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Haemostatic Potential of Medicinal Plants and Their Phytochemicals

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Abstract: Haemorrhage associated with traumatic injury is responsible for over 35% of pre-hospital deaths and over 40% of deaths within the first 24 hours.Some important pharmacological aspects of plants such as haemostatic potential remain underexplored due to lack of scientific validation for the medical use of plant extracts/active compounds in bleeding control. In this study, an ethnobotanical survey of medicinal plants, which are used to stop bleeding, was done. Information was gathered from local herbalists, elderly people, literature search through various books and previously reported research papers in scientific databases (Pubmed, Science Direct, Scopus, Chem Spider, PubChem). Information about plants used to treat bleeding, plant parts used, mode of preparation, possible compounds and mechanism of action and dosage was collected and recorded. The collected information revealed 92 medicinal plants belonging to 59 families which are used against bleeding. Members of the Asteraceae family (12%) were the most prominent, followed by Moraceae (6%), Poaceae (5%) and Euphorbiaceae (4%). Leaves and underground plant parts were reported to be the most commonly used plant parts. The most prominent methods of herbal administration used were intravenous and as an ointment on the body surface. These plant extracts can be used efficiently and in a managed proportion to develop an effective remedy for bleeding/haemorrhages.

Keywords: Medicinal plants • Haemorrhage • Asteraceae • Natural coagulants

Introduction

Haemorrhage: Cuts and wounds are inescapable in our life. But in case of excessive/ severe bleeding (haemorrhage) at the site of injury, wounds can be life-threatening. The severity of the injury is commonly associated with the degree of overall blood loss.Low blood pressure due to blood loss can lead to immediate complications, including the multiple organ failure and life-threatening infections (Heckbert et al., 1998). After a traumatic injury, haemorrhage is responsible for over 35% of pre-hospital deaths and over 40% of deaths within the first 24 hours (Kauvar et al., 2006). Obstetric haemorrhage is the world's leading cause of maternal mortality, responsible for an estimated 127000 deaths annually (Kumar, 2016). Postpartum haemorrhage (PPH) is the most common type of obstetric haemorrhage and accounts for the majority of the 14 million cases that occur each year (WHO, 2007).

Prevention of haemorrhages and bleeding complications is possible by using agents that initiate or fasten the haemostasis process in the body. Haemostatic agents (Aprotinin, Epsilon-aminocaproic acid and Tranexamic acid, desmopressin, recombinant coagulation protein) improve haemostasis by stimulating fibrin formation, or inhibiting fibrinolysis.Unfortunately, the limited number of available drugs, the adverse effect associated and strict selection criteria for being accepted for a drug (undesirable effect of drugs on patients suffering from myocardial infarction), result in a small number of patients being eligible. Hence, there is a need for an alternative treatment that is faster, cheaper, safer, and effective.Treating haemorrhage / bleeding using medicinal plants is a common practice in many parts of the world. There are several herbs

that have been prescribed by Ayurvedic medicineto treat haemorrhage, and some of them have been used since ancient times.

Haemostasis: Haemostasis, a natural process to stop bleeding after injury, is critical for survival. Haemostasis involves a complex cascade of reactions which initiates at the site of injury as a counter response as soon as an injury is confronted by the body.

Fibrinolysis: After clotting and coagulation are complete (generally between 3–6 minutes after injury) the unneeded clot is dissolved and removed by a process called fibrinolysis.

Plants as a factory of natural medicines

Plant extracts have been a vital element of ethno medicine since ancient times (Petrovska, 2012). Knowledge about medicinal plants is documented in old written manuscripts and also orally transferred. In India, Ayurveda is a rich Hindu heritage that documents medicinal plants and their potential uses, including plants that show haemostatic activity. Plants still form a base of medicines for various diseases. Allopathic medicine can cure a wide range of diseases; however, the escalating prices and side effects (toxicity) are forcing people to incline towards the herbal medicine. The Plant-based medicines are notonly cheap but are also safehaving no side effects when used in managed proportion.

Plants are being examined and evaluated scientifically for their medicinal potency. Most of the plant extracts have been evaluated by researchers for their anti-inflammatory, antidiarrheal, analgesic, anti-cancerous, antimicrobial, antidiabetic and antihemorrhagic activities but some other important pharmacological aspects such as haemostatic potential remain underexplored. There is a need for continued exploration and examination of plants for the presence of more potent coagulants, for analysing toxicity and optimum dose to develop an efficacious remedy for bleeding and with faster action.

