

The Active Ingredients and Therapeutic Effects of Cinnamon: A Review Article

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ABSTRACT: Cinnamon is used in knocking and medicine for many centuries and in different countries. Several researches about cinnamon have exhibited its curative potentials, which include: immunomodulatory, gastroprotective, antidiabetic, antilipemic, antihypertensive, antitumor, antioxidant, antifungal, antiviral, antimicrobial. Cinnamaldehyde, Eugenol and Beta-caryophyllene are the major active ingredients in cinnamon. The mode of action for the therapeutic effects indicating the anti-diabetic and antihypertensive activities of cinnamon and its chemical components have not been deeply investigated. May systematic review articles have found that the taking the extracts or having cinnamon tea have potential antidiabetic effects. Researches about the action of cinnamon on hypertension still debated. However, a number of experimental trials have found significant antihypertensive effect for cinnamon. This review cast a brief light on the active ingredients and the activity of cinnamon in the reduction of high blood pressure and hyperglycemic status.

1. INTRODUCTION

Cinnamon, is the general name of *Cinnamomum*, which belongs to family Lauraceae, has been used knocking and medicine for many centuries and in different countries.. Several researches about cinnamon have exhibited its curative potentials, which include: immunomodulatory, gastroprotective, antidiabetic, antilipemic, antihypertensive, antitumor, antioxidant, antifungal, antiviral, antimicrobial. Two hundred species of the genus *Cinnamomum* have been specified as a potential economical and medicinal herb (Barceloux, 2009).

The majority of this research is centered around cinnamon bark powder a composition of cinnamon essential oil in small quantities with fiber, minerals, vitamins, carotenoids, flavonoids, antioxidants. The quills are curls of bark taken from the tree and left to dry as they contain these valuable components. Essential oil sacs found within the cambium typically measure between 2–10 microns in diameter. The yield of essential oil from the cinnamon bark is about 1–4%, which comes from these specific sacs located in the tree's bark (Stevens & Allred, 2022).

Cinnamon, medicinally speaking, has historically been used as a carminative agent which implies it was used to treat the different issues that may result in anorexia and dyspepsia or even nausea and vomiting. Beyond this point there are other anecdotal uses of cinnamon such as therapy for bleeding ulcers and hemorrhage alongside being considered a warming agent plus stimulant. Cinnamon is also suggested as having anti-cancer properties although scientific evidence to support these claims (Hajimonfarednejad et al., 2019). According to Amran et al. (2023), cinnamon bark oil's main constituent is cinnamonaldehyde alpha.-Muuroolene, copaene, and tau-Muurolol. These chemical compounds are thought to have hepatoprotective characteristics.

ACTIVE INGREDIENTS

The essential contributor of the sweetening and spicy aroma in cinnamon is cinnamaldehyde, a phenylpropanoid that is naturally produced via the shikimate pathway in plants. It has a chemical formula C_9H_8O and consists of a an aldehyde group, a short carbon chain, and a benzene ring. This compound makes up about half to nine-tenths of cinnamon oil's total chemical composition; the actual percentage varies based on plant species and part. Although cinnamaldehyde typically imparts this distinctive fragrance note by itself, in whole cinnamon bark essential oil there are many other constituents that contribute to create a rich complex aroma different from isolated cinnamaldehyde as single note (Stevens.2020).

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A compound derived from guaiacol with an allyl chain substitution, eugenol belongs to the phenylpropanoid class of compounds which are synthesized from the amino acid phenylalanine along the shikimate pathway. It has a molecular formula of $C_{10}H_{12}O_2$ and is composed of a benzene ring with an ether group in ortho-conformation and a hydroxy group along with the allyl chain para to the hydroxy group. Typically found as the main constituent in essential oil obtained from cinnamon leaf, eugenol is present in about 2–13% in oils derived from bark; it can be characterized as a member of the phenol class of compounds with these specific structural features (Stevens & Allred, 2022).

Beta-caryophyllene is a bicyclic sesquiterpene found in various spice and flavoring plants, one of which is cinnamon. This molecule is synthesized by plants through the mevalonate pathway, where it is derived from precursor molecules of acetyl-CoA. In nature, beta-caryophyllene is found together with alpha-humulene (previously known as alpha-caryophyllene) which has a structure that differs due to ring-opening. Beta-caryophyllene stands out in nature due to its unique nine-membered double-ring structure (an uncommon trait) coupled with a pleasant sweet aroma and taste factors that have made it a research subject of interest. Typically, beta-caryophyllene constitutes less than 10% of cinnamon oil (PubChem, 2019).

