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Herbal anticoagulant therapy: A Review on anticoagulant property of plants

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ABSTRACT

Herbal medicines have been used for the various diseases and disorders since ancient era. The aim of this review is to focus on the herbal remedies for anticoagulant purpose. Now a days the use of allopathic medicines is exaggerated which leads to side effects and adverse reactions of drugs. To avoid such reactions use of herbal medicine is indicated. This review explored various plants like *Thymus atlanticus*, *Selaginella*, *Terminalia bellerica*, *Tulbaghia violacea*, *Tridax procumbens*, *Porana volubilis*, *Panax notoginseng*, *Petroselinum crispum*, Green and Brown algae, Grape seed, *Gracilaria debilis*, *Ferulago carduchoram*, *Erigeron canadensis*, *Fagonia arabica*, *Codium fragile*, *Cyamopsis tetragonoloba*, *Bauhinia forficata*, *Careya arborea*, *Artemisia dracuncululus*, *Angelica shikokiana*, *Syzygium cumini*, *Melastoma malabathricum*, *Rhaponticum acaule*, *Cinnamomum cassia* showing anticoagulant activity. The data for this review is collected mainly from sciencedirect and pubmed.

KEYWORDS: Coagulation, Herbal anticoagulant therapy, Anticoagulant plants

INTRODUCTION

Thrombotic disorders such as deep vein thrombosis, pulmonary emboli, ischemic stroke, hypercoagulable states, strokes and heart attacks are the main causes of morbidity and mortality in developed countries (1). Therefore, anticoagulants play an important role for the prevention and treatment of thromboembolic disorders (2, 3). Anticoagulant drugs consisting of warfarin heparins, vitamin K antagonists, and their derivatives have been used for the treatment. Although their efficacy remains undisputed, the deleterious life-threatening side effects of these drugs have also been well documented (4, 5).

Herbal anticoagulant therapy can be used as the alternative sources for the development of new anticoagulant agents due to their biological activities (6). The use of herbal medicine provides an alternative to overcome the limitations of available anticoagulants such as warfarin and heparin which have bleeding complication, as well as uncertainty of the newer anticoagulant drugs dosing in some patient populations such as patient with underlying chronic diseases (7). This review highlights on documented plants which are used as antithrombotic or anticoagulant as mentioned in folklore medicine.

Cyamopsis tetragonoloba

Cyamopsis tetragonoloba belongs to family Fabaceae. It contains gum residues, saponins and polyphenols. Its pharmacological activity is anticoagulant and antimicrobial. Mestechkina et al reported the anticoagulant activity. Seeds contain galactomanna. It exhibited platelet aggregation ability in vitro. *C. tetragonoloba* must be avoided in patients on anticoagulant therapy because it can enhance anticoagulation potential of anticoagulant agents (8).

Pulmonaria officinalis

Pulmonaria officinalis belongs to the family Boraginaceae. It contain flavonoids, vitamin C, B-complex; minerals-iron, copper, silver, manganese and nickel. Its pharmacological activity is astringent and anticoagulant. It is also used in cough, asthma, colds, bronchial and catarrhal afflictions, inflammation, wounds, swellings, infected sores, diarrhea and hemorrhoids. Byshevskii et al. reported the anti-coagulant activity of this plant. Anti-coagulant glycopeptides is found in the ammonia extract. Anticoagulant activity was at the stage of fibrinogen conversions (9).

Cinnamomum cassia

Cinnamomum cassia belongs to the family Lauraceae. It contain coumarin, cinnamyl acetate, hydroxycinnamaldehyd, cinnamaldehyde and N-acetyl-l-cysteine. It is used as aromatic, anti-coagulant, in depression, rheumatism and muscle pains. Kim et al. reported the anti-coagulant activity. Extract has found effective in inhibition of platelet coagulation (10).

Petroselinum crispum

Petroselinum crispum belongs to the family Apiaceae. It contain flavonoids, dihydroxycoumarin, apiin, and apigenin. It is used as carminative, antioxidant, immunomodulant, antispasmodic, diuretic, emmenagogue, expectorant, antirheumatic, antimicrobial and laxative, in flatulence, dyspepsia, colic, dysuria, bronchitis, dysmenorrhoea, functional amenorrhoea and myalgia. Gadi et al. reported that aqueous extract inhibits in vitro and ex vivo platelet aggregation and prolongs bleeding time in rats. Inhibition of platelet aggregation may be due to phenolic compounds present in the extract (11).

Tridax procumbens

Tridax procumbens L. belongs to the family Asteraceae. It contain bis-bithiophene, oleonic acids, lupeol, beta-amyrenone and taraxasteryl acetate. It is used as insecticidal, anti-inflammatory, hair tonic, antiviral, anti-oxidant and antibiotic, in wounds and inflammation. A study was conducted to investigate the anticoagulant activity. Anti-coagulant activity was comparable to heparin and chondroitin sulphate (12).