Ethno-Pharmacological Data Collection

All the information for this review was obtained from different books, the electronic database such as Google Scholar, PubMed, local herbalists, elderly people and from a range of publications reporting and validating the haemostatic potential of plants.

Plants with Haemostatic Potential

Details of 92 plants were obtained, which are known to exhibit haemostatic activity. Asteraceae is the most common plant family among these plants (12%). Parameters such as prothrombin time (PT), activated partial thromboplastin time (APTT), clotting time (CT), bleeding time (BT) and time of recalcification of plasma were used by researchers to evaluate the potential of these plants and validate their use as a remedy for bleeding (Table 1).

Table 1 Plants exhibiting haemostatic activity with the possible coagulants present in them

S. No.	Plant	Family	Coagulant	Parts used	References
1.	*Acacia Arabica* L.	Fabaceae	Alkaloid	Gum	Raoof et al., 2013
2.	*Acalypha australis* L.	Euphorbiaceae	Tannin	Whole plant	Li, 2002
3.	*Ageratum conyzoides* L.	Asteraceae	Tannin	Leaf	Bamidele et al., 2010
4.	*Agrimonia eupatoria* L.	Rosaceae	Tannin	Whole plant	Li, 2002
5.	*Anacardium occidentale* L.	Anacardiaceae	Tannin, alkaloid	Stem bark	Arokoyo et al., 2015
6.	*Annona senegalensis* Pers.	Annonaceae	Tannin	Leaf	Dandjesso et al., 2012
7.	*Ardisia japonica* (Hornst.) Blume	Primulaceae	Alkaloid	Whole plant	Li, 2002
8.	*Artemisia annua* L.	Asteraceae	Not reported	Whole plant	Wang et al., 2009
9.	*Artocarpus altilis (Parkinson ex. F.A. Zorn) Forsberg*	Moraceae	Protease	Latex	Singh et al., 2015
10.	*AspidiumfalcatumSw.*	Aspidiaceae	Tannin	Whole plant	Li, 2002

11.	*Biota chinensis* Hort.	Cupressaceae	Not reported	Twig	Li, 2002
12.	*Biota orientalis*L.	Cupressaceae	Not reported	Twig	Li, 2002
13.	*Bletilla hyacinthine* R.Br.	Orchidaceae	Not reported	Tuber	Li, 2002
14.	*Callicarpa macrophylla* L.	Verbenaceae	Tannin, flavone	Leaf,root	Li, 2002
15.	*Capsella bursa-pastoris* (L.) Medicus	Brassicaceae	Alkaloid	Whole plant	Li, 2002
16.	*Carduus acaulis* Thunb.	Asteraceae	Not reported	Leaf, stem	Li, 2002
17.	*Carduus crispus* L.	Asteraceae	Not reported	Leaf, stem	Li,2002
18.	*Caraduus japonicas* Franch.	Asteraceae	Not reported	Leaf,stem	Li, 2002
19.	*Carica papaya* L.	Caricaceae	Tannin, alkaloid	Leaf	Patil et al., 2013
20.	*Cassia absus*Linn	Caesalpiniaceae	Not reported	Seed	Varier, 2010
21.	*Cassytha filiformis*	Lauraceae	Alkaloid, tannin	Aerial part	Dandjesso et al., 2012
22.	*Cephalanoplossegtum*	Asteraceae	Alkaloid	Aerial part	Li, 2002
23.	*Chromolaena odorata*	Asteraceae	Not reported	Leaf	Pandith et al., 2012
24.	*Cissampelos mucronate*	Menispermaceae	Alkaloid, tannin	Aerial part	Dandjesso et al., 2012
25.	*Cissus quadrangularis* Linn.	Vitaceae	Not reported	Whole plant	Varier, 2010
26.	*Citrus medica* Linn.	Rutaceae	Not reported	Fruit	Varier, 2010
27.	*ClinopodiumChinense*(Benth.)	Lamiaceae	Not reported	Whole plant	Li, 2002
28.	*Cornusflorida*L.	Cornaceae	Tannin	-	Li, 2002
29.	*Cotyledon fimbriatum* Turcz	Crassulaceae	Not reported	Whole plant	Li, 2002
30.	*Curcuma longa* Linn.	Zingiberaceae	Not reported	Rhizome	Varier, 2010
31.	*Cynodondactylon*(Linn.) Pers.	Poaceae	Not reported	Whole plant	Varier, 2010
32.	*Daemonoropsdraco*Blume.	Arecaceae	Not reported	Fruits	Li, 2002
33.	*Dioscoreacirrhosa*L.	Dioscoreaceae	Tannin	Tuber	Li, 2002
34.	*Dioscoreahispida*Dennst.	Dioscoreaceae	Tannin	Tuber	Li, 2002
35.	*Dipsacus asper*	Caprifoliaceae	Dipsacus saponin C	Whole plant	Song et al.,2012
36.	*Eclipta alba* Hassk.	Asteraceae	Alkaloid	Aerial part	Li, 2002
37.	*Ecliptaerecta*L.	Asteraceae	Tannin, nicotine	Aerial Part	Li, 2002
38.	*Ficus hispida*Linn.f.	Moraceae	Not reported	Fruit	Varier, 2010
39.	*Ficus microcarpa*Linn.f.	Moraceae	Not reported	Bark,leaf	Varier, 2010
40.	*Ficus palmata*Forsk.	Moraceae	Not reported	Latex	Bhatt et al.,2010
41.	*Ficus religiosa* Linn.	Moraceae	Not reported	Latex	Varier, 2010
42.	*Gardenia augusta*(L.)Merrill.	Rubiaceae	Not reported	Fruit,flower,bark	Li, 2002
43.	*Gardenia jasminoides*Ellis	Rubiaceae	Not reported	Fruit, flower,bark	Li, 2002
44.	*Hippophaërhamnoides* L.	Elaeagnaceae	Not reported	Fruit	Bal et al., 2011
45.	*Houttuynia cordata* Thunb.	Saururaceae	Not reported	Aerial part	Li, 2002
46.	*Imperataarundinacea*Cyrill.	Poaceae	Not reported	Root	Li, 2002
47.	*Imperata cylindrica* L.Beauv.	Poaceae	Not reported	Root	Li, 2002
48.	*Iris lacteal* Pall. subsp. chinensis(Fisch.)Kitag	Iridaceae	Not reported	Seed,flower, leaf,root	Li, 2002
49.	*Jatropha curcas*L.	Euphorbiaceae	Alkaloid, tannin	Leaf	Azikiwe et al., 2014
50.	*Jatropha gossypifolia*L.	Euphorbiaceae	Alkaloid, tannins	Stem latex	Odula et al., 2005
51.	*Jatropha multifida*	Euphorbiaceae	Not reported	Plant sap	Dougnon et al., 2012
52.	*Loropetalumchinense*(R.Br.) D.Oliver	Hamamelidaceae	Flavones	Whole plant	Li, 2002

