Antithrombotic activity of turmeric (Curcuma longa): A review

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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.

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);
**Table 1**: Dietary supplement category as antithrombotic properties

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

**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), kurkuma (Arabic), toormerik (Armenian), halodhi (Assamese), haldi, halad (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), hindi (Hindi), kurkuma (Hungarian), curmeric (Icelandic), kunyit (Indonesian), kunyit (Italian), tamerikkku, 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), curcumā (Romanian), imbir zholtyj (Russian), marmari (Sanskrit), kurkuma (Slovak), turmeric (Spanish), gurkmeja (Swedish), manjal (Tamil), haridra (Telugu), kha min chan (Thai), gaser (Tibetan), hint safari (Turkish), kurkuma (Ukrainian), zard chub (Urd), 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, curcin (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%), sabine (0.6%), cineol (1%), borneol (0.5%), zingiberene (25%) and sesquiterpenes (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.
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 diazoyl crude enzyme fractions of turmeric species viz., C. aromatic, 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, dysmenorrhea, 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 helpful the body in numerous ways.

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