Indian J. Agric. Res., 50 (2) 2016 : 101-106
Print ISSN:0367-8245 / Online ISSN:0976-058X

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Antithrombotic activity of turmeric (*Curcuma longa*): A review

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Received: 17-10-2015 Accepted: 30-01-2016 DOI: 10.18805/ijare.v50i2.9586

ABSTRACT

The venous and arterial thromboembolic disorders are still be the major cause of morbidity and mortality worldwide. Now a days, the concept of "healthy diets" is very popular in the present lifestyle. So, the use of antithrombotic agents is of considerable interest in the role of natural food products and their bioactive components in the prevention and treatment of these disorders. Moreover, epidemiologic studies have provided evidence that foods with the thrombolytic/fibrinolytic effect could reduce the risk of thrombosis. "Blood thinner foods" have the antiplatelet, anticoagulant, and/or fibrinolytic properties. Natural foods that contain salicylates can mimic some of the antiplatelet effects of cardiovascular drug like aspirin. Fruits (i.e., grapefruit, guava, kiwi, pineapple, and watermelon), vegetables (i.e., alfalfa, beans, corn, potato, radish, and zucchini), and spices (i.e., chili, curry, ginger, rosemary and turmeric) are reported that they are containing salicylates compounds. Turmeric (*Curcuma longa*) is a small rhizomatous perennial herb belonging to Zingiberaceae family originating from Southeastern Asia. It is a folk remedy for applying on fresh cuts to stop bleeding and for the healing of wound. Further, turmeric has been shown to possess anticancer, antidiabetic, antifertility, anti-inflammatory, antimicrobial and antioxidant properties. Its phytochemical substances are alkaloids, curcuminoids, flavonoids, glycosides, saponins, which all of these contribute to its remedial properties. This article provides a brief overview of the antithrombotic activity of turmeric, *C. longa* to further provide an up-to-date review showing its importance.

Key words: Antithrombotic activity, Blood thinner food, *Curcuma longa*, Salicylates compounds, Turmeric.

When blood vessels are teared, platelet aggregation occurs rapidly to form blood plugs or thrombi at the sites of vessel injury or in regions where blood flow is disturbed (Lee, 2006). These thrombi are the complications of many diseases such as atherosclerosis, heart attacks, stroke, and peripheral vascular disease (Prandoni, 2009). Drugs as thrombolytic agents are used to dissolve these blood clots and in the management of thrombosis in patients (Apu *et al*., 2013). These thrombolytic agents such as alteplase, anistreplase, streptokinase, tenecteplase, urokinase, and so forth, are used all over the world for the treatment (Ali *et al*., 2014), but their use is associated with bleeding risk, anaphylactic reaction and lacks specificity (Daley *et al*., 2015). There are a number of foods (plants, herbs, fruits, and vegetables) and supplements that are known to thin the blood as "Natural Blood Thinners or Blood Thinner Foods" (Sugerman, 2013). These foods may be the alternative to currently used as antiplatelet and anticoagulant agents that potentially most effective for arterial and venous clot prevention, respectively, and as fibrinolytic agent that for dissolving clots, because they constitute a rich source of bioactive chemicals as shown in Table 1 (Urrutia *et al*., 2011).

Curcuma longa

General description: *Curcuma longa* commonly known as turmeric, is used for the food applications as an active ingredient in curries and mustards (Kim *et al*., 2014) and used as food additives like coloring, flavoring substance and food preservative. Moreover, it is also one of the most extensively investigated medicinal plant species. The name turmeric originated from the Arabic name "kurkum" (Goel *et al*., 2008). In recent years, turmeric has received much attention worldwide due to its wide spectrum of pharmacological activities. The numbers of scientific literature during 2000-2015 showed 10,818; 7,703; and 95, 200 hits on "curcumin" according to the ScienceDirect, PubMed, and Google Scholar database, respectively, search on October 10, 2015. Among them are book, classical article, clinical trials, journal article, patent application and reviews. Moreover, the Panel on Food Additives and Nutrient Sources added to Food provides a scientific opinion re-evaluating the safety of curcumin. The Panel agreed with The Joint FAO/WHO Expert Committee on Food Additives that curcumin is not carcinogenic. The Panel concluded that the present database supports an ADI of 3 mg/kg bw/day (EFSA, 2010).