53.	*Luffa aegyptiaca* Mill.	Cucurbitaceae	Vitamin A, B, C	Fruit, fiber	Li, 2002
54.	*Luffa cylindrical* L.Roem.	Cucurbitaceae	Not reported	-	Li, 2002
55.	*Mentha asiatica*	Lamiaceae	Not reported	Root	Eisenman, 2013
56.	*Musa sapientum*	Musaceae	Alkaloid, tannin	Plant sap	Klotoé et al., 2012
57.	*Newbouldialaevis*Seem.	Bignoniaceae	Tannin	Leaf	Dandjesso et al., 2012
58.	*Ophioglossumvulgatum*L.	Ophioglossaceae	Not reported	Whole plant	Li, 2002.
59.	*Polygonum bistorta* L.	Polygonaceae	Not reported	Stem, root	Li, 2002
60.	*Psidium guajava* L.	Myrtaceae	Not reported	Leaf	Jadhav et al., 2013
61.	*Pyrola decorata*H. Andres	Ericaceae	Not reported	Whole plant	Li, 2002
62.	*Pyrola rotundifolia* L.	Ericaceae	Not reported	Whole plant	Li, 2002
63.	*Quercus pubescens*Willd.	Fagaceae	Not reported	Fruit	Jadhav et al., 2013
64.	*Rheum officinale* Baill.	Polygonaceae	Not reported	Rhizome	Li, 2002
65.	*Rubia chinensis* Regel &Maack	Rubiaceae	Not reported	Root	Li, 2002
66.	*Rubia cordifolia* Thumb.	Rubiaceae	Not reported	Root	Li, 2002
67.	*Saccharum officinarum* Linn.	Poaceae	Not reported	Stem	Varier, 2010
68.	*Santalum album* Linn	Santalaceae	Not reported	Heartwood	Varier, 2010
69.	*Sedum aizoon*L.	Crassulaceae	Not reported	Whole plant	Li, 2002
70.	*Streblus asper* Lour.	Moraceae	Not reported	Root	Varier, 2010
71.	*Symplocoscochinchinensis*(Lour.) Moore ssp. laurina(Retz.)Nooteboom	Symplocaceae	Not reported	Bark	Varier, 2010
72.	*Syzygiumjanbos*(Linn) Alston	Myrtaceae	Not reported	Bark	Varier, 2010
73.	*Tabernaemontanadivaricata* (L.) R. Br. ex. Roem. and Schult.	Apocynaceae	Protease	Latex	Singh et al.,2015
74.	*Tagetes erecta*L.	Asteraceae	Not reported	Leaf	Dasgupta et al., 2014
75.	*Tectona grandis* Linn.f.	Verbenaceae	Not reported	Leaf	Varier, 2010
76.	*Terminalia bellirica*(Gaertn.) Roxb.	Combretaceae	Not reported	Fruit	Varier, 2010
77.	*Terminalia chebula*Retz.	Combretaceae	Not reported	Fruit	Jadhav et al., 2013
78.	*Thespesia populnea*(Linn)Soland ex Correa	Malvaceae	Not reported	Whole plant	Varier ,2010
79.	*Thevetia peruviana* (Pers.) K. Schum.	Apocynaceae	Not reported	Latex	Jadhav et al., 2013
80.	*Thymus vulgaris* L.	Lamiaceae	Alkaloid	Leaf	Raoof et al., 2013
81.	*TrachycarpuswagnerianusBeccari*	Arecaceae	Tannin	Seed	Li, 2002
82.	*Trapa natans*Linn.var.bispinosa (Roxb.) Makino	Trapaceae	Not reported	Fruit	Varier, 2010
83.	*Tribulus terrestris*Linn.	Zygophyllaceae	Not reported	Seed	Varier, 2010
84.	*Tridax procumbens* Linn	Asteraceae	Not reported	Leaf	Kale et al., 2008, Trivedi, 2009
85.	*Vetiveriazizanioides*(linn.) Nash	Poaceae	Not reported	Root	Varier, 2010