Filipendula ulmaria

Filipendula ulmaria belongs to the family Rosaceae. It is used as aromatic and anti-inflammatory, in inflammation, arthritis, diarrhea, peptic ulcer, diphtheria and pneumonia. It contains flavonoids, vitamins, tannins, polyphenols, ellagitannins, phenolic acids, methyl gallate 3-O-beta-glucoside and rugosins. It contains heparin like compounds which bounds to the protein in complex form. This complex has anticoagulant and anti-fibrinolytic activity (13).

Paeonia anomala

Paeonia anomala belongs to the family Paeoniaceae. It contains acetophenone, ellagic acid, tert-butylhydroperoxide, methyl gallate, ethyl gallate, fischeroside B and quercetin derivatives. It is used as antithrombotic, thrombolytic and anticoagulant, in hepatoma and thrombosis. A study reported the anticoagulant activity of this plant. Anti-coagulant activity may be due to presence of heparin like fragments present in *P. anomala* (14).

Ferula communis

Ferula communis L. belongs to the family Apiaceae. It consists of ferulenol, fertdin, anisate, oxajaeskeanadiolyl and costic acid. It is used as antioxidant and anti-hemolytic, in cardiovascular disorders. A study reported the

anticoagulant activity of *F. communis*. Author reported that hemorrhage increases as a consequence of blood coagulation disturbance after administration of 4-hydroxycoumarins compound isolated from *F. communis* (15).

Panax notoginseng

Panax notoginseng belongs to the family Araliaceae. It consist of ginsenoside Rh4, ginsenoside Rh1, notoginsenoside S, notoginsenoside T ginsenoside Re, notoginsenoside R1 and ginsenoside Rd. It is used in bleeding, angina pectoris and memory loss. It is used as anti-hemorrhagic, antihypertensive and anti-hypercholesterolemic. Activity of *P. notoginseng* on platelet aggregation and plasma coagulation was studied. Bleeding time in rat model was found to be increased (16).

Ocimum sanctum

Ocimum sanctum, commonly known as holy basil, tulsi belongs to the family Lamiaceae. It have varieties of medicinal properties such as hypoglycaemic and hypolipidemic activity, immunomodulatory activity, antimicrobial activity, anti-ulcer activity, antioxidant activity, anti-inflammatory activity, anti-stress activity chemopreventive and radioprotective activity, anticoagulant activity, etc. Other uses may include common cold, headache, cough, influenza, earache, fever, colic pain, sore throat, bronchitis, asthma, hepatic diseases, malarial fever, as an antidote for snake bite and scorpion sting, flatulence, migraine headaches, fatigue, skin diseases, wound, insomnia, arthritis, digestive disorders, night blindness and diarrhoea (17). It consists of glycosides, alkaloids, flavonoids, steroids, saponins, tannins, etc. It also contains cirsilineol, circimaritin, apigenin, isothymusin, eugeno, eugenol, methyl eugenol, rosameric acid, carvacrol and sesquiterpine hydrocarbon caryophyllene. Two flavonoids orientin and andvicenin from aqueous leaf extract of *Ocimum sanctum* are also present (18).

Zingiber officinale

Zingiber officinale, commonly known as ginger, adrakh comes under the family Zingibaraceae. It is widely used as stomachic, aromatic, carminative, stimulant and flovouring agent, in mouth washes, ginger beverage and liquors. It works against nausea and vomiting (antiemetic) during motion sickness and seasickness. Apparently, this effect is not mediated through the central nervous system (CNS), but rather, ginger's active principles act directly on the gastrointestinal tract. It is also found that it has efficacy in motion sickness and control parasitic infection. It also has anticoagulant effect (19). It consists of carbohydrates, lipids, terpenes, phenolic compounds, amino acids, protein, phytosterols, vitamins and minerals. Terpene components of ginger include β -bisabolene, zingiberene, α -farnesene, β -sesquiphellandrene, and α -curcumene, and phenolic compounds include gingerol, paradols, and shogaol so it is also used:

- To reduce vomiting in patients treated with cytotoxic compounds.
- To promote digestion and as anti-flatulent or carminative to reduce gas and bloating.
- To improve blood circulation.
- To lower blood glucose in the treatment of diabetes.
- To treat migraine headache.
- As a sialagogue, to promote salivation (20).