Taxonomical classification: The taxonomy of *C. longa* is in the Kingdom (Plantae); Subkingdom (Tracheobionta);

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Table 1: Dietary supplement category as antithrombotic properties

Antithrombotic properties	Dietary supplement category
Antiplatelet property	-Sunflower, *Gundelia tournifortii* in Jordan (Halabi *et al*., 2005) -Turmeric, *Curcuma longa* in Korea (Lee, 2006) and in India (Prakash *et al*., 2011) -Lotus, *Nelumbo nucifera* in India (Durairaj and Dorai, 2010) -Thorn tree, *Acacia leucophloea*, in Pakistan (Imran *et al*., 2012) -Bamboo, *Phyllostachys pubescens* in Korea (Jin *et al*., 2013)
Anticoagulant property	-Lime, *Citrus aurantifolia* in Nigeria (Adepoju and Adeyemi, 2010) -Horseweed, *Erigeron canadensi*, in Poland (Pawlaczyk *et al*., 2011) -Corn, *Zea mays* in Brazil (Melo-Silveira *et al*., 2012) -Horseradish, *Moringa oleifera*; Oregano, *Coleus aromaticus*; and Kamias, *Averrhoa bilimbi* in Philippines (Dayaganon *et al*., 2013) -Hwanggeumchal Sorghum, *Sorghum bicolor* in Korea (Kim *et al*., 2013) -Strawberry, *Fragaria vesca* in Poland (Pawlaczyk *et al*., 2013)
Fibrinolytic property	-Rue, *Ruta graveolens* in Iraq (Jawad Jafar, 2008) -Fern, *Drynaria quercifolia* in Bangladesh (Ramjan *et al*., 2014) -Black ebony, *Maba buxifolia* in India (Srinivasa Reddy *et al*., 2015)

Superdivision (Spermatophyta); Division (Magnoliophyta); Class (Magnoliopsida); Subclass (Zingiberidae); Order (Zingiberales); Family (Zingiberaceae); Genus (Curcuma); Species (*C. longa*) (Lal, 2012).

Nomenclature: The origin of *C. longa* is not certain, but it is thought to be originated from tropical regions like Southeast Asia, most probably from India (Deb *et al*., 2013). Nowadays, it is cultivated also in Indonesia, Thailand, China, and Japan as well as throughout the African continent. The vernacular name of *C. longa* is also known as Indian saffron, turmeric (English), kurkum (Arabic), toormerik (Armenian), halodhi (Assamese), haldi, halud (Bengali), kurkuma (Bulgarian), hsanwen (Burmese), curcuma (Catalan), wat gam (Chinese), indijski šafran (Croatian), zluty koren (Czech), gurkemeje (Danish), geelwortel (Dutch), kurkumo (Esperanto), harilik kurkuma (Estonian), zardchubeh (Farsi), keltajuuri (Finnish), curcuma long, safran des Indes (French), curcuma, Indischer safran (German), kourkoumi (Greek), halad (Gujrati), kurkum (Hebrew), haldi (Hindi), kurkuma (Hungarian), turmeric (Icelandic), kunyit (Indonesian), kunyit (Italian), tamerikku, ukon (Japanese), arishina (Kannada), romiet (Khmer), gang-hwang (Korean), khi min khun (Lao), kurkuma (Latvian), ciberzole (Lithuanian), kunyit basah (Malay), manjal (Malayalam), halad (Marathi), haldi (Nepali), gurkemeie (Norwegian), kurkuma (Polish), açafrão da Índia (Portuguese), haldi (Punjabi), curcumã (Romanian), imbir zheltyj (Russian), marmarii (Sanskrit), kurkuma (Slovak), turmérico (Spanish), gurkmeja (Swedish), manjal (Tamil), haridra (Telugu), kha min chan (Thai), gaser (Tibetan), hint safrani (Turkish), kurkuma (Ukrainian), zard chub (Urdu), botnghe (Vietnamese) (Chakraborty *et al*., 2011, Lal, 2012).