86.	*Vigna radiata* (Linn) Wilczek var. sublobata (Roxb.) Verdc.	Fabaceae	Not reported	Root	Varier, 2010
87.	*Vitex negundo* Linn.	Verbenaceae	Not reported	Flower	Varier, 2010
88.	*Vitis vinifera* Linn.	Vitaceae	Not reported	Fruit	Varier, 2010
89.	*Woodfordia fruticose (*Linn) Kurz	Lythraceae	Not reported	Flower	Varier, 2010
90.	*Zanthoxylum rhetsa*(Roxb.) DC.	Rutaceae	Not reported	Fruit	Jadhav et al., 2013
91.	*Zingiber officinale* Roscoe	Zingiberaceae	Alkaloid	Rhizome	Jadhav et al., 2013
92.	*Ziziphus mauritiana*Lam.	Rhamnaceae	Not reported	Fruit	Varier, 2010

As it is evident from the Table 1, Li (2002) and Varier (2010) documented most of the plants exhibiting haemostatic activity. But there is no valid in vitro and in vivo scientific study that evaluates their haemostatic activity.

Studies on the haemostatic activity of plant extracts

a. In vitro:

Odula et al. (2005) studied the coagulating and anti-coagulating activity of *Jatropha gossypifolia*and found that latex from the stem of plant reduces blood clotting time. This procoagulant activity was assumed as a result of precipitation of clotting factors. The activity was evaluated on the basis of bleeding Time (BT) and (clotting time) CT. But active compounds and proper dosage were unidentified. Kale et al. (2008) reported haemostatic activity of the ethanolic extract of the fresh juice of leaves of *Tridaxprocumbens*. The activity was evaluated by determining CT. In the succeeding year, Wang et al. (2011) and Edemeka and Ogwu, (2009) screened the fraction of *Artemisia annua* L. and *Ocimumgratissimum*respectively in vitro by plasma recalcification time. The haemostatic active extracts of *A. annua* plants shortened the clotting time. Aqueous and methanol extract of *O. gratissimum* significantly shortened the APTT of normal and factor VII-deficient plasma samples. Its coagulating constituents were unidentified.

