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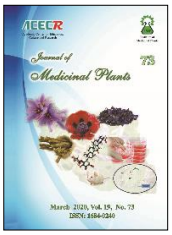

Review Article

Cinnamon inhibits platelet function and improves cardiovascular system

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Abstract

Background: Cinnamon belongs to the Lauraceae family and is one of the most common spices that are used as traditional medicine in the world. The bark and leaf of cinnamon contain essential oils and derivatives including cinnamaldehyde, cinnamic acid and several other compounds such as polyphenols. Moreover, anti-inflammatory and lipid lowering properties of cinnamon has been proven. **Objective:** The goal of this review is to find out whether cinnamon extract was used as an anticoagulant and anti-aggregation properties for the platelets or not. **Methods:** Using the search engine tools such as PubMed and Scopus, the articles that were studied cinnamon and its effects on platelets function and cardiovascular disease were under reviewed. **Results:** This article presents a comprehensive analysis of cinnamon compounds and their effects on platelet function and cardiovascular disease. **Conclusion:** Taken together, data show that cinnamon extract can inhibit platelet function and as a complementary medicine were used in cardiovascular disorder.

1. Introduction

Spices, pungent or aromatic substances, are dietary adjuncts which acquire from dried parts of plants including seeds, fruits, leaves, roots, bark and other parts of the tropical plants. They give the food a pleasant taste and smell. Early records indicate that spices were used as a medicine and food preservative in Egypt, Asia, Greece and Rome. The use of spices as medications and food flavors continued in the Middle Ages [1]. Currently, there is a high tendency to identify natural products with low side effects for prevention of diseases [2].On the other hand, diet-related factors play an important role in development of several human diseases such as cardiovascular disease [3]. Since the

Abbreviations: CA, cinnamonaldehyd; Sp, species; US, United State; AA, Arachidonic acid; PGG, Prostaglandin G; PGH, Prostaglandin H; HDL-c, High density Lipoprotein; LDL-c, Low Density Lipoprotein

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onset of human civilization, plants have become an integral part of society due to their medicinal and nutritional properties. So far, many commercial medicines have been made from herbal medicine, which includes digitoxin from *Digitalis purpurea* (foxglove) and salicin (the source of aspirin) from *Salix Alba* (willow bark) and emphasize the crucial role of plants for modern medicine production [4]. Among the spices,cinnamon is one of the most important which is used by people over the world and contains iron, manganese, fiber and calcium [5]. The genus Cinnamomum (commonly named cinnamon) belongs to the Lauraceae family and contains over 250 evergreens and shrubs that is mostly found in Asia and Australia. Cinnamon leaf and bark are used extensively as spices and sources of volatile oil [6].A number of cinnamon species include *C. cassia* (cassia or Chinese cinnamon, the most common commercial type), *C. burmannii* (Korintje, Padang cassia, or Indonesian cinnamon), *C. loureiroi* (Saigon cinnamon, Vietnamese cassia, or Vietnamese cinnamon), *C. verum* (Sri Lanka Cinnamon, Ceylon cinnamon or *C. zeylanicum*) and *C. tamale* (Indian cinnamon). Remarkably, Cinnamomum cassia is not true cinnamon but it is a very similar spice called cassia [6].

2. Methods

In this review, search engines such as PubMed and, Scopus were applied to review articles that are related to cinnamon and its effects on platelets function and cardiovascular disease.

3. Results

In this study, we first review cinnamon compounds and then evaluate the traditional uses of cinnamon, safety and its effect on the platelets. Then, in the discussion section, we evaluated the effect of cinnamon on lipids, platelets and cardiovascular diseases.

3.1. Cinnamon compounds

Cinnamon mainly contains essential oil and other derivatives, such as cinnamaldehyde, cinnamic acid, cinnamate and many other compounds such as polyphenols[7]. The chemical constituents of essential oil vary based on cinnamon species and different parts of the plants (leaf, bark and…) and include L-bornyl acetate, caryophyllene oxide, γ-eudesmol, β-caryophyllene, T-cadinol, δ-cadinene, trans-β-elemenone, cadalene, trans-cinnamaldehyde, α-pinene, camphene, β-pinene, limonene, citronellal, citronellol, citral, cinnamyl acetate, eugenol, L-borneol, caryophyllene oxide, E-nerolidol, α-cubebene, α-terpineol, terpinolene, and α-thujene (Table 1) [8-10].