CLINICAL EFFECTS

Lowering blood glucose level

The precise pharmacological pathways responsible for cinnamon's antidiabetic effects remain largely unknown. However, in a recent systematic review, the investigators delved into this particular realm, seeking to unearth the potential pharmacological underpinnings of cinnamon's hypoglycemic and hypolipidemic efficacy. They didn't stop there; clinical recommendations surrounding cinnamon and its active components were also brought to light through this review. These weren't 16 randomized control trials involving over a thousand patients tracked anywhere between 7 to 17 weeks— painted an interesting picture when synthesized. The meta-analysis revealed marked improvements in glycolipid levels among diabetic individuals who ingested cinnamon vis-a-vis those on a placebo regimen; adverse effects were scanty with only one recorded case. Their takeaway from these findings was straightforward: cinnamon wields a considerable sway over both lipid and glucose metabolism orchestration quite affirming indeed! Patients with HbA1c of 8% experienced a stronger impact. The conclusion drawn by the writer was that cinnamon could be used as a lipid-lowering and hypoglycemic remedy in medical settings, where its safety is guaranteed (Zhou et al., 2022).

The study by Allen et al. (2013) involved a systematic review and meta-analysis where they searched for randomized control experiments that assessed the effects of cinnamon on glycemia and lipid levels. They found that consuming cinnamon is significant linked to a drop in levels of triglycerides, LDL-C, total cholesterol, and fasting plasma glucose while elevating HDL-C levels; though no significant impact on hemoglobin A1c was found. The high heterogeneity greatly limits practical application as details such as preferred dose and therapy duration remain unclear making it difficult to translate these findings into patient care (Allen et al., 2013).

An experimental study conducted by Moridpour et al. (2024) was aimed at investigating the impact of cinnamon intake on control of blood glucose for T2DM patients through a meta-analysis. They found out that more than 20 different randomized control trials all showed the same results where cinnamon supplementation was associated with statistically significant reductions in hemoglobin A1C (Mean difference: -0.67; $p = 0.011$), Homeostatic Model Assessment for Insulin Resistance (Mean difference: -1.32; $p < 0.001$) and fasting blood sugar (Mean difference: -1.32; $p < 0.001$), while there was no notable change in serum insulin levels among those who took part as patients with T2DM when compared with the control group. The researchers thus concluded that cinnamon has a significant effect in reducing these indicators of glycemic control, according to their analysis findings which were reported through the metanalytic experimental study.

Cinnamaldehyde is one of the principle compounds derived from Cinnamon that has found use as a fragrance agent— be it in your kitchen or an industry natural flavorant. Over the past decades, studies have emerged looking into its role as a beneficial agent in diabetes management and its related complications. The evidence keeps piling up: cinnamaldehyde can lower glucose and lipid levels which helps diabetics by improving insulin sensitivity through increased glucose uptake at adipose and muscle tissues; it also helps restore pancreatic islet function, amongst other benefits. On top of all this, cinnamaldehyde has the potential to metabolize into different compounds once inside your body. However, there is also mention of toxicity concerns surrounding this compound (Zhu et al., 2017).

Reduction of blood pressure

The effect of cinnamon on hypertension is still a subject of debate. The intake of cinnamon did lead to a decrease in the average ambulatory SBP level, although not significantly clinically but with statistical significance, and it also moderately improved the lipid profile. Hence, the use of cinnamon could be seen as an adjunctive therapy approach for people suffering from stage 1 hypertension. (Shirzad et al., 2021).

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The outcome of the systematic review and meta-analysis which was carried out to ascertain the impact of cinnamon intake on hypertension shows that it significantly lowered systolic and diastolic blood pressure among people with insulin-dependent diabetes (Jamali et al., 2020).

Mousavi et al. (2020) conducted a systematic review and meta-analysis on impact of cinnamon intake on systolic and diastolic blood pressure among adults. The results indicated that cinnamon supplementation led to a notable decrease in SBP (Weighted Mean Differences (mean difference): -6.23 mmHg, $P = 0.006$) as well as DBP (mean difference: -3.93 mmHg, $P = 0.001$). The trials demonstrated more pronounced effects on SBP with lower doses of cinnamon (≤ 2 grams), longer duration (≥ 3 months) and younger participants (< 50 years old) while also managing to reduce DBP.

In their study, Jalali et al. (2020) performed a systematic search using various online databases (Web of Sciences, Scopus, Embase, and PubMed) to find RCTs that looked into the impact of cinnamon intake on diastolic or systolic blood pressure (SBP or DBP) in patients with insulin-independent diabetes up to the publication date of 10 December 2019. The Egger regression test was utilized to assess potential publication bias; approximately 5 full-text articles were part of this meta-analysis. Results pooled from studies involving more than three hundred participants showed a significant decrease in both DBP and SBP after cinnamon intake with no publication bias detected. They suggested that cinnamon could be useful for lowering blood pressure among insulin-dependent diabetic patients.

