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# A Comprehensive Review of Currently Researched Medicinal Herbs with Anticoagulant Potential

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***Abstract***—*Various herbal preparations have been used since ancient times to solve clotting problems. It is considered more affordable to target the side effects of synthetic coagulants, relying mainly on herbal medicines. According to the World Health Organization (WHO), 80 percent of the world's population depends on primary health care. Important pharmacological effects have been observed when using herbal medicines. This article provides an updated and comprehensive review of plants and phytoconstituents known to have antiplatelet and anticoagulant effects. The review presents various bioactive compounds and secondary metabolites, such as alkaloids, tannins, saponins, glycosides, flavonoids, coumarins, sesquiterpenes and polyphenols, which are said to be responsible for antiplatelet and antithrombotic effects. The purpose of this study is to document the effects of natural anticoagulants. Analysis of selected literature showed that many plants contain bioactive compounds with antiplatelet and anticoagulant effects. These herbal ingredients act against factors that play an important role in thrombosis by disrupting primary and secondary hemostasis. The potential of herbal ingredients to fight various diseases suggests the need for further research. Referenced articles were retrieved from Google Scholar, PubMed, ScienceDirect and Elsevier, focusing on articles published in English-language journals. Together, this study highlights the importance of new phytoconstituents to minimize the adverse effects of current anticoagulants*.

***Keywords***— *Thromboembolism; flavonoids; medicinal plants; phytoconstituents*.

## I. Introduction

Thrombosis is the formation of blood clots in the veins, causing deep vein thrombosis and pathological diseases of the blood vessels and heart. If a blood clot forms in an artery, it can lead to myocardial infarction, gangrene, or limb stroke [1]. According to a report by the WHO Program on Traditional Medicine (2002), about 17.3 million people died of coronary heart disease in 2008 due to thrombotic diseases such as cardiovascular disease, and an estimated 23.6 million people worldwide by 2030. the population may die. affects CAD [2]. According to the National Health and Nutrition Examination Survey (NHANES) 2013-2016. About 18.2 million people in their 20s have coronary heart disease in the United States, and men are at greater risk than women [3]. Pandemic anticoagulants for COVID-19 play an important role in anti-thrombotic complications caused by excessive blood clotting. This condition, also known as coagulopathy, has been associated with COVID-19 [4].

## II. Occurance Of Thromboemabolism

Thromboemabolism offenly occurs in organs i.e. (Myocardial infraction) and in contrast. Kidney, intestinal and eyes in this organ arterial thromboemabolism is occurs [5].

Complications include pulmonary embolism, deep venous thrombosis (DVP) in the veins, and systemic arterial embolism in the arteries.

Acute pulmonary embolism made 81% of complications observed (n=25) [6].

*Thrombosis:*

Thrombosis is characterized by events that essentially involve activation of platelets, and conversion of soluble fibrinogen into insoluble polymerised fibrin.

*Arterial Thrombi:*

Example of major formed in the arteries are under

1. Arteries of limbs: atherosclerosis, diabetes mellitus, buerger's disease, Raynaud's disease
2. Aorta: aneurysm, arteritis.
3. Coronary arteries: atherosclerosis
4. Cerebral artery: atherosclerosis vasculitis
5. Mesenteric artery: atherosclerosis, arteritis
6. Renal artery

*Venous Thrombosis:*

1. Veins of lower limbs: deep veins of legs, various veins.
2. Renal vein: amyloidosis.
3. Pulmonary vein: CHF, pulmonary hypertension.
4. Hepatic and portal vein: portal hypertension.
5. Superior vena cava: infection in head and neck.
6. Inferior vena cava: extension of thrombus from hepatic vein.
7. Mesenteric vein volvulus, intestinal obstruction.
8. Popliteal, femoral and iliac veins: postoperative stage, postpartum [7].

## III. Current Treatment Strategies And It's Limitations

Anticoagulating agent play a crucial role as a antithrombosis i.e. In thrombotic disorders such as peripheral arterial disease, cardiovascular disease.

Predominantly it includes various classes, such as anticoagulant, antithrombic, fibrinolytic, antiplatelets they decrease the forming clots or prevent clot formation.

The most obvious complication of these drugs is bleeding. They have higher risk of gastrointestinal bleeding. Protamine sulfate has some disadvantages due to its adverse allergic reactions.

A study in a243 patients who underwent cardiac surgery. In which 26 patients shows unfavorable reactions [8].