Dougnon et al. (2012)reported that theaddition of the sap of *Musa sapientum* in the whole blood induced a reduction of CT**.** The effect was not dose-dependent. It's mechanism of action was explained by vasoconstriction and cell aggregation (mediated by tannin). Phytochemical analysis revealed the presence of alkaloids, tannins, coumarins, reducing compounds, anthocyanins and leuco-anthocyanins. *M.sapientum*is very common in the South – Benin (West Africa) as a treatment of bleeding. This plant is also used in India and Brazil for haemostasis. Phytochemistry and in vitro haemostatic properties of some medicinal plants sold as anti-hemorrhagic in Benin were studied by Dandjesso et al. (2012). *Annona senegalensis* (Leaves), *Newbouldialaevis* (Leaves), *Cassythafiliformis*(Aerial part), *Cissampelosmucronata* (Aerial part) are the four species of medicinal plants commonly sold by herbalists in South Benin for the treatment of bleeding. Hydro alcoholic extracts of these plants reduced plasma re-calcification time and validated their coagulant properties. The coagulation activity is related to the presence of tannin in these plant extracts. The phytochemical study of these plants revealed that *C. mucronata* contains alkaloids and tannins; *A. senegalensis* contains tannins, mucilages and reducing compounds; *C. filiformis* contains alkaloids, tannins and *N. laevis* contains tannins, triterpenoids, mucilages and reducing compounds.

Jadhav et al. (2013) screened ten Indian herbs for haemostatic activity in vitro. Of the ten plants evaluated, aqueous extracts of *Quercus pubescens, Thevetia peruviana* proved to have significant haemostatic activity, whereas alcoholic extracts of *Zingiber officinale, Zanthoxylumrhetsa*and petroleum ether extracts of *Psidumguajava*,

Terminalia chebula, *Zanthoxylumrhetsa* confirmed the haemostatic activity.

Blood coagulation activity of the marigold leaf extract was reported by Dasgupta et al. (2014). Activity was evaluated on the basis of PT. Leaf extract showed very good blood coagulation properties in the microlitre range. However, the active compounds were not identified. In the same year, Badgujar (2014) evaluated the haemostatic activity of latex from three plants belonging Euphorbiaceae family. These were *Euphorbia nivulia* Buch. -Ham., *Pedilanthustithymaloides*(L.) Poit and *Synadeniumgrantii* Hook F. The activity was assessed by the determination of bleeding/clotting time test of the fresh experimentally-induced wound in mice. In vitro studies were also done on the blood sample of human, goat, buffalo and ox by detecting the procoagulant activity of latex of these plants. *E. nivulia* latex showed the best blood clotting activity followed by *P. tithymaloides* and *S. grantii.* The haemostatic activity was reported due to the presence of the protease in the latex. In another study, Singh et al. (2015) estimated the proteolytic activity of crude extract of plants *Tabernaemontanadivaricata* (L.) R. Br. ex. Roem. and Schult. and *Artocarpusaltilis* (Parkinson ex. F.A. Zorn) Forsberg and found that crude enzymes from both plants exhibited coagulant activity on human platelet poor plasma. A significant reduction in clotting time was exhibited by *T. divaricata* compared to *A. altilis*.Ohkuraet al. (2015) screened for the haemostatic activity of popular Chinese medicinal herbs and concluded that extracts of Alpinia Rhizome, Areca, Artemisia Leaf, Cassia Bark, Danshen Root, Ephedra Herb, Epimedium Herb, Forsythia Fruit, Great Burdock Achene, Moutan Bark, Perilla Herb, Red Paeony Root, Schizonepeta Spike, Senticosus Rhizome, Sweet Annie, Uncaria Thorn and Zanthoxylum Peel shorten the coagulation time of blood.

b. In vivo: Geranium (*Pelargonium zonale*) has been traditionally used as a local haemostatic medicine in some Andean region. Paez and Hernandez (2003) studied its haemostatic effect using bleeding rat model and found that leaf juice of *P. zonale* shortened the bleeding time by 50% as compared to control group. They also proved that haemostatic agent gelatin sponge showed the similar effect as geranium juice. Ankaferd Blood Stopper®, which has been approved in the management of external haemorrhage and dental surgery bleedings in Turkey, comprises a standardized mixture of plants viz. *Thymus vulgaris, Glycyrrhiza glabra, Vitis vinifera, Alpinia officinarum and Urtica dioica.*Cipilet al. (2009) reported in vivo haemostatic effect of the medicinal plant extract Ankaferd Blood Stopper® in rats pretreated with warfarin.Bamidele et al. (2010) reported haemostatic activity of methanolic leaf extract of *Ageratum conyzoides* by determining BT, PT, CT in albino rats and the activity was due to the possible interaction of extract with both intrinsic and extrinsic pathways. Bal et al. (2011) described that fruits of *Hippophaėrhamnoides* L. have haemostatic effects.