In the year 2020, Hadi et al. have gone through the process of conducting a meta-analysis. To do this, they referred to systematic review. The databases that they searched were Google Scholar, ISI Web of Science, Cochrane Library, Scopus, and PubMed in order to find out randomized clinical trials (RCTs) that studied the impact of cinnamon supplementation on blood pressure. The results were positive: there were significant reductions in both systolic (mean difference: -5.17 mmHg, $p = 0.01$) and diastolic blood pressure (mean difference: -3.36 mmHg, $P \leq 0.001$) after cinnamon intake as seen from meta-analysis of 9 RCTs with 641 participants. These findings were significant only under certain conditions as revealed by subgroup analyses when cinnamon was administered at dosages of ≤ 2 g/day and for more than 8 weeks' time period plus in people with a baseline BMI of ≥ 30 kg/m² indicating that cinnamon intake can relieve hypertension by a moderate level.

In 2021, Ghavami et al. conducted a research study which designed to produce a meta-analysis and systematic review based on randomized controlled trials (RCTs) that looked into the impact of cinnamon on blood pressure (BP). From an initial pool of 927 records, only 8 trials were chosen due to their large sample sizes exceeding 500 participants. The combined effect size pointed towards no change in SBP even after the intake of cinnamon (with a mean difference of -0.61 mmHg, $P = 0.111$). However, when looking at cinnamon intake over a long period (≥ 8 weeks), there was a significant impact on SBP (mean difference: -1.25 mmHg, $P = 0.012$). Further analysis revealed that cinnamon did indeed have a significant effect on DBP (mean difference: -0.93 mmHg, $P = 0.003$) results echoed by both subsets in terms of duration and high dose (> 1500 mg/day) for cinnamon intake with regard to DBP effects being favorable although the same could not be said for SBP's findings.

The herb component was reported to induce low BP by inhibiting calcium cellular gates an effect reported earlier (Xue et al. 2011). Similarly, it was observed that the biochemical components in cinnamon can either indirectly affect the renin-angiotensin system or cause vasodilation effects directly (Ajbli Eddouks 2020). Another study noted that phytoconstituent of cinnamon exhibited antihypertensive activity by causing peripheral vasodilation further implying the potential mechanisms behind cinnamon's hypotensive effect. In addition, it was found that the antihypertensive impact of cinnamon may be linked with improving lipid profile characteristics due to its high potassium content— findings from two separate studies suggested this relationship (Mousavi et al., 2020 ; Abdelrahman et al., 2023).

CONCLUSIONS

Cinnamon is used in knocking and medicine for many centuries and in different countries. Several researches about cinnamon have exhibited its curative potentials, which include: immunomodulatory, gastroprotective, antidiabetic, antilipemic, antihypertensive, antitumor, antioxidant, antifungal, antiviral, antimicrobial. Cinnamaldehyde, Eugenol and Beta-caryophyllene are the major active ingredients in cinnamon. The mode of action for the therapeutic effects indicating the anti-diabetic and antihypertensive impacts of cinnamon and its chemical components have not been deeply investigated. May systematic review articles have found that the taking the extracts or having cinnamon tea have potential antidiabetic effects. Researches about the action of cinnamon on hypertension still debated. However, a number of experimental trials have found significant antihypertensive effect for cinnamon.

REFERENCES

- 1) Abdelrahman, I. A., Ahad, A., Raish, M., Bin Jardan, Y. A., Alam, M. A., & Al-Jenoobi, F. I. (2023). Cinnamon modulates the pharmacodynamic & pharmacokinetic of amlodipine in hypertensive rats. Saudi pharmaceutical journal : SPJ : the official publication of the Saudi Pharmaceutical Society, 31(9), 101737. <https://doi.org/10.1016/j.jsps.2023.101737>

