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REVIEW

Antidiabetic effects of cinnamon (*Cinnamomum sp.*) and the influence of the compounds it contains

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Abstract

Background: Cinnamon (*Cinnamomum sp*.) is a traditional Indonesian herbal plant that has been used as a medicinal agent for centuries. Numerous studies have been conducted, demonstrating the benefits of cinnamon, including its use as an antidiabetic agent. **Objective:** This review aims to examine the antidiabetic effects of cinnamon (*Cinnamomum sp.*) and the influence of the compounds it contains. **Method:** This literature review was compiled using electronic databases like PubMed, Science Direct, and Google Scholar with the keywords "*Cinnamon or Cinnamomum*" and "*antidiabetic or hyperglycemia*". The inclusion criteria focused on in vitro and in vivo studies from 2019 to 2024 that examine the blood glucose-lowering effects of cinnamon (*Cinnamomum* sp.). A total of 15 relevant articles were obtained for review. **Result:** Cinnamon contains secondary metabolites such as sinamaldehyde, polyphenols, flavonoids, tannins, cinnamic acid, and sinamal acetate, which can inhibit the enzymes α-glucosidase, maltase, and α-amylase, thereby inhibiting carbohydrate hydrolysis and reducing the increase in blood glucose levels. **Conclusion:** The antidiabetic effects of cinnamon's secondary metabolites were highlighted in a literature review. Both in vitro and in vivo studies have indicated that these compounds lower blood glucose levels by enhancing insulin sensitivity, thereby slowing the rise in blood glucose.

Introduction

Diabetes mellitus (DM) is a chronic metabolic disorder characterised by defects in insulin secretion and action, leading to dysregulated carbohydrate, lipid, and protein metabolism. It results from chronic hyperglycaemia due to insufficient insulin secretion by the pancreas or impaired insulin action in peripheral tissues (WHO, 2019). In 2021, 537 million people worldwide had diabetes, with projections of 643 million by 2030 and 783 million by 2045. Indonesia ranks fifth in the number of diabetics, with 19.5 million cases, following China, India, Pakistan, and the United States (IDF Diabetes Atlas, 2021).

Elevated blood glucose levels, indicative of hyperglycaemia in diabetes mellitus, are attributed to either inadequate insulin secretion or reduced cellular responsiveness to insulin. In general, diabetes is divided into two types, namely Type 1 DM and Type 2 DM. Type 1 DM generally begins to occur in childhood or early adulthood (WHO, 2019). The hallmark of Type 1 DM is the inadequate production or deficiency of insulin resulting from pancreatic beta cell impairment. Whereas Type 2 DM results from a relative insulin deficiency due to pancreatic beta cell dysfunction that causes the pancreas to no longer produce enough insulin, or the cells no longer respond to the secreted insulin. As a result, cellular glucose uptake is impaired, leading to increased accumulation of glucose in the blood (Ajibade *et al*., 2019).

Diabetes necessitates long-term management. The length of treatment may cause unwanted side effects. Antihyperglycemic treatment can be given orally or by injection. Oral hyperglycaemic drugs are from the group of insulin secretion boosters, dipeptidyl peptidase-4 enzyme inhibitors (DPP-4 inhibitors), α-glucosidase inhibitors, and Sodium Glucose Co-Transporter-2 inhibitors (SGLT-2 inhibitors). Injectable drugs include GLP-1 1-RA, insulin, and a combination of insulin and GLP-1 1-RA (PERKENI, 2021). However, there is no comprehensive solution for diabetes therapy due to drug shortages, side effects and limitations of the mode of administration, such as adverse reactions from long-term subcutaneous injection and problems with poor gastrointestinal absorption. Therefore, there is a need for new antidiabetic drugs that are both highly efficient and have minimal side effects.

Currently, the world is aggressively pursuing research on new treatments for diabetes. In addition to pharmacological therapy, there are many options for complementary therapy to treat hyperglycaemia due to its fewer side effects than chemical drugs. Herbal plants can serve as an alternative to chemical drugs for treating various diseases (Gahtori *et al.,* 2023). Herbal plants are a rich source of bioactive compounds, including tannins, alkaloids, flavonoids and steroid resins, which confer significant therapeutic potential. Non-pharmacological treatment with herbal plants has fewer side effects, is more affordable, and is easily accessible, making it a safer and more cost-effective option. One of the plants that has benefits as an antidiabetic is cinnamon.

