Thrombolytic Property of Herbal Plants: A Short Review

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Since, ancient time medicinal plants have been using to treat various human ailments. Blood clotting causes various heart associated diseases like myocardial infarction, deep vein thrombosis and renal vein thrombosis. Thrombolytic drugs are being employed to lyse the thrombus (blood clot) formed in the arteries. The modern systems of medicines have certain limitations and serious consequences which can alter the normal hemostasis process. Herbal medicines are known for their safety and efficacy in treating diseases effectively without producing any untoward effects. The present review provides the medicinal importance of some plants as thrombolytic agents. The source for the present review was taken from literature survey carried through the findings from suitable keywords in databases, PubMed, Google Scholar and Web of Science and Scopus, etc. This review provides the detailed information on medicinal plants and phytochemical compounds as thrombolytic agents.

Keywords: Efficacy; Herbal Plants; Hemostasis; Thrombolytic Activity; Thrombosis.

Hemostasis means regulating the blood loss consequent to bleeding. It should not confuse with similar word homeostasis which means maintenance of the body’s internal environment within physiological limits. In the blood vessels, the blood normally circulates in a fluid state. But if it is drawn from the body, it thickens and forms a gel called a clot. The process is called cloting or coagulation. Natural human circulatory or blood vessel systems are presented with two contending qualification to confirm the feasibility of the entity or organism: tissue intromission must be conserve at any movement, and the bleeding must be rapidly ceased at sites of blood vessel injury. Cardiovascular illness caused by formation of thrombus is one of the most dangerous conditions which is rapidly increasing at an alarming rate in current times. Hemostasis and fibrinolysis represent the important dynamics for stopaging the free flow of blood at sites of damage or injury and reinstate blood vessel capacity or potency during process of recovery of wound or healing correspondingly. The term hemostasis or coagulation refers to the transformation of...
dispersible fibrinogen into insoluble fibrin. This technique occurs by step by step process of enhancing the enzymatic activation in which the formation of an inactive state of plasma proteins into an active protease (serine) product. Thrombin serves as the central serine protease of the coagulation cascade. Blood clot formation is a censorious step in the vascular related diseases which includes myocardial infarction, hypoxia (anoxia), hypertension, sudden heart blockage and infarction disorders that stand for a considerable number of mortality in Worldwide. Intense research activity in the antithrombotic field was devoted to compounds showing antiaggregatory potency during the last three decades of the 20th century. Among the huge number of synthetic molecules tested, only very few of them found in clinical use. Intravenous tissue plasminogen activator infusion is the fastest way to initiate thrombolytic therapy; however, poor recovery can be expected in up to 50% of patients. Tissue plasminogen activator delivery to the thrombus is dependent on the residual flow to and around the arterial obstruction when given intravenously. Though, thrombolytics which includes aspirin, warfarin, antiplatelet (Clopidogrel) and heparin have shown efficacy and are widely dispensed medications in many cardiovascular and cerebrovascular diseases, the main adverse effects of use of these medications were an increased incidence of over bleeding. The current epidemiological data stated that 11% of all diseased persons who were administered thrombolytics have presented adverse effects like hemorrhage. About 0.3-1.3% had significant adverse drug reactions like intracranial hemorrhage. These drugs are contraindicated in the present scenario in thrombolytic therapy.

To get cleanse of problems developed due to the formation of a clot in the blood or thrombus to remodify function to the affected area, fibrinolytic therapy is required. The agent which is having the thrombolytic activity also known as clot busters which shows long term benefits for survivors, who have just a 5% death rate at one year. Fibrinolytic substance is being used in blood vessels or venous thrombosis, pulmonary (lung) embolism, myocardial infarction formation of clot in the arteries (arterial thromboembolism), and acute ischemic stroke etc.