## IV. Antithrombic effects of phytoconstituents

According to the World Health Organization, herbal medicines are an alternative to synthetic drugs used by about



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80% of the world's population. From an ancient time humans are depend on medicinal plant to maintain their health. Phytochemicals are widely found in herbs, shrubs, vegetables, fruits, seeds, etc. Recent study is clearing that to prevent the thrombosis by synthetic drug are showing adverse effect but to avoid the adverse effects recently several studies is demonstrating the anticoagulating, antiplatelet, antithrombic, fibrinolytic activities of phytoconstituents such as coumarin, alkaloids, flavonoids, anthraquinone, naphthalene, stilbenes, xanthos.

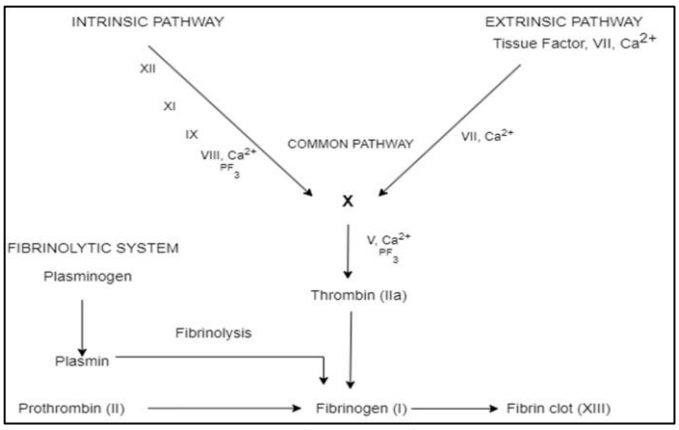


Fig. 1 Schematic representation of pathways of Coagulation Mechanism and Fibrinolytic System

Researchers are studying plant sources through reverse pharmacology to understand the therapeutic effects and effectiveness of secondary metabolites proposed in the World Health Organization's Traditional Medicine Strategy 2014-2023. In line with WHO traditional medicine strategy 200-2005[8,9,10].

## V. Mechanism of Blood Coagulation

Hemostasis is the mechanism that led to cessation of bleeding from a vessel. In this process multiple interdependent Paths. It prevent and stop bleeding homeostasis two interconnection can elaborate in primary and secondary hemostasis[11].

- Primary hemostasis: Primary hemostasis show effect by adhering, activating, and aggregating. To prevent blood loss from injured vascular endothelium [12].
- Secondary hemostasis: Secondary hemostasis involved the activating of plasmatic coagulation protein, and it leading to the positive and negative feedback mechanism. Extrinsic and intrinsic or contact pathway which is play crucial role in formation of clot by covalent stabilized fibrin network [12].

## VI. Pathways To Understanding The Antithrombotic Effects Of Natural Compounds From Plant Sources

Since ancient time human civilization depends on the natural resources of medicine. Humans are depend on the source directly or indirectly. Herbal anticoagulant have the potential to treat various communicable and non-communicable disease [13]. This has proven to be the case in the presence of a variety of natural chemicals, including natural medicinal actives, fenolix, flavonoids, polyeshooks, proteins, peptides, peptides, talepen, alkaloids, and more. Credits the presence of various bioactive compounds. The other. Multiple evidence is shown that the plant-generated bioactive compound gradually became the first treatment choice for creating a bioactive compound gradually and the first treatment selection for the thrombus-induced cardiovascular and cerebrovascular disease [14]. Pharmacologically active constituent in the plant existing anticoagulant effect by acting various site of coagulation casket. The casket is compose by various factors like intrinsic, extrinsic, common pathway, vascular endothelial, fibrinolytic system platelets etc. [15]. The secondary metabolites of plants i.e. Phenolic or polyphenolic compounds are distributed in overall plants. These aromatic structure have substitution on various positions of hydroxyl group. That phenolic group classification are include Flavonoids, tannins, stilbenes, lignans, phenolic acids etc. That compound are widely distributed in medicinal plants and eventually responsible for the pharmacological activity.

Flavonoids are comes under an extensive group of phenolic compounds fifteen carbon atoms in three consecutive rings (C6-C3-C6) label respectively A, B and C. Based on the chalcone, flavan, anthocyanin and proanthocyanidin C-ring substituents and degree of saturation, flavonoids can be divided into different groups, including flavones, flavonols, dihydrochalcones, isoflavones, auronans, flavans ketones, flavanones [16].