3.2. Safety

Cinnamon has been used in food applications and as medicinal remedies from ancient times. It is the most frequently consumed spices and is both safe and relatively inexpensive. According to the United States Food and Drug Administration (USFDA), cinnamon spp., including common and cassia cinnamon are generally safe and well tolerated in amounts commonly found in food [14]. Cinnamon oil is also being listed and recognized as safe and is exempt from toxicity data requirements by the US Environmental Protection Agency (EPA) [14, 15].

3.3. Traditional uses of cinnamon

Cinnamon is traditionally used as a cure for cold, diarrhea, pain killer, stomach illnesses, digestive problems and also helps to eliminate bad breath [15-17]. Cinnamon extract also has antimicrobial [18-23], antifungal [24, 25] and anti-

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Table 1. Chemical constituents of volatile oil in different parts of *C. zeylanicum* [11-13]

Part of the plant	Major compounds	Amount of compounds
Leaf	Eugenol	87.3%
	Bicyclogermacrene	3.6%
	α-Phellandrene	1.9%
	β-Caryophyllene	1.9%
Bark	E-Cinnamaldhyde	97.7%
	δ-Cadinene	0.9%
	α-Copaene	0.8 %
	α-Amorphene	0.5%
Bud	*α*-Copaene	23.05%
	α-Bergamotene	27.38%
	α-Humulene	6.19%
	δ-Cadinene	5.97%
Fruit Stalk	Cinnamyl acetate	36.59%
	Caryophyllene	22.36%
	α-Humulene	5.49%
	T-Cadinol	4.90%

parasitic [26, 27] properties which can treat infection diseases. Moreover, the chemical composition of cinnamon has an anti-inflammatory [8, 10, 28, 29], anticancer and anti-oxidative [34-38] properties.

3.4. The role of platelets in cardiovascular disease

Globally, cardiovascular disease is one of the major causes of mortality [39]. Given this, ischemic heart disease is expected to be the leading cause of death by 2020 and is responsible for one out of every three deaths in the world [40, 41]. Since platelet hyperactivity is involved in arterial thrombosis and atherosclerosis, platelets play a vital role in cardiovascular disease [42]. Consequently, antiplatelet therapy is proven to reduce the risk of cardiovascular disease[43]. Antiplatelet drugs are classified based on mechanism of action on the platelets, which involve drugs that inhibit adhesion, activation, and aggregation. Aspirin, among the commonly used drugs, inhibits platelet activation [44], although, its ordinary use is associated with gastrointestinal bleeding [45]. With this in mind, there is an effort to reduce these side effects using traditional medicine such as cinnamon.

3.5. Inhibitory effect of cinnamon on platelets

Since inhibition of platelets, reduces the burden of cardiovascular disease, the use of cinnamon has been evaluated by many researchers, and there are many studies in this field. Various studies in this regard are subdivided into two categories: in vitro and invivo studies.

3.5.1. In vitro studies

Study of cinnamon components showed, eugenol, amygdala tone, cinnamic alcohol, 2-hydroxy cinnamaldehyde, 2-methoxy cinnamaldehyde, and conifer aldehyde have the most antiaggregatory effect. This group showed that some of cinnamon ingredients have mild anticoagulant effects and inhibit platelet aggregation more effectively than aspirin [46]. Other studies have also shown that eugenol can inhibit platelet aggregation induced by various agonists (especially arachidonic acid) by inhibiting thromboxane A2 (TXA2) [47, 48]. Therefore, it

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seems that the platelet aggregation is diminished indirectly by inhibiting the thromboxane A2 synthesis. Hung et al. have shown that cinhalaldehyde (CA) can inhibit in vitro platelet aggregation induced by collagen, thrombin, arachidonic acid and adenosine diphosphate (ADP) [49]. CA repress the release of arachidonic acid (AA) from platelet membrane phospholipids and then reduces thromboxane A2 production (an eicosanoid and metabolite of AA) [50]. Other in vitro studies in human platelet, rat isolated aorta and guinea-pig isolated trachea showed CA, a new lignan, isolated from *Cinnamomum philippinense*, is a novel dual thromboxane synthase inhibitor and TXA2 receptor antagonist which can restrain PRP aggregation induced by AA, collagen and U-46619 [51].