Contraindications for thrombolytic therapy

Thrombolytics were predominantly safe and effective in correcting thrombosis, but excess bleeding (hemorrhage) is the major adverse effect. The current epidemiological data stated that 11% of all diseased persons who were administered thrombolytics have presented adverse effects like hemorrhage. About 0.3-1.3% had significant adverse drug reactions like intracranial hemorrhage. These drugs are contraindicated in

Animal survallance on this earth has been made acceptable only because of the important role played by plants. Medicinal plants are the plants or their parts used for the protecting the health care of an individual as they probably contains a large number of functional groups which shows therapeutic activity against various dysfunctions of organs or tissues or systems in the body. The future of the plants as sources of medicinal agents for use in investigation, prevention, and treatment of diseases is very promising. Herbal preparations contain a wide variety of chemical constituents like tannins, salicylate, and coumarins and proved as clot lysis or thrombolytic agents. Therefore herbal preparations would be used in the place of synthetic drugs to avoid unwanted effects.
vascular lesions, severe uncontrolled hypertension, brain tumor, peptic ulcer and pregnancy.

**Methodology**

Published articles in connection with thrombolytic activity of various herbal plants were retrieved from PubMed, Science Direct, Taylor and Francis, BMC, ACS, Google scholar, Web of Science, Scopus and other literature database. Some articles were found by tracking citations from publications. The research key words used were thrombolytic activity and herbal plants. In this review briefly discussed the recent scientific findings regarding the thrombolytic activities of various herbal plants and indicated the areas where further study is required. The literature collections were restricted to publications in English language.

**Medicinal plants having thrombolytic activity**

Various studies have been reported the thrombolytic properties of plant parts and their isolated forms of few plants (Table 1). In the present review the scientific data of each reported medicinal plants were presented hereunder.

**Camellia sinensis**

*C. sinensis* belongs to the *Theaceae* family. *C. sinensis* is commonly known as green tea. The herb is resident of the Asian and Southeast region for many years. *C. sinensis* is being widely consuming in countries like India, North Africa, North East Asia and China and Pakistan. *C. sinensis* has been proved to have a wide variety of useful pharmacological and physiological actions. Leaves were used as probiotic activities. Warfarin effect is reduces in persons taking an excessive concentration of *C. sinensis* and also found hemorrhage development. *In vitro* thrombolytic potential *C. sinensis* reported that about 95.24% and 90.34% of clot lysis observed for methanolic extract and aqueous extract, respectively at 800 µg/mL concentration in dose dependent manner.

**Allium sativum**

*A. sativum* (garlic) represent the *Amaryllidaceae* family. *A. sativum* bulb is used in the conditions like hyperlipidaemia and heart related diseases. It blocks thromboxane formation and counteracts with thrombocytes functions and also reduces platelet aggregation. In addition, the plant has fewer complications like postoperative bleeding and epidural hematoma. Scientific studies, advises the avoidance of the supplements of garlic preparation with warfarin therapy, as this combination will causes serious complications. Anti-coagulant property of garlic extract was achieved by preventing or prolonging the time required for clot formation thereby alters the coagulation mechanism. Ethanolic extract at 10 µg/mL dose displayed the potential fibrinolytic activity and time factors exposure was influenced.

**Terminalia bellerica**

It belongs to the *Combretaceae* family. It is one of the compositions of well-established preparation known as “Triphala” which is being using in a wide variety of pharmacological and physiological actions in hair care, as a laxative, leucorrhoea, liver diseases and gastrointestinal

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**Fig. 1. Coagulation process**

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Damaged platelets or tissue cells secrete Thromboplastin

Prothrombin → Thrombin

Ca²⁺

Fibrinogen → Fibrin

Ca²⁺

Fibrin + Cells → Clot

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### Table 1. List of medicinal plants having active constituents responsible for thrombolytic activity