Plant description: *C. longa* is a perennial herb, grows to a height of 60-90 cm. Its leaves are very large, in tuft up to 1.2 m or more long, including the petiole which is about as long as the blade, oblong lanceolate, tapering to the base (Chakraborty *et al*., 2011). Its flowers are yellow, between 10-15 cm in length and they group together in dense spikes, which appear from the end of spring until the middle session. No fruits are known for this plant. The rhizome is yellowish-brown with a dull orange interior that looks bright yellow when powdered. Rhizome measures 2.5-7.0 cm in length, and 2.5 cm in diameter with small tuber branching off (Lal, 2012).

Phytochemical substances: The nutritional composition of 100 g of turmeric are 50 mg ascorbic acid, 6.8 g ash, 0.2 g calcium, 69.9 g carbohydrate, 8.9 g fat, 390 Kcal food energy, 47.5 g iron, 4.8 mg niacin, 260 mg phosphorus, 200 mg potassium, 8.5 g protein, 0.19 mg riboflavin, 30 mg sodium, 0.09 mg thiamine, and 6.0 g water (Lal, 2012). On the other hand, *C. longa* contains carbohydrates (69.4%), fat (5.1%), fiber (2.6%), minerals (3.5%), protein (6.3%) and moisture (13.2%) (Trinidad *et al*., 2012). Phenolic diketone, curcumin (diferuloylmethane) (3-4%) is responsible for the yellow color, and comprises curcumin I (94%), curcumin II (6%) and curcumin III (0.3%) (Yadav *et al*., 2013). The essential oil (5.8%) obtained by steam distillation of rhizomes has α-phellandrene (1%), sabinene (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpines (53%) (Yadav *et al*., 2013). Chemical constituents of *C. longa* have been extensively investigated by Li et al. (2011). They reported that at least 235 compounds, primary phenolic compounds and terpenoids have been identified from the species, including 22 diarylheptanoids and diarylpentanoids, 6 monomeric phenylpropene and 2 other phenolic compounds, 68 monoterpenes, 105 sesquiterpenes, 4 diterpenes, 3 triterpenoids, 4 steroids, 5 fatty acids, and 16 other compounds.

Traditional uses: From review of literature regarding the traditional uses or phytochemical properties of *C. longa* are shown in Table 2.

Table 2: The traditional uses or phytochemical properties of *C. longa*

Phytochemical properties	References
Anticancer activity	Basnet and Skalko-Basnet, 2012; Heger *et al*., 2014; Shanmugam *et al*., 2015; Zong *et al*., 2012
Anti-inflammatory activity	Panahi *et al*., 2015
Antimicrobial activity	Gupta et a., 2015; Kamble and Dahake Pavan, 2015
Antifungal activity	Wuthi-udomlert *et al*., 2000
Anti-lipidemia activity	Han *et al*., 2015; Li *et al*., 2010; Sahebkar 2014
Hepatoprotective activity	Adaramoye *et al*., 2010; Baxla *et al*., 2013; Kim *et al*., 2012; Kim *et al*., 2014; Salama *et al*., 2013; Sengupta *et al*., 2011; Varalakshmi and Abhinov, 2015
Gastrointestinal protective activity	Taylor and Leonard, 2011; Thong-Ngam *et al*., 2012
Neuroprotective activity	Issuriya *et al*., 2014
Cardiovascular protective activity	Sahebkar, 2015; Shin *et al*., 2014; Wongcharoen *et al*., 2012
Bone and joint protective activity	Panahi *et al*., 2014