Cinnamomum sp., a member of the Lauraceae family, is extensively utilised in traditional and complementary medicine (Hussain *et al*., 2019). Traditionally, cinnamon is recognised as a spice with medicinal properties for various diseases. The biological effects of cinnamon have been scientifically proven. Cinnamon food products are typically available in the form of native roll pieces or natural powder (Ilmi *et al*., 2022). Cinnamon is one of the complementary therapy options for diabetes. Cinnamon contains bioactive compounds that play a role in diabetes, specifically cinnamaldehyde, which can help reduce blood glucose levels. Cinnamon is a source of various compounds, including polyphenols, eugenol, quercetin, cinnamic acid and many more. These compounds play a role in inhibiting α-amylase and α-glucosidase in the blood. Therefore, this narrative review aims to determine the antidiabetic effectiveness of various cinnamon (*Cinnamomum sp.*) compounds (Silva *et al.*, 2022).

Methods

This article is written using the narrative review method. The writing of this narrative review is taken from valid and credible sources. A comprehensive literature search was performed across PubMed, ScienceDirect, Google Scholar, and the official websites of the International Diabetes Federation and the World Health Organisation using the keywords “(Cinnamon or Cinnamomum) and (antidiabetic or hyperglycaemia)”. The inclusion criteria used include articles or journals that feature in vivo and in vitro tests reviewing the activity of cinnamon plants (Cinnamomum sp.) in lowering blood glucose, published between 2019 and 2024. The exclusion criteria used were articles that studied the compounds contained in cinnamon, the tests used, the solvents used, and the pharmacological mechanisms related to lowering blood glucose levels.

Results

Cinnamon (*Cinnamomum sp.)* is a family of Lauraceae that is mainly used as an herbal medicine (Table I). The genus Cinnamomum comprises 250 species native to China, Southeast Asia, and Australia. Cinnamon is a tree that grows to be about 10-15 meters tall. Cinnamon has two main species: *Cinnamomum zeylanicum* Blume (native cinnamon, also known as *Cinnamomum verum*) and *Cinnamomum cassia* (Chinese cinnamon, also known as *Cinnamomum aromaticum*). C. *zeylanicum* is native to South India and Sri Lanka. C. *cassia* is native to Vietnam and China. C. *burmani* originates from Indonesia, specifically the Java and Sumatra regions (Wijenayaka *et al.,* 2022).

Cinnamon is one of the natural ingredients that is also a biological wealth of Indonesia, possessing therapeutic potential due to its secondary metabolites. Cinnamon contains cinnamaldehyde compounds, cinnamic acid, polyphenols, tannins, eugenol, and many other essential oils known to have antidiabetic effects. Apart from being antidiabetic, cinnamon also exhibits antioxidant, anti-inflammatory, antimicrobial, antihypertensive, and antilipemic properties (Sari *et al*., 2023).

Table I: Classification of cinnamon (*Cinnamomum* sp.*)*

Kingdom	Plants
Sub kingdom	Tracheobionta
Class	Magnoliopsida
Subclass	Magnoliopsida
Subdivision	Spermatophyta
Division	Magnoliophyta

Cinnamon (*Cinnamomum* sp.) is composed of many compounds with efficacious biological activities. The chemical processes involved in extracting from different parts of the Cinnamomum plant resulted in variations in the properties of the resulting extract. Essential oils, typically extracted from the leaves, bark and root bark of Cinnamomum plants, exhibit a consistent spectrum of monoterpene hydrocarbons.

However, the main compounds are different. Cinnamon aldehyde is the primary constituent of cinnamon bark. Leaf oil contains eugenol, while root bark oil contains camphor (Błaszczyk *et al.,* 2021).

The bark of the cinnamon plant is the predominant part utilised. The primary secondary metabolite in cinnamon is cinnamaldehyde, which contributes significantly to its aroma (Table II). Cinnamon bark sources bioactive compounds, including catechins and procyanidins, which are classified within the flavan-3-ols subgroup of flavonoids and act as antidiabetic agents.