<table>
<thead>
<tr>
<th>No</th>
<th>Plant name</th>
<th>Family</th>
<th>Active constituents</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td><em>Cyamopsis tetragonoloba</em></td>
<td>Fabaceae</td>
<td>Gum residues, saponins and polyphenol</td>
<td>14</td>
</tr>
<tr>
<td>2</td>
<td><em>Pulmonaria officinalis</em></td>
<td>Boraginaceae</td>
<td>Flavonoids, vitamins like C and B, Al(^+), Mn(^+), nickel and Fe(^{2+})</td>
<td>15</td>
</tr>
<tr>
<td>3</td>
<td><em>Petroselinum crispum</em></td>
<td>Apiaceae</td>
<td>Flavonoids, dihydroxycoumarin, apiin, and apigenin</td>
<td>15</td>
</tr>
<tr>
<td>4</td>
<td><em>Tridax procumbens L.</em></td>
<td>Asteraceae</td>
<td>Taraxasterylacetate, lupeol, oleic acids.</td>
<td>15</td>
</tr>
<tr>
<td>5</td>
<td><em>Paeonia anomala</em></td>
<td>Paeoniaceae</td>
<td>Acid like ellagic, Acetophenone, (\tau)-butylhydroperoxide, methyl and ethyl gallate, quercetin, fischeroside B</td>
<td>15</td>
</tr>
<tr>
<td>6</td>
<td><em>Ferula communis L.</em></td>
<td>Apiaceae</td>
<td>Ferulol, fertdin,anisate, oxajaeskeanadiyl and costic acid</td>
<td>15</td>
</tr>
<tr>
<td>7</td>
<td><em>Panax notoginseng</em></td>
<td>Araliaceae</td>
<td>Ginsenoside Rh4, Rh1, notoginsenoside S, notoginsenoside T ginsenoside Re</td>
<td>15</td>
</tr>
<tr>
<td>8</td>
<td><em>Cinnamomum cassia</em></td>
<td>Lauraceae</td>
<td>Derivatives of coumarin, cinnamyl acetate, hydroxyl cinnamaldehyde, and (N)-acetyl-l-cysteine</td>
<td>16</td>
</tr>
<tr>
<td>9</td>
<td><em>Filipendula ulmaria</em></td>
<td>Rosaceae</td>
<td>Flavonoids, tannins and vitamins, tannins, polyphenol, ellagitannins, phenolic acids, methyl gallate</td>
<td>17</td>
</tr>
<tr>
<td>Plant name</td>
<td>Family</td>
<td>Part used</td>
<td>Functions</td>
<td>Mode of action</td>
</tr>
<tr>
<td>--------------------------</td>
<td>-------------------------</td>
<td>-----------------</td>
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<td>-----------------------------------------------------</td>
</tr>
<tr>
<td><em>Cyamopsis tetragonoloba</em></td>
<td>Fabaceae,</td>
<td>Seeds</td>
<td>Thrombolitics</td>
<td>Increases prothrombin time</td>
</tr>
<tr>
<td><em>Panax notoginseng</em></td>
<td>Araliaceae</td>
<td>Roots</td>
<td>Thrombolitics</td>
<td>Increases prothrombin time</td>
</tr>
<tr>
<td><em>Ferula communis</em></td>
<td>Apiaceae</td>
<td>Leaves</td>
<td>Thrombolitics</td>
<td>Increasing the clotting time</td>
</tr>
<tr>
<td><em>Paeonia anomala</em></td>
<td>Paeoniaceae</td>
<td>Fruits and roots</td>
<td>Anti coagulants</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Filipendula ulmaria</em></td>
<td>Rosaceae</td>
<td>Flowers</td>
<td>Thrombolitics</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Pulmonaria officinalis</em></td>
<td>Boraginaceae</td>
<td>Aerial parts</td>
<td>Thrombolitics</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Cinnamomum cassia</em></td>
<td>Lauraceae.</td>
<td>Bark</td>
<td>Thrombolitics</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Petroselinum crispum</em></td>
<td>Apiaceae</td>
<td>Aerial parts</td>
<td>Thrombolitics</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Careya arborea</em></td>
<td>Lecythidaceae</td>
<td>Bark</td>
<td>Thrombolytic</td>
<td>Prolongs the thrombin time by decreasing the clotting factors</td>
</tr>
<tr>
<td><em>Terminalia bellerica</em></td>
<td>Combretaceae</td>
<td>Fruit</td>
<td>Thrombolytic</td>
<td>Antithrombotic and thrombolytic</td>
</tr>
<tr>
<td><em>Allium cepa</em></td>
<td>Amaryllidaceae</td>
<td>Bulb</td>
<td>Thrombolytic</td>
<td>Prolongs prothrombin time</td>
</tr>
<tr>
<td><em>Moliniera recurpata</em></td>
<td>Hypoxidaceae</td>
<td>Leaves</td>
<td>Antithrombotic</td>
<td>Increases the prothrombin time</td>
</tr>
<tr>
<td><em>Curcuma longa</em></td>
<td>Zingiberaceae</td>
<td>Root and rhizome</td>
<td>Antithrombotic</td>
<td>Suppresses the ability of platelet adhesion</td>
</tr>
</tbody>
</table>
disorders. Fruits are being reported as anticoagulant and thrombolytic activity. In addition it also acts as anthelmintic, antidepressants, antianxiety and antiplasmodial activity. *In vitro* thrombolytic activity of methanolic leaf extract showed moderate amount of (32.95%) of clot lysis when compared with standard streptokinase.