The terpenes or isoprenoids presenting to large group of essential oils which consist of isoprene Molecules where each molecule contains five carbon atoms with double bonds. Based on the amount of isoprene Molecules, terpenes can be classified as monoterpenes (2 Isoprene molecules), sesquiterpenes (3 isoprene molecules) and Diterpenes (4 isoprene molecules) [17]. The alkaloids are derived from of amino acids and tertiary nitrogen atom is present in the basic moiety with heterocyclic ring but it having exception like caffeine, paclitaxel, colchicine. Alkaloids are classified on the basic of skeletal ring tropane alkaloids, indole alkaloids, isoquinoline alkaloids, pyrazolidine alkaloids. Multiple Studies have shown that alkaloids isolated from medicinal plants Showed antiplatelet activity in various experiments models [18]. Substances that prevent the formation of blood clots work Through multiple mechanisms including platelet inhibition Aggregation and formation of blood clots (antiplatelet agents), Inhibit and disrupt the coagulation system expansion of plaques (antagonists). Natural phenols, including polyphenols and flavonoids Effectiveness as preventive and alternative medicine Cardiovascular complications caused by blood clots. They have been reported to have antiplatelet and antithrombotic effects oxidative stress reduce [19]. Decrease intracellular Ca2+ mobilization, inhibit platelet phospholipase C, ameliorate intraplatelet cyclic adenosine monophosphate (cAMP) level [20].

Dual roles of quercetin in platelets: Phosphoinositide-3-kinase and MAP kinases inhibition, and cAMP-dependent vasodilator-stimulated phosphoprotein stimulation [21]. Antagonise TXA2 receptor [22] Flavonoids inhibit platelet function through binding to the thromboxane A2 receptor. [23]



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and antagonize thrombin receptor [24]. Apigenin inhibits platelet adhesion and thrombus formation and synergizes with aspirin in the suppression of the arachidonic acid pathway [25].

TABLE 1. Phytochemicals, Mechanism action of herbal source

| Botanical Name | Family | Parts used | Effect/activity | Phytochemicals | Mechanism of Action | References |
|---|---|---|---|---|---|---|
| Angelica keiskei (Miq.) Koidz | Apiaceae | Stem | Antithrombotic-anti-coagulant | Xanthoangelol B | Inhibit platelet aggregation | [26] |
| Angelica keiskei (Miq.) Koidz | Apiaceae | Aerial Parts | Anti-coagulant, antiplatelet | Z-Ligustilide | Inhibit platelet aggregation | [27] |
| Abelmoschus manihot (L.) Medik | Malvaceae | Plant | Antiplatelet | Total flavone | Inhibit platelet aggregation | [28] |
| Andrographis paniculata (Burm.f.) Nees | Acanthaceae | Plant | Antiplatelet | Diterpenoids | Inhibit platelet aggregation | [29] |
| Anemarrhena asphodeloides Bunge | Liliaceae | Rhizomes | Antiplatelet; antithrombotic | Timosaponin A-III, timosaponin B-II, anemarsaponin B | Inhibit ADP-induced platelet aggregation | [30] |
| Apium graveolens Linn | Apiaceae | Seeds | Antithrombotic, antiplatelet | 3-N-Butylphthalide (NBP)l-3-nbutylphthalide (NBP) | Inhibit platelet aggregation | [31] |
| Achyranthes bidentatata Blume | Amaranthaceae | Plant | Anticoagulant | Polysaccharides | Inhibit platelet aggregation | [32] |
| Allium sativum L. | Liliaceae | Cloves | Antiplatelet | Allicin, adenosine,parafnic polysulfdes | Prolonged coagulation time | [33] |
| Aesculus hippocastanum L | Sapindaceae | Bark | Anticoagulant | Aescin (coumarin) | Preventing oxidative damage of fibrinogen | [34] |
| Berberis vulgaris L. | Berberidaceae | Plant | Antiplatelet | Berberine | Inhibit platelet aggregation | [35] |
| Campomanesia xanthocarpa (Mart.) O.Berg | Myrtaceae | Leaf | Antithrombotic, antiplatelet | Flavonoids | Inhibit platelet aggregation | [36] |
| Cyperus rotundus L. | Cyperaceae | Tuber | Antiplatelet | (+)-nootkatone(sesquiterpenoid) | Inhibit collagen-, thrombin | [37] |
| Cornus mas L | Cornaceae | Dried fruits | Anticoagulant | Anthocyanins, polyphenols | Inhibit platelet aggregation | [38] |
| Cassytha fliformis L. | Lauraceae | Fresh herb | Antiplatelet | Aporphinoid alkaloids | Inhibit platelet aggregation | [39] |
| Curcuma aromatica Salisb. | Zingiberaceae | Rhizome | Antiplatelet | Curcumin | Inhibit AA-, collagen-, & ADP-induced platelet aggregation | [40] |
| Chrysanthemum indicum L | Asteraceae | Antiplatelet | Antiplatelet | Chlorogenic acid | Inhibit platelet aggregation | [41] |
| Cinnamomum cassia Nees. | Lauraceae | Bark and twigs | Antiplatelet | Eugenol, amygdalactone, cinnamic alcohol, 2-hydroxycinnamaldehyde, 2-methoxycinnamaldehyde, coniferaldehyde | Inhibit platelet aggregation | [42] |
| Citrus hassaku Yu.Tanaka | Rutaceae | Fruits | Antiplatelet | Prunin | Inhibit platelet aggregation | [43] |
| Coptis chinensis Franch. | Ranunculaceae | Rhizome | Antiplatelet | Berberine | Inhibited thromboxane synthesis | [44] |
| Carthamus tinctorius L. | Compositae | Plant | Antithrombotic | Hydroxysafor yellow A | Inhibited thromboxane synthesis | [45] |
| Cnidoscolus aconitifolius (Mill.) | Euphorbiaceae | Leaf | Anticoagulant | Kaempferol-3- o-glucorhamnoside and 15(S)-HPETE | Juan Pablo Quintal Martínez | [46] |
| Caesalpinia sappan L | Leguminosae | Heartwood | Antiplatelet | Brazilin | Inhibited collagen-induced platelet aggregation | [47] |
| Curcuma longa L. | Zingiberaceae | Rhizome | Antiplatelet, anticoagulant, antithrombotic | Ar-turmerone, curcumin | Inhibited platelet aggregation | [48] |
| Cudrania tricuspidata Bureau | Moraceae | Roots | Antiplatelet | Cudratricusxanthone A (CTXA) | Inhibit platelet aggregation | [49] |
| Cubeb | Piperaceae | Fruit | Anticoagulant | Kaempferol-3- o-glucorhamnoside and 15(S)-HPETE | Inhibit platelet aggregation | [50] |
| Callicarpa nudifora Hook. & Arn | Lamiaceae | Leaves | Antiplatelet | Triterpenoids | Inhibit platelet aggregation | [51] |
| Centella asiatica L. (Urb) | Apiaceae | Herb | Antiplatelet | Cafeoyl quinic acid compounds | Inhibition of platelet activation and coagulation | [52] |