Dougnon et al. (2012)studied the haemostatic potential of the sap of *Jatropha multifida* in wistar rats and found a significant reduction in bleeding time. The phytochemical screening showed the presence of tannins, flavonoids, saponins, leucoanthocyanes, mucilage and reducing compounds in the sap of *J. multifida*. The haemostatic power of the sap was explained by the strong presence of tannins and flavonoids. In vivo and in vitro haemostatic activity of *Chromolaena odorata* leaf extract was investigated by Pandith et al. (2012). In vitro haemostatic mechanisms were tested using platelet aggregation and blood coagulation tests in sheep plasma. Ethanol extract from the dried leaves decreased the bleeding time in vivo. Song et al. (2012) discovered that *Dipsacus asper*, known to have analgesic and anti-inflammatory effects, potently induced procoagulant activities in platelets. Dipsacus saponin C (DSC) was identified as a key active ingredient in plant induced procoagulant activities. Extracts of *Zingiber officinale* Roscoe, *Thymus vulgaris* L. *and Acacia arabica* L. was found to contain a higher percentage of alkaloids and was effective in coagulation as it decreased both BT and CT and increased platelets, RBC, WBC and

calcium count (Raoof et al., 2013). The study was done on lab mice. *Carica papaya* leaf extract was found to increase the platelet count and also to decrease the clotting time in thrombocytopenic rats as reported by Patilet al. (2013). Aqueous extract of *C. papaya* leaves at a concentration of 400mg/kg and 800mg/kg was given to cyclophosphamide-induced thrombocytopenic rats for a period of fifteen days. Blood was withdrawn at the various time intervals to determine the platelet count. Azikiweet al. (2014) carried out some in-vivo and in-vitro haemostatic studies of the leaf extracts of *Jatropha curcas* in rats and scientifically demonstrated its possible coagulant activity. The phytochemistry and acute toxicity testing were done. Acute toxicity level was 28.28mg/kg (IP). Phytochemistry revealed the presence of alkaloids, resin, oils, saponins, flavonoids, tannins and glycosides. Blood clotting time was shortened by both aqueous and ethanolic extract. The possible mechanism of action of the extract was described by the enhancement of carboxylation of trans-carboxylic acid (glutamate) residue, mimicking that of vitamin K or aggregation of platelets. Recently, Arokoyoet al. (2015) reported that methanolic stem bark extract of *Anacardium occidentale* L. possesses haemostatic activity as it significantly decreased BT, PT, CT and APTT in the albino rat in a dose-dependent manner and increased platelet count. The anti-hemorrhagic activity of the leaf extract of *Sidacorymbosa* was evaluated in Wistar albino rats by John-Africa and Aboh, 2015. The haemostatic activities of the extract were investigated using the tail bleeding time and amount of bleeding in rats. Phytochemical screening confirmed the presence of tannins, saponins, alkaloids, flavonoids, carbohydrates, terpenes and sterols.

Plant-based coagulants and mechanism of action

Various coagulants or coagulation inducing agent that are reported to be present in plant extracts are:

i. Concanavalin A and other legume lectins (phytohaemagglutinin): Concanavalin A is a lectin originally extracted from jack bean. It directly agglutinates erythrocytes irrespective of blood groups. Concanavalin A interacts with different receptors (made up of structures like sugars, glycoproteins, glycolipids), including blood group markers.

ii. Alkaloids: Alkaloids are a class of naturally occurring organic nitrogen-containing bases. They are found primarily in plants and fungus. Alkaloids are derived from various amino acids such as ornithine, lysine, phenylalanine etc. About 5,500 alkaloids are known and they comprise the largest single class of secondary plant substances (Raoof et al., 2013). Some well-known alkaloids are: Nicotine, caffeine, morphine, colchicine, ergots, strychnine, quinine, reserpine.

Ergonovine (from fungus *Claviceps purpurea*) is used to reduce uterine haemorrhage after childbirth.

iii. Phenols:

Tannins, also called Tannic acid, have been reported to accelerate blood clotting. Tannins are known as an astringent agent. Astringent activity favors vasoconstriction, which is the initial step in haemostasis (Dougnonet al., 2012). Phenolic compounds of high molecular weight, containing hydroxyls and other suitable groups, form effectively strong complexes with macromolecules like protein and precipitate proteins (Ashok and Upadhyaya, 2012). Tannins follow the same mechanism in coagulating blood. Tannins are known to precipitate the clotting factors, thus helping in haemostasis (Dougnon et al., 2012). Their phenolic hydroxyl groups form strong hydrogen bonds with the protein (Crozier et al., 2009) rendering insoluble proteins that increase blood viscosity and slow down the movement of red blood cells. Thus, facilitates their aggregation. Increased aggregation produced locally in each capillary will instantly interrupt blood flow (Mchedlishvili et al., 2002).

iv. Vitamins (A, B, C): They are reported to be involved in the early synthesis of collagen fibers (Kumarasamyrajaet al., 2012). Collagen is one of the major activators of the platelet response after injury. Collagen is the only matrix protein which supports both platelet adhesion and complete activation. When collagen becomes exposed to flowing blood, platelets rapidly adhere, spread,

become activated and begin to form an aggregate (Farndale et al., 2004).