Table II: Example compound chemistry in part of the plant cinnamon (Błaszczyk *et al.*, 2021)

Plant parts	Compound
Fruit	Cinnamyl acetate Coumarin
Leaf	Eucalyptus Cinnamaldehyde
Bark	Cinnamaldehyde Tannin

Compounds with antidiabetic activity in Cinnamon

Cinnamaldehyde

Cinnamaldehyde is the most abundant compound found in cinnamon. This compound is cinnamaldehyde, also known as cinnamal 3-phenylpropenal or β-phenylacrolein, and its chemical structure is C6H5CH=CHCHO. Cinnamaldehyde in cinnamon is 49.75% in trans-cinnamaldehyde form and 20.26% in the form of sinamal acetate. Cinnamaldehyde is a metabolite secondary in cinnamon obtained through the distillation process of the bark. This compound includes a group of polyphenols, which are derived from secondary metabolites. This compound has potential as an antidiabetic agent because it enhances the transport of glucose by GLUT-4 in adipose and skeletal muscle cells, which may hinder the improvement in blood glucose levels (Dewi *et al.*, 2022).

Polyphenols

Polyphenols are compounds found in many plants. Proanthocyanidin is one type of polyphenol compound. Proanthocyanidin is an insulin mimetic and works as an enzyme inhibitor of α-amylase and α-glucosidase digesters. This is useful in the hydrolysis process of carbohydrates, as it hinders the improvement of blood glucose levels (Attahmid *et al*., 2021).

Flavonoids

Flavonoids are one of the compounds contained in cinnamon. Flavonoids include phenolic compounds that consist of a heavy molecule, composed of 2-phenylchromone from a derivative of sour acetate. Compound phenolic effects hypoglycaemia, flavonoids exhibit anti-inflammatory, antioxidant, antithrombotic and antiviral properties. As antioxidants, flavonoids play a role in inhibiting phosphodiesterase and alleviating oxidative stress in patients with DM (Azzahra *et al*., 2022). This compound plays a role in the decline of blood sugar levels by inhibiting α-glucosidase, maltase, and α-amylase. Flavonoids also function to stimulate the uptake of glucose into the muscle under the regulation of GLUT-4 (Anggraini, 2020).

Tannin

Tannin plays a role as an antidiabetic because it increases the process of glycogenesis, which causes a rapid decline in blood glucose levels. This compound has the ability to convert glucose into glycogen, which is then stored within the cell. (Dewi *et al*., 2022). With the increase in tannin compounds, the activity of glycogenesis increases, leading to a decrease in blood glucose levels.

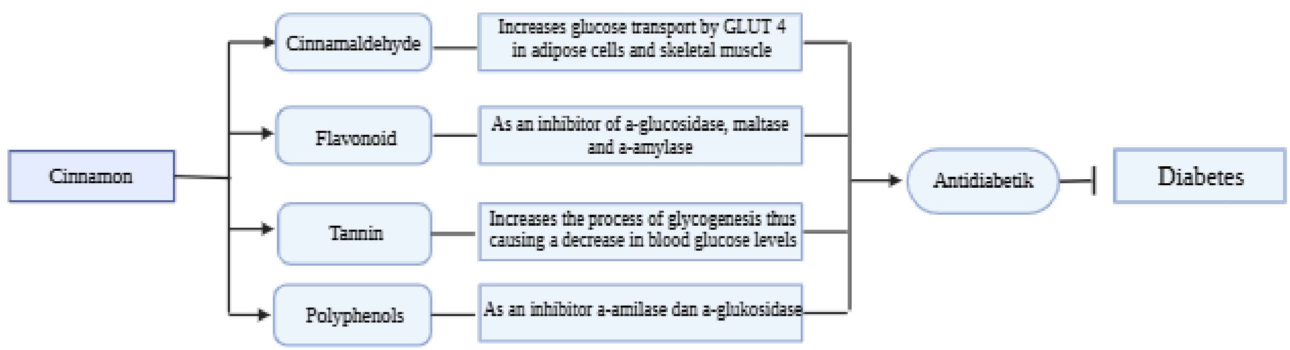

Figure 1: Compounds in cinnamon containing antidiabetic agents

Table III outlines research studies examining the efficacy of cinnamon in lowering blood glucose levels. These studies encompass various parameters, including the type of tests conducted, active compounds identified, solvents utilised, inclusion criteria for subjects, and the pharmacological mechanisms associated with the reduction of blood glucose levels.