**Typha angustifolia**

*Typha angustifolia* belongs to the family of Typhaceae and it is commonly known as elephant grass or cattail. Various parts of the plant are edible; including dormant sprouts on the roots and bases of the leaves, ripen pollens, the stem, and the starchy roots. The medicinal use of the plant includes treatment of renal calculi, uncontrolled bleeding in uterus, abscesses, infection with tapeworm, diarrhea, and dysentery. Modern research on pollen grains of angustifolia showed that presence of sterols, terpinoids, flavonoids and glycosides and these secondary active metabolites possess various pharmacological activities like immune suppression, antiplatelet aggregation and lipid lowering property. *In vitro* fibrinolytic activity of methanolic leaf extract showed 58±2.32 % of clot lysis.

**Zingiber officinale**

*Z. officinale* belongs to the family of Zingiberaceae. Roots used in the treatment of motion sickness disorder and rheumatism. It inhibits the thromboxane synthetase and thereby reduces the platelets aggregation. Excess intake of ginger in the diet may cause bleeding with warfarin. The methanolic extracts of *Z. officinale* showed moderate thrombolytic activity (30.13% clot lysis) at test concentration of 10 mg/mL.

**Salvia miltiorrhiza**

This *S. miltiorrhiza* belongs to the family of Lamiaceae. Rhizomes possess various pharmacological and physiological actions. It shows beneficial pharmacological uses in the various circulatory disorders. The complications are gastric cancer, bleeding and pleural hemorrhage with warfarin. Previous studies suggested that blood clotting mechanism is altered by various factors like enhancement of fibrinolytic efficacy, promotion of antithrombin III like action and inhibition of platelet aggregation. A purified extract of this plant containing its major constituents, cryptotanshinone, tanshinone I, and tanshinone IIA can protect against liver toxicity in vivo and *in vitro*. *S. Miltiorrhiza* was shown to possess unique efficacy in treating thromboangiitis obliterans.

**W edelia trilobata**

*W. trilobata* is a flowering plant belongs to the family of Asteraceae. It is used to treat hepatitis infections and to reduce the menstrual pain and unspecified female complaints. The plant has various medicinal activities, such as antidiabetic, antimicrobial, antitumor, liver protectant, and CNS depressant. The reports indicated the maximum blood clot lysis (57.89%) effects of leaf extracts of *W. trilobata*.

**Triclisia dictyophylla**

*Tr. dictyophylla* belongs to the family of Menispermaceae. The aqueous root extract of *T. dictyophylla* showed anti-platelet activity. The aqueous root extract of *T. dictyophylla* prolonged the *in vitro* whole human blood clotting time at concentrations of 50 and 100 mg/mL, complete anticoagulation effect was achieved.