Conclusion

Nature has provided a large variety and number of plants which contain biologically active and important compounds that show impressive blood coagulating activity. This review is an attempt to explore the haemostatic activity of such plants through documented and undocumented resources. The main obstacle to the development of an effective medicine for bleeding from these plant extracts is the lack of knowledge about their in-vivo activity, mechanism of action, toxicity and possible coagulants (compounds). There is a need for continuous exploration and evaluation of plants for the presence of more potent coagulants, for analysing toxicity and optimum dose to develop an efficacious remedy for bleeding and with faster action. The plant list documented in this review may prove valuable in the trend of plant medicine development for bleeding / haemorrhages.

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References

Arokoyo DS, Bamidele O, Babatunde LD, Adebisi O (2015). Hemostatic effect of methanolic stem bark extract of *Anacardium occidentale* L. in male albino rats. *J Med. Medic Sci.*, 6:58-65.

Ashok PK, Upadhyaya K (2012). Tannins are Astringent. *J Pharma. Phytochem.* 1:45-50.

Azikiwe CCA, Ifezulike CC, Amazu LU, Nwabali MO (2014). Hemostatic effect of *Jatropha curcas* (Linn) in rats. *Drug Discovery*. 8:16-20.

Badgujar SB (2014). Evaluation of hemostatic activity of latex from three Euphorbiaceae species.*J Ethnopharmacol*. 151:733-739.

Bal LM, Medab V, Naika SN, Satya S (2011). Sea buckthorn berries: A potential source of valuable nutrients for nutraceuticals and cosmoceuticals. *FOOD RES INT*. 44:1718-1727.

Bamidele O, Akinnuga AM, Anyakudo MMC, Ojo OA, Ojo GB, Olorunfemi,JO, Johnson OP (2010). Hemostatic effect of methanolic leaf extract of *Ageratum conyzoides* in albino rats.*J. Med. Plants Res*. 4:2075-2079.

Bhatt A, Baunthiyal M., Pandey, A., Dangwal, H, Singh, A.K., 2010. Ethnobotanical uses of plants for curing diseases and ailments by people of Pauri Garhwal. *J. Mountain Res*. 5:129-139.

Cipil HS, Kosar A, Kaya, A, Uz B, Haznedaroglu IC, Goker H, Ozdemir O, Koroglu M, Kirazil S, Firat HC (2009). In vivo hemostatic effect of the medicinal plant extract Ankaferd Blood Stopper in rats pretreated with warfarin. *Clin Appl Thromb Hemost* 15:270-276.

Crozier A, Jaganath IB, Clifford MN, Dietary phenolics: chemistry, bioavailability and effects on health. *Nat. Prod. Rep*. 26:1001-1043.

Dandjesso C, Klotoé JR, Dougnon TV, Sègbo J, Atègbo JM, Gbaguidi F, Fah L, Fanou B, Loko F, Dramane K (2012). Phytochemistry and hemostatic properties of some medicinal plants sold as anti-hemorrhagic in Cotonou markets (Benin). *Indian J Sci Technol*. 5:3105-3109.

Dasgupta N, Ranjan S, Saleh MA Arabi Mohammed, Jadon PS, Melvin SS, Harris AD, Chakraborty AR, Ramalingama C (2014). Extraction based blood coagulation activity of marigold leaf: Acomparative study.*Comp Clin Path*. 23:1715-1718.

Dougnon TV, Klotoé JB, Sègbo J, Atègbo JM, Edorh,AP, Fernand G, Hounkpatin AS, Dandjesso C, Fah L, Fanou B, Dramane K, Loko F (2012). Evaluation of the phytochemical and hemostatic potential of *Jatropha multifida* sap.*Afr. J. Pharm. Pharmacol*. 6:1943-1948.

Edemeka DBU, Ogwu AS (2009). Blood coagulation activities of leaf extracts of *Ocimumgratissimum* plant in man. *J Herbs Spices Med Plants*. 7:9-14.

Eisenman SW, Zaurov DE, Struwe L (2013). *Medicinal Plants of Central Asia*: Uzbekistan and Kyrgyzstan. Heidelberg Dordrecht London New York. Springer.

Farndale RW, Sixma JJ, Barnes MJ, de Groot PG (2004). The role of collagen in thrombosis and haemostasis. *J ThrombHaemost*. 2:561–73.