Table III: Test type, compound, solvent, criteria subject, action pharmacology decreased blood glucose levels from cinnamon plant (*Cinnamomum* sp.)

Test type	Compound chemistry	Solvent	Criteria subject	Mechanism action	Results	Reference
In vitro	Cinnamaldehyde, quercetin, eugenol	Ethanol 95%	Powder wood sweet extracted with solvent	Inhibition α-amylase enzyme	Decrease glucose blood	(Nawaz *et al.,* 2023)
In vitro	Polyphenols	Ethanol 80%	Cinnamon dry destroyed with a machine hammer size 0.8 mm, then extracted with solvent.	Inhibition α-amylase enzyme	Decrease glucose blood	(Yusuf *et al.,* 2021)
In vitro	Sour cinnamate, cinnamaldehyde	Sodium citrate 0.01 M	Powder wood sweet extracted with solvent	Induce translocation through track AMPK signal	Decrease glucose blood	(Nazareno *et al.,* 2022)
In vitro	Cinnamaldehyde, eugenol, coniferaldehyde	Ethanol watery	Powder wood sweet extracted with solvent	Inhibition of α-glucosidase and α-amylase enzymes	Decrease glucose blood	(Das *et al.,* 2022)
In vitro	Normal compound	Ethanol, methanol and aqueous	Extract wood sweet	Inhibition of α-glucosidase and α-amylase enzymes	Decrease glucose blood	(Vijayakumar *et al.,* 2022)
In vitro	Tannins, phenols, terpenoids	Ethanolic, methanolic, aqueous, and acrbose	Extract wood sweet	Inhibition of α-glucosidase and α-amylase enzymes	Decrease glucose blood	(ALmohaimeed *et al.,* 2021)
In vivo	Sour cinnamate, cinnamaldehyde, methyl polymer hydroxide	Methanol	Three tens tail mouse, wistar albino male	Show activity antihyperglycemic with lower blood glucose in 28 of 30 mice	Decrease glucose blood	(Sivaranjani *et al.,* 2021)
In vivo	No mentioned	Saline solution	Three ten Mouse Sprague-Dawley male	There is an antihyperglycemic, antioxidant, and anti-inflammatory effect due to the existence of BDNF up-regulation and cytokine down-regulation mechanisms, which reduce inflammation, as well as work directly to reduce hyperglycemia in the body.	Decrease glucose blood	(ALmohaimeed *et al.,* 2021)
In vivo	Normal compound	Ethanol, methanol and aqueous	Mouse wistar albino male	There is an antihyperglycemic effect in rat test samples	Decrease glucose blood	(Vijayakumar *et al.,* 2022)
In vivo	Polyphenols, Cinnamaldehyde, Acid cinematography	Methanol	Mouse wistar albino male	The effect of antihyperglycemic caused the existence of various phytoconstituents in screening phytochemicals. MECB has a profit to control glucose blood levels	Decrease glucose blood	(ALmohaimeed *et al.,* 2021)

Effect of cinnamon in diabetes

In vitro and in vivo studies have demonstrated the antidiabetic activity of Cinnamomum plant extracts, attributed to the inhibition of α-amylase and α-glucosidase enzymes. This can be proven in research: cinnamon powder extracted with a 95% ethanol solvent contains compounds such as cinnamaldehyde, quercetin, and eugenol, which are capable of inhibiting enzymes a-amylase and a-glucosidase, thereby reducing blood glucose levels (Nawaz *et al*., 2023). Based on Table II, in vitro cinnamon tests were conducted using several solvents, including ethanol, methanol, aqueous solutions, and sodium citrate. The use of solvents in cinnamon extract affects the level of its antidiabetic activity. Cinnamon extract with ethanol exhibits greater inhibition than with methanol, aqueous, and sodium citrate solvents (Vijayakumar *et al*., 2022).