3.5.2. In vivo studies

CA markedly prolonged the hemorrhage and coagulation times in mice. Antithrombotic effects of CA were also demonstrated in mouse and rat models [49, 52, 53]. in vivo prohibition of thrombosis formation by CA may be due to inhibition of platelet aggregation and the mechanism may be associated with interaction of platelet and smooth muscle cell via platelet-derived TXA2 [50], a potent agonist for platelet activation and clot formation [54]. So TXA2 reduction by CA may contribute to reduction of platelet thrombosis. In vivo studies in mice and guinea-pigs showed CA can prolong tail bleeding time of mice and appears to be a promising approach to antithrombotic therapy [51].

4. Discussion

Traditional medicine has minimal side effects and become very popular [55] in the improvement of ischemic heart disease [56]. Among traditional medicine, cinnamon extract has anticoagulant and antiaggregation properties for the platelets. Furthermore, it would be suggested that cinnamon can reduce other risk factors associated with cardiovascular disease, such as hyperlipidemia and hyperglycemia.In this regard, it was shown that administration of cinnamon to hypercholesterolemic rats, increased HDL-cholesterol levels and decreased the concentration of triglyceride and low density lipoprotein -cholesterol (LDL-C) levels [57]. Cinnamon supplementation (1.5 g/day for 60 days) in patients with type 2 diabetes mellitus also was accompanied by increasing in high density lipoprotein-cholesterol (HDL-C) levels and reduction in triglyceride and cholesterol [58, 59].

Interestingly, control of blood glucose, improve lipid profiles [60]. In this regard, water-soluble polyphenol polymers [61] or methylehydroxychalcone polymers [62] from cinnamon potentiate insulin action [63] which can be associated with reduction in glucose and subsequently lipid levels. On the other hand, hyperlipidemia is associated with increased platelet activity following various agonists and procoagulant state. It seems that cholesterol plays critical role in activating of platelets [64, 65]. Therefore, platelets of hypercholesterolemic patients with high levels of low density lipoprotein (LDL), exhibit high aggregability and enhanced activity [66, 67]. Platelets are activated by native LDL (nLDL) through apoE Receptor [68] and Oxidized low density lipoprotein (Ox-LDL) via CD36 and scavenger receptor-A (SRA) [69, 68]. Absorption of cholesterol by the platelets is associated with increased sensitivity to epinephrine and adenosine diphosphate (ADP) [70]. On the other hand,hypercholesterolemia is associated with high mean platelet volume (MPV) and low platelet count and platelets are more susceptible to activation [71].

The cinnamon water extract also inhibits differentiation of monocytes into macrophages by

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reducing the expression of CD11b, CD36 and SRA [72], so indirectly reduces foam cells formation and ultimately limits the formation of atherosclerotic plaque. Fig. 1 demonstrates the effect of cinnamon on lipid profile and platelet function.