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|---|---|---|---|---|---|---|
| Dalbergia odorifera T. Chen | Fabaceae (Leguminosae) | Heartwood | Antiplatelet | Sesquiterpenes | Inhibit platelet aggregation | [53] |
| Dioscorea zingiberensis C.H. Wright | Dioscoreaceae | Rhizome | Antithrombotic, anticoagulant, antiplatelet | Dioscin-steroidal saponins | Antithrombotic | [54] |
| Diospyros kaki Thunb | Ebenaceae | Leaves, fruits | Anticoagulant, antithrombotic | Diosmin (diosmetin 7-O-rutino-side),a disaccharide derivative | Inhibited thrombin-catalysed fibrin formation | [55] |
| Euphorbia neriifolia L. | Euphorbiaceae | Roots, leaves | Antithrombotic | Flavonoids, polyphenols | Prolonged bleeding time & clotting time | [56] |
| Evodia rutaecarpa A.Juss | Rutaceae | Dried unripened fruit | Antiplatelet | Rutaecarpine | Prolonged bleeding time, antiplatelet aggregation | [57] |
| Erigeron canadensis L. | Asteraceae | Whole plant | Anticoagulant, antiplatelet | Polyphenolic polysaccharide | Inhibited thrombin | [58] |
| Ficus religiosa L | Mulberry | Stem bud | Antiplatelet | Phenylmalonic acid | Inhibit platelet aggregation | [59] |
| Ginkgo biloba L | Ginkgoaceae | Leaf | Antiplatelet activity | Ginkgolides A, B, and C | Antithrombotic | [60] |
| Glycyrrhiza uralensis | Leguminosae | Rhizome | Antithrombotic | Isotrifoliol | Inhibit platelet aggregation | [61] |
| Galbulimima baccata F.M.Bailey | Himantandraceae | Bark | Antithrombotic | Galbulimima alkaloids-himbacine | Antiplatelet aggregation | [62] |
| Houttuynia cordata | Saururaceae | Plant | Antiplatelet | Alkaloids | Antiplatelet aggregation | [63] |
| Hernandia nymphaefolia J.Presl | Hernandiaceae | Trunk bark | Antiplatelet | Aporphine compounds | Antiplatelet aggregation | [64] |
| Illigera luzonensis Merr | Hernandiaceae | Roots | Antiplatelet | Aporphine alkaloids | Inhibits fibrinogen & platelet aggregation | [65] |
| Ilex paraguariensis A.St. | Aquifoliaceae | Fruits | Antithrombotic, antiplatelet | Chikusetsusaponin IVa | Antiplatelet aggregation | [66] |
| Leonurus | Lamiaceae sibiricus | Aerial parts | Antiplatelet | Leonurine | Antiplatelet aggregation | [67] |
| Lonicera japonica Thunb. | Caprifoliacea | Plant | Antiplatelet | Protocatechuic acid | Inhibit aggregation of red blood cells | [68] |
| Lycopus lucidus Turcz. | Lamiaceaeae | Plant | antiplatelet | - | Inhibit thrombosis | [69] |
| Liriope muscari L.H.Bailey. | Asparagaceae | Plant | Anti-thrombotic | D39, a natural saponin | Inhibit thrombosis | [70] |
| Lindera obtusiloba Blume | Lauraceae | Leaf | Antiplatelet, antithrombotic | quercitrin and afzelin | Inhibit platelet aggregation & collagen-induced thromboxane | [71] |
| Melicope semecarpifolia Merr. | Rutaceae | Root, bark | Antiplatelet | quinoline alkaloids, | Antiplatelet aggregation | [72] |
| Moringa oleifera | Moringaceae | leaf | anti-coagulant | Cc extract of morigna | Prolonged bleeding time & clotting time | [73] |
| Magnolia officinalis | Moringaceae | Leaf | Antiplatelet | Extract of moringa oleifera | Antiplatelet aggregation | [74] |
| Nelumbo nucifera Gaertn. | Nelumbonaceae | fruits ;whole plant | anti-coagulant; antithrombotic | neferine, alkaloid; flavonoids in hydroalcoholic extract respectively | Inhibitory effect on platelet activation, adhesion & aggregation | [75] |
| Origanum majorana L. | Lamiaceae | plant | Antiplatelet | hydroquinone-D-glucopyrano-side (Coumarin ) | Inhibition of platelet adhesion & aggregation | [76] |
| Osmanthus fragrans Lour. | Oleaceae | seeds | Antiplatelet | secoiridoid glucoside | Inhibit platelet aggregation | [77] |
| Panax ginseng Meyer | Araliaceae | root | Antiplatelet | Ginsenoside Rg1, Ginsenoside Rg3, Ginsenoside Rp4.Ginse-noside Ro (an oleanane-type saponin | Antiplatelet aggregation | [78] |
| Piper longum L. | Piperaceae | Dried fruits | Antiplatelet | piperlongumine,a pyridone alkaloid | Inhibit AA-, collagen-, & PAF-induced platelet aggregation | [79] |
| Polygonum Amplexicaule Radix | Polygonaceae | Leaf rhizome | Antithrombic | 11-O-galloylbergenin | Antiplatelet aggregation | [80] |
| Paeonia suffruticosa | Paeoniaceae | dried root bark | Antiplatelet | - | Inhibit platelet aggregation & blood coagulation | [81] |