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- 2) Allen, R. W., Schwartzman, E., Baker, W. L., Coleman, C. I., & Phung, O. J. (2013). Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis. *Annals of family medicine*, 11(5), 452–459. <https://doi.org/10.1370/afm.1517>
- 3) Amran, D.A.; Karim H. Al-Derawi, K.H and Al-Saadi, S.A. (2023). Phytochemical constituents of bark essential oils of *Cinnamomum zeylanicum* Blume and effects on liver tissue of rats. *University of Thi-Qar Journal of Science*. 10(2): 165-170.
- 4) Barceloux D. G. (2009). Cinnamon (*Cinnamomum* species). *Disease-a-month : DM*, 55(6), 327–335. <https://doi.org/10.1016/j.disamonth.2009.03.003>
- 5) Ghavami, A., Haghghian, H. K., Roshanravan, N., Ziaei, R., Ghaedi, E., Moravejolahkami, A. R., & Askari, G. (2021). What is the Impact of Cinnamon Supplementation on Blood Pressure? A Systematic Review and Meta-Analysis. *Endocrine, metabolic & immune disorders drug targets*, 21(5), 956–965. <https://doi.org/10.2174/1871530320666200729143614>
- 6) Hadi, A., Campbell, M. S., Hassani, B., Pourmasoumi, M., Salehi-Sahlabadi, A., & Hosseini, S. A. (2020). The effect of cinnamon supplementation on blood pressure in adults: A systematic review and meta-analysis of randomized controlled trials. *Clinical nutrition ESPEN*, 36, 10–16. <https://doi.org/10.1016/j.clnesp.2020.01.002>
- 7) Hajimonfarednejad, M., Ostovar, M., Raei, M. J., Hashempur, M. H., Mayer, J. G., & Heydari, M. (2019). Cinnamon: A systematic review of adverse events. *Clinical nutrition (Edinburgh, Scotland)*, 38(2), 594–602. <https://doi.org/10.1016/j.clnu.2018.03.013>
- 8) Jalali, R. Mahmoodi, M. Parisa Moosavian, S. Ferns, G.A. and Sohrabi, Z. (2020) Cinnamon supplementation improves blood pressure in type 2 diabetic patients: A systematic review and meta-analysis of randomized controlled trials. *Clin Diabetol*;9(4):259-266.
- 9) Jamali, N., Jalali, M., Saffari-Chaleshtori, J., Samare-Najaf, M., & Samareh, A. (2020). Effect of cinnamon supplementation on blood pressure and anthropometric parameters in patients with type 2 diabetes: A systematic review and meta-analysis of clinical trials. *Diabetes & metabolic syndrome*, 14(2), 119–125. <https://doi.org/10.1016/j.dsx.2020.01.009>
- 10) Moridpour, A. H., Kavyani, Z., Khosravi, S., Farmani, E., Daneshvar, M., Musazadeh, V., & Faghfour, A. H. (2024). The effect of cinnamon supplementation on glycemic control in patients with type 2 diabetes mellitus: An updated systematic review and dose-response meta-analysis of randomized controlled trials. *Phytotherapy research : PTR*, 38(1), 117–130. <https://doi.org/10.1002/ptr.8026>
- 11) Mousavi, S. M., Karimi, E., Hajishafiee, M., Milajerdi, A., Amini, M. R., & Esmailzadeh, A. (2020). Anti-hypertensive effects of cinnamon supplementation in adults: A systematic review and dose-response Meta-analysis of randomized controlled trials. *Critical reviews in food science and nutrition*, 60(18), 3144–3154. <https://doi.org/10.1080/10408398.2019.1678012>
- 12) PubChem Beta-Caryophyllene. [(accessed on 27 August 2019)]; Available online: <https://pubchem.ncbi.nlm.nih.gov/compound/5281515>
- 13) Shirzad, F., Morovatdar, N., Rezaee, R., Tsarouhas, K., & Abdollahi Moghadam, A. (2021). Cinnamon effects on blood pressure and metabolic profile: A double-blind, randomized, placebo-controlled trial in patients with stage 1 hypertension. *Avicenna journal of phytomedicine*, 11(1), 91–100.
- 14) Stevens N. (2020) Cinnamon Bark Essential Oil and a Novel Essential Oil Blend as Potential Modulators of Glucose Metabolism. Ph.D. Thesis. University of Miami; Miami, FL, USA: [(accessed on 1 December 2021)]. Available online: <https://scholarship.miami.edu/esploro/outputs/doctoral/Cinnamon-Bark-Essentialoil-and-a/991031454482202976>
- 15) Stevens, N., & Allred, K. (2022). Antidiabetic Potential of Volatile Cinnamon Oil: A Review and Exploration of Mechanisms Using In Silico Molecular Docking Simulations. *Molecules (Basel, Switzerland)*, 27(3), 853. <https://doi.org/10.3390/molecules27030853>
- 16) Zhu, R., Liu, H., Liu, C., Wang, L., Ma, R., Chen, B., Li, L., Niu, J., Fu, M., Zhang, D., & Gao, S. (2017). Cinnamaldehyde in diabetes: A review of pharmacology, pharmacokinetics and safety. *Pharmacological research*, 122, 78–89. <https://doi.org/10.1016/j.phrs.2017.05.019>
- 17) Zhou, Q., Lei, X., Fu, S., Li, Z., Chen, Y., Long, C., Li, S., & Chen, Q. (2022). Efficacy of cinnamon supplementation on glycolipid metabolism in T2DM diabetes: A meta-analysis and systematic review. *Frontiers in physiology*, 13, 960580. <https://doi.org/10.3389/fphys.2022.960580>