Careya arborea

Careya arborea Roxb. belongs to the family Lecythidaceae is known as "Kumbhi" in Ayurveda. It contains alkaloids, terpenoids, flavonoids, saponins and tannins mainly (21). It has pharmacological activities such as analgesic, antidiarrhoeal, hepto-protective, CNS activities of the methanolic extract, antitumor, antileishmanial, antimicrobial and antioxidant activities of stem bark. The bark is used in treatment of tumors, bronchitis, astringents,

antidote to snake- venom and skin diseases (22). The methanolic bark extract shows anticoagulant activities when compared with the standard warfarin. Methanolic bark extract prolonged the time taken for blood clotting and there was a significant ($*p<0.05$) increase in the activated Partial Thromboplastin Time, Prothrombin Time and Thrombin Time (23).

Melastoma malabathricum

Melastoma malabathricum Linn. belongs to family Melastomataceae. It contains alkaloids, amides, triterpenoids, flavonoids and tannins (24). It has antidiarrhoeal (25), antibacterial, wound healing activities (26), the aqueous extract of leaves used as antinociceptive, anti-inflammatory, antipyretic (27), gastroprotective effects (28), antioxidant activity (29). The aqueous leaf extract shows potent anticoagulant property. In vitro the results showed that activated Partial Thromboplastin Time (aPTT) of plasma samples with different concentrations of the leaf extract (100-1000 $\mu\text{g/ml}$) was markedly prolonged in a concentration-dependent manner ($p<0.001$), but was otherwise for Prothrombin Time (PT) and Thrombin Time (TT). The anticoagulant activity of aqueous leaf extract affects the intrinsic pathway of the coagulation cascade by causing clotting factor(s) deficiency (30).

Gloriosa superba

Gloriosa superba Linn. commonly known as “Glory lily” belongs to family- Lilaceae. Gloriosine and colchicines are phytochemicals used for treatment of gout and rheumatism. It is used as analgesic, anti-inflammatory, antitumour, in treatment of snake bite and also used in skin diseases, respiratory disorders and in Familial Mediterranean Fever (FMF) (31). Extracts are used as antimicrobial (32) and anthelmintic activity (33). The leaves extracts shows anticoagulant properties by inhibiting thrombin induced clotting, with IC_{50} value of 2.97 mg/ml (34).

Bauhinia forficata

Bauhinia forficata belongs to family Leguminosae. It contains flavonoids, flavonols, glycosides, kaempferitrin, astragalins, β -sitosterol, organic acids, quercitrosides, rhamnose, saponins and etc. Leaves can be used for treatment of diabetes, as a diuretic for kidney and urinary disorders (including polyuria, cystitis and kidney stones), as a blood cleanser and to build blood cells, for high cholesterol. It has hypoglycemic activity (35) and antioxidant activity (236). Aqueous extract shows anticoagulant, antifibrinolytic properties (37).

Eichhornia crassipes

Eichhornia crassipes belongs to family Pontederiaceae. It consist of tannins, flavonoids, alkaloids, terpenoids, steroids, phenolic contents, anthraquinones, quinone & cardiac glycosides (38). The plant possesses anticoagulant activity due to presence of polysaccharides from the methanol extract of leaf (39).

Jatropha curcas

Jatropha curcas L. belongs to family Euphorbiaceae is commonly grown in rural areas in India. It is used for the treatment of paralysis, sciatica, dropsy, rheumatism, dysentery, diarrhoea, and certain skin diseases (40). Coagulant activity showed that whole latex significantly ($P<0.01$) reduced the clotting time of human blood. Diluted latex, prolonged the clotting time. At high dilutions, the blood did not clot at all (41).

Porana volubilis

Porana volubilis belongs to family Convolvulaceae. The plant have polysaccharide which showed the highest anticoagulant activity. The polysaccharide contains mainly galactose, galacturonic acid, and mannose (42).

Erigeron canadensis

Erigeron canadensis belongs to family Asteraceae. It consists of volatile oil (including limonene, terpineol, and linalool), flavonoids, terpenes, plant acids, and tannins. Traditionally, it is used in diarrhoea, dysentery, astringent to stop bleeding, diuretic and etc. The polyphenolic polysaccharide preparation from *Erigeron canadensis* may potentially useful in anticoagulant therapy (43).

CONCLUSION

The present review highlights anticoagulant agents which can be obtained from plants. The phytochemicals from herbal plants are found to have biological activities such as anticoagulant properties. Therefore, the use of herbal medicine provides an alternative to overcome the limitations of available anticoagulants such as warfarin and heparin which have bleeding complication, as well as uncertainty of the newer anticoagulant drugs dosing in some patient populations such as patient with underlying chronic diseases. Beside their wide spread usage traditional medicines have not been evaluated scientifically with regard to their safety and efficacy. The review explored various herbal medicines that require more exploitation up to desired level, and these report could be a better target for the development of alternatives to synthetic anticoagulant drugs.

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