Antiplatelet property: Drugs that inhibit platelet aggregation are called antiplatelet drugs. They include Thromboxane synthesis inhibitors like low dose aspirin, Phosphodiesterase inhibitors, Purinergic receptor antagonists, Glycoprotein IIb/IIIa receptor antagonists and other drugs like epoprostenol (Unnikrishnan and Nishteswar, 2015). Even turmeric is traditionally applied on fresh cuts to stop bleeding by the rural and tribal population of India (Shivalingu *et al*., 2015), but there is no report explaining the possible involvement of turmeric in stopping the bleeding. Earlier, Srivastava *et al*. (1995) reported the ethereal extract of turmeric inhibited arachidonate-induced platelet aggregation and showed inhibitory effects at several steps of the arachidonic acid cascade in platelets. Lee (2006) studied the antiplatelet activities of *C. longa* rhizome-derived materials using a platelet aggregometer and compared with those of aspirin as antiplatelet agent. The active constituent from the rhizome of *C. longa* was isolated and characterized as *ar*-turmerone by various spectral analyses. At 50% inhibitory concentration value, *ar*-turmerone was effective in inhibiting platelet aggregation induced by collagen and arachidonic acid. In comparison, *ar*-turmerone was significantly more potent platelet inhibitor than aspirin against platelet aggregation induced by collagen. These results suggested that *ar*-turmerone could be useful as a lead compound for inhibiting platelet aggregation induced by collagen and arachidonic acid (Lee, 2006). In additional, Mayanglambam *et al*. (2010) have shown that curcumin inhibited platelet aggregation and dense granule secretion induced by GPVI agonists through interfering with the kinase activity of Syk (spleen tyrosine kinase) and subsequent activation of PLCγ2.

Anticoagulant property: Manikandan *et al*. (2004) reported the anticoagulation activity of curcumin has shown that curcumin extends the blood clotting times as proved by prothrombin time, thrombin time and activated partial thromboplastin time analysis in comparison with the control blood sample. Moreover, Kim *et al*. (2012) also reported that curcumin and its derivative (bisdemethoxycurcumin) prolonged activated partial thromboplastin time and prothrombin time significantly and inhibited thrombin and activated factor X activities.

Fibrinogenolytic property: In recently, Shivalingu *et al*. (2015) reported the possible involvement in blood coagulation cascade with respect to procoagulant activity by reducing the human plasma clotting time from 172 s (control) to 66 s, 84 s, 88 s, 78 s, and 90 s from the dialyzed crude enzyme fractions of turmeric species *viz*., *C. aromatica*, *C. longa*, *C. caesia*, *C. amada* and *C. zedoria*, respectively. They concluded that turmeric species are rich in serine and cysteine proteases that exhibited procoagulant associated with fibrinogenolytic activity.

Clinical trial: The use of turmeric extract or turmeric oil as a spice and household remedy has been known to be safe for centuries. Joshi *et al*. (2003) revealed the safety and tolerance of turmeric through human clinical trials. Ahmad *et al*. (2011) also confirmed that curcumin even at a high dose of 1000-2000 mg/day does not produce any harmful effect on human body. Chakraborty *et al*. (2011) verified the pathogenesis of *C. longa* drug in 129 cases (59 males and 79 females). Study shows that *C. longa* can be considered as an important medicine for relieving various clinical conditions like anorexia, dyspepsia, abdominal colic, constipation, laryngitis, dry cough, dysmenorrhoea, lumbago, headache, vertigo, conjunctivitis, toothache and anxiety neurosis. Thus, curcumin has the potential for the development of modern medicine for the treatment of various disease that is reviewed and updated the potential therapeutic effect by Choudhary and Sekhon (2012).

CONCLUSION

In conclusion, plants, herbs, fruits and vegetables may serve as the best alternative sources for the development of new antithrombotic agents due to their biological activities. Recent researches were found that turmeric has essential therapeutic benefits and have the ability to protect consumers from bleeding disorders. *Curcuma longa* is the source of various chemical constituents which are used for the treatment of many fatal or life threatening diseases.

Turmeric is not only spice, it is quite help the body in numerous ways.

ACKNOWLEDGMENTS

This review article was funded in part by the Thailand Research Fund and the Commission on Higher Education: Research Grant for Mid-Career University Faculty. Thanks should be addressed to the members of the Fish Research Unit, Department of Pathobiology, Faculty of Science, Mahidol University for their support. The author also many thanks to anonymous referees and editor for their perceptive comments on, and positive criticism of this review article.

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