Auto-phosphorylation and slow dephosphorylation of the insulin receptor

A tetrameric configuration characterises the insulin receptor, which is assembled from two extracellular a-subunits and two b-subunits. Upon insulin's interaction with the a-subunit, the transmembrane b-subunit mediates the cellular insulin response by initiating intracellular tyrosine kinase activity. This results in autophosphorylation of the beta subunit tyrosine residue. Increased autophosphorylation and decreased dephosphorylation of the insulin receptor affect increased insulin sensitivity (Figure 2) (Wijenayaka *et al*., 2022).

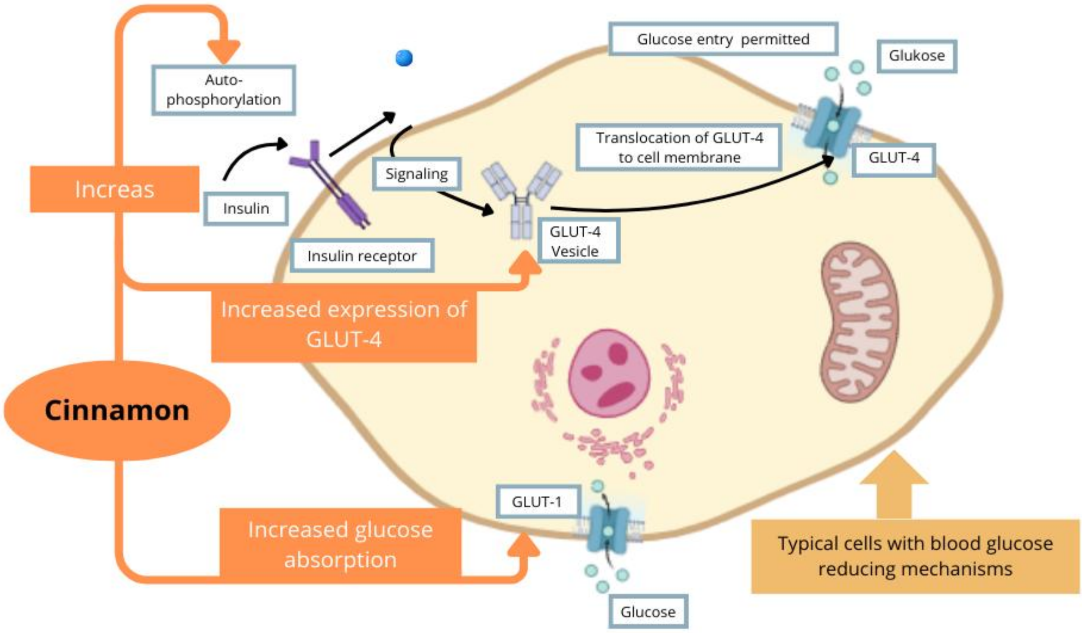

Figure 2: Mechanism of cinnamon's action on diabetes

Translocating glucose transporter 4 (GLUT 4)

The primary glucose transporter in adipose tissue and skeletal muscle is GLUT4, which is regulated by the hormone insulin. During diabetes mellitus, GLUT4 is reduced due to a lack of or inadequate insulin sensitivity. Cinnamomum extracts have been shown to enhance the phosphorylation of adenosine monophosphate-activated protein kinase (AMPK) and acetyl-CoA carboxylase (Wijenayaka *et al*., 2022).

Effect on GLUT's glucose transport activity

The GLUT1 gene, located on human chromosome 1, encodes the glucose transporter protein 1 (GLUT1). This gene is found in many cells that proliferate during embryonic development, such as the heart muscle, human erythrocytes, and astrocytes, which affect basal glucose absorption (Pragallapati, 2019).

Conclusion

Based on this narrative review, cinnamon contains compounds that have the potential to be antidiabetic. Cinnamon has the potential to treat diabetes due to its chemical composition, which includes cinnamaldehyde, polyphenols, tannins, flavonoids, and cinnamic acid, all of which are found in the bark. This chemical content can decrease the activity of α-amylase and α-glucosidase. The antidiabetic effect of cinnamon can reduce blood glucose levels. The collective evidence from in vitro and in vivo studies supports the potential of Cinnamomum as an antidiabetic agent.

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