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|---|---|---|---|---|---|---|
| Paeonia lactiflora Pall. | Paeoniaceae | plant | antiplatelet and anti-coagulant | Paeoniflorin, Benzoylpaeoniflorin, Benzoyloxypaeoniflorin, Methyl gallate. | Inhibit platelet aggregation & blood coagulation | [82] |
| Rollinia mucosa Jacq. | Annonaceae | stems | antiplatelet | N-methoxycarbonyl aporphine alkaloids,romucosine A (1), romucosine B (2), romucosine C (3), andromucosine D (4 | Inhibit platelet aggregation & prolonged aPTT | [83] |
| Ruta graveolens L. | Rutacaeae | root and aerial parts | antiplatelet | The quinoline alkaloid graveo-linine | Inhibit platelet aggregation | [84] |
| Rhus verniciflua (Syn.Toxicoden-dron vernicifluum) | Anacardiaceae | herb | antiplatelet | Isomaltol, Pentagalloyl glucose | Inhibition of platelet-activating factor | [85] |
| Rheum palmatum L. | Polygonaceae | aerial parts | antiplatelet | Two stilbenes- trans-resveratrol- 3-O-β-d-glucopyranosid (I) and rhaponticin (II) | Antiplatelet aggregation | [86] |
| Rehmannia glutinosa (Gