, was also significantly inhibited by CBEO. Furthermore, CBEO significantly modulated global gene expression and altered signaling pathways, many of which are important in inflammation, tissue remodeling, and cancer biology. The study shows that CBEO is a promising antiinflammatory agent; however, further research is required to clarify its clinical efficacy.

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