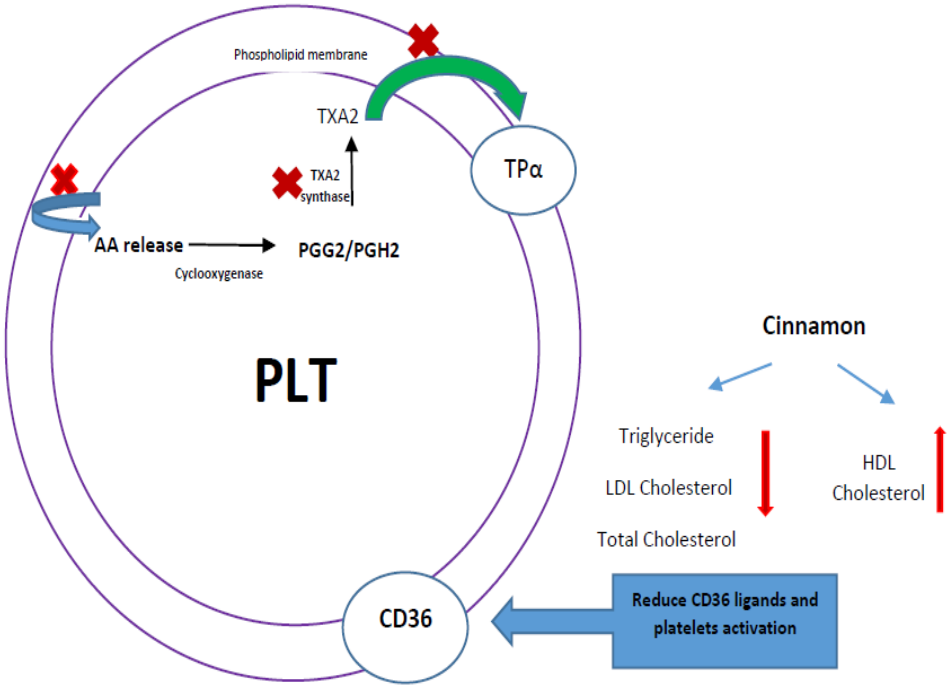

Fig. 1. Cinnamon effect on platelets and lipid profile. The antiaggregation effect of cinnamon on platelets is mediated by inhibition of arachidonic acid (AA) release from platelet membrane phospholipids and reduction of thromboxane A2 (TXA2) production. Cinnamon also decreases triglyceride, LDL cholesterol and total cholesterol and increases HDL cholesterol in serum. Since LDL and Ox-LDL are high affinity ligands for CD36 which lead to platelet activation, a reduction in LDL levels by cinnamon, decreases platelet activation.

5. Conclusion

Cinnamon, as a spice, has been used for many years to taste the foods, but also possesses great medicinal values. Several studies have shown that cinnamon could be effective and safe in treatment of serious illnesses including cardiovascular disease.

In addition to cinnamon water extract, different cinnamon compounds have inhibitory effects on platelet function and lipid levels. Since lipid lowering effect of cinnamon can ultimately lead to decreased platelet activation, it seems that, both mechanisms are ultimately associated with inhibition of platelet activation and thus are accompanied by a reduction of risk for cardiovascular disease.

Therefore, cinnamon can help prevent heart disease and reduce its symptoms. Further studies are needed to examine the effectiveness of this herbal medicine in the treatment and prevention of cardiovascular disease.

Author contributions

Concept: Mahdieh Mehrpouri, Mohsen Hamidpour

Literature Search: Mohsen Hamidpour, Rafie Hamidpour, Mahdieh Mehrpouri

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Conflict of interest

The authors declare that there is no conflict of interest.

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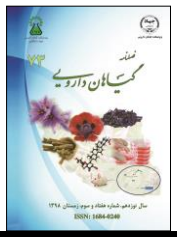

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مقاله مروری

دارچین موجب مهار عملکرد پلاکتی شده و سیستم قلبی عروقی را بهبود می‌بخشد

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اطلاعات مقاله

گل‌واژگان:
دارچین
عملکرد پلاکتی
بیماری قلبی عروقی

چکیده

مقدمه: دارچین متعلق به خانواده برگ بو می‌باشد و یکی از رایج‌ترین ادویه‌هایی است که به عنوان داروی سنتی در جهان مورد استفاده قرار می‌گیرد. پوست و برگ دارچین حاوی روغن‌های ضروری و مشتقات از جمله الدهیدی دارچین، اسید دارچین و چندین ترکیب دیگر مانند پلی‌فنول‌ها می‌باشد. عصاره دارچین یکی از پرکاربردترین داروهای سنتی است که دارای خواص ضد التهابی و کاهش دهنده چربی می باشد. **هدف:** هدف از مرور مقالات رسیدن به این نکته که آیا دارچین دارای خاصیت ضد انعقادی و ضد تجمع پلاکتی می‌باشد. **روش بررسی:** با استفاده از ابزارهای موتورهای جستجو مانند PubMed و Scopus، مقالاتی در مورد تأثیرات دارچین بر عملکرد پلاکت‌ها و بیماری‌های قلبی و عروقی مورد بررسی قرار گرفت. **نتایج:** در این مقاله، یک تجزیه و تحلیل جامع از ترکیبات دارچین و تأثیر آنها بر عملکرد پلاکت و بیماری قلبی عروقی ارائه شده است. **نتیجه‌گیری:** روی هم رفته نتایج بر گرفته از مرور مقالات نشان داد که عصاره دارچین عملکرد پلاکتی دارد و به عنوان یک دارو مکمل می‌تواند در بیماری‌های قلبی عروقی استفاده کرد.

مخففها: (CA) cinnamonaldehyd; (Sp) species; (US) United State; (AA) Arachidonic acid; (PGG) Prostaglandin G; (PGH) Prostaglandin H; (HDL-c) High density Lipoprotein; (LDL-c) Low Density Lipoprotein

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