Heckbert SR, Vedder NB, Hoffman W, Winn RK, Hudson LD, Jurkovich GJ, Copass MK, Harlan JM, Rice CL, Maier RV (1998). Outcome after hemorrhagic shock in trauma patients. *J Trauma*. 45:545-549.

Jadhav S., Kulkarni C, Salunkhe S, Deshpande A, Bhise S (2013). Screening of Indian herbs for hemostatic activity. *J drug delivTher*. 3:81-85.

John-Africa LB, Aboh M (2015). Evaluation of the Hemostatic Activities of *Sidacorymbosa* in Rats. *Br J Pharm Res*. 5:431-436.

Kale MA, Shahi SR, Somani VG, Shamkuwar PB, Dhake AS (2008). Hemostatic activity of the leaves of *Tridaxprocumbens* Linn. *Int J Green Pharm*. 2:54-55.

Kauvar DS, Lefering R, Wade CE (2006). Impact of hemorrhage on trauma outcome: an overview of epidemiology, clinical presentations, and therapeutic considerations. *J Trauma*. 60: S3-11.

Kumar N (2016). Postpartum hemorrhage; a major killer of woman: review of current scenario. ObstetGynecol Int J. 4(4):00116.

Kumarasamyraja D, Jeganathan NS, Manavalan R (2012). A review on medicinal plants with potential wound healing activity. *Int J Pharma Sci.* 2:105-111.

Li TSC (2002). *Chinese and Related North American Herbs*: Phytopharmacology and Therapeutic values. Boca Raton London New York Washington D.C.:CRC Press.

McHedlishvili G, Varazashvili M, Gobejishvili L (2002). Local RBC aggregation disturbing blood fluidity and causing statis in microvessels. *Clin HemorheolMicrocirc*. 26:99-106.

Oduola T, Adeosun GO, Oduola TA, Avwioro GO, Oyeniyi AM (2005). Mechanism of action of *Jatropha gossypifolia* stem latex as a hemostatic agent. *Eur J Gen Med*. 2:140-143.

Ohkura N, Yokouchi H, Mimura M, Nakamura R, Atsumi GI (2015). Screening for hemostatic activities of popular Chinese medicinal herbs in vitro. *J intercultethnopharmacol*. 4:19-23.

Paez X, Hernandez L (2003). Topical hemostatic effect of a common ornamental plant, the geraniaceae Pelargonium zonale. *J CLIN PHARMACOL*. 43:291-295.

Pandith H, Thongpraditchote S, Wongkrajang Y, Gritsanapan W (2012). In vivo and in vitro hemostatic activity of Chromolaenaodorata leaf extract. *Pharm Biol.* 50:1073-1077.

Patil S, Shetty S, Bhide R, Narayanan S (2013). Evaluation of platelet augmentation activity of *Carica papaya* leaf aqueous extract in rats. *J PharmacognPhytochem*. 1:57-60.

Petrovska BB (2012). Historical review of medicinal plants'usage. *Pharmacogn Rev*. 6:1-5.

Raoof AW, Zahraa Abdul-Elah Al-Naqqash, Abdul-Latif M jawad, Salah M Mushan(2013). Evaluation of the activity of crude alkaloids extracts of *Zingiber officinale* Roscoe, *Thymus vulgaris* L. And *Acacia Arabica* L. as coagulant agent in lab mice. *J Biomed Biotechnol*. 1:11-16.

Singh MK, Usha R, Hithayshree KR, Bindhu OS (2015). Hemostatic potential of latex proteases from Tabernaemontanadivaricata (L.) R. Br. ex. Roem. and Schult. and Artocarpusaltilis (Parkinson ex. F.A. Zorn) Forsberg. *J Thromb Thrombolysis*. 39:43-49.

Song JS, Lim KM, Kang S, Noh JY, Kim K, Bae ON, Chung JH (2012). Procoagulant and prothrombotic effects of the herbal medicine, *Dipsacus asper* and its active ingredient, dipsacus saponin C, on human platelets. *J ThrombHaemost*. 10:895-906.

Trivedi PC (2009). *Medicinal Plants Utilization and Conservation*. 2nd ed. Jaipur, India: Aaviskar Publishers

Varier PS (2010). *IndianMedicinal Plants; a compendium of 500 species*. Volume 2,3,4-5. Kottakal: Orient Longman, Universities Press.

Wang B, Sui J, Yu Z, Zhu L (2011). Screening the hemostatic active fraction of *Artemisia annua* L. in-vitro. *IranJ Pharm Res*. 10:57-62

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