**Aporosa wallichii Hook. f**

This plant belongs to Th Phyllanthaceae family. This study showed that this plant has an acceptable level of the free radical scavenging property and thrombolytic property along with cytotoxic activity. *In vitro* thrombolytic model the methanolic extract exhibited 24.5% of clot lysis at 100 µL.

**Melissa officinalis**

It is belongs to the family of Lamiaceae is a perennial aromatic herb, it is generally applied for the preparations of food and cosmetics related products. An *in vitro* thrombolytic model of methanolic extracts of leaves and stem showed 25.87±1.089, 41.482 ± 0.948 % clot lysis, respectively.

**Enhydra fluctuans**

*E. fluctuans* is a small genus of marsh herb, available in tropical and subtropical regions. Leaves of the plant are used as a laxative and also used in the treatment of the skin and nervous system. The phytochemical analysis displayed that the crude extract contains tannin, alkaloid, and saponins; it could be predicted that these phytochemicals may be responsible for its clot lysis activity. *An in vitro* thrombolytic model of methanolic extract showed 31.25% of clot lysis.
**Luffa cylindrica**

*L. cylindrica* Linn belongs to the family of Cucurbitaceae. Originally the literature report revealed the folk claims of *L. cylindrica*. The plant is having a potent thrombolytic property which is beneficial in treating heart attacks and pulmonary embolism and atherothrombosis. In an *in vitro* study the ethanolic extract showed 45% of clot lysis.

**Angelica sinensis**

*A. sinensis* is herbal plant belongs to family Apiaceae. Primarily it is used in menses in females. The plant also exhibits a fibrinolytic activity by blocking the activation and aggregation of platelets. A study on rabbits revealed that prothrombin time was increased after its consumption.

**Wedelia chinensis**

The family of *W. chinensis* (Osbeck) Merr is Asteraceae. It is also known as Chinese Wedelia and herb of sunflower. Fruits, stems and leaves possess medicinal importance. The plant leaves possess pharmacological activities in the conditions of kidney dysfunction, cold, wounds, and amenorrhea. The other medicinal uses are treatment of wounds, seminal weakness, astringent, bitter, acrid, anti-inflammatory and cardio protection and hepatitis. The methanolic leaf extract of *W.chinensis* (osbeck) Merr showed significant clot lysis 24.48% at 100 µg/mL concentration with reference to streptokinase as standard.

**Vigna unguiculata**

*V. unguiculata* Linn is a herbal plant of Fabaceae family. It possesses a wide variety of physiological and pharmacological properties. Few reports suggest that methanolic extract of *V. unguiculata* Linn (seed) showed significant thrombolytic activity with 40.33% of clot lysis at 10 mg/mL concentration.

**Punica granatum**

*P. granatum* belongs to the family of Lythraceae. Pomegranate fruits has been considered as a healing food owing to its vast advantageous biological effects against several diseases since ancient times. It is widely used in the preparation of ayurvedic blood tonic. Ethanolic and aqueous extract of fruit and peel of plant was used for *in vitro* thrombolytic activity by using streptokinase as standard. Ethanolic extract of fruit and peel showed moderate amount of *in vitro* clot lysis (59%) at 100 µg/mL concentration.

**Murraya koenigii**

It belongs to the family of Rutaceae. Leaves and roots are medicinally useful. Leaves possess promising thrombolytic property. In an *in vitro* thrombolytic model of an aqueous extract exhibited the remarkable clot lysis (22.14%) effect at a concentration of 10 mg/mL.

On extensive literature search, the reports suggest majorly the plant constituents have possessed their antithrombotic properties through prolonging the prothrombin time or by preventing the platelet aggregations. As per literature information’s few other antithrombotic plant sources with their probable mode of actions are depicted in the Table 2.
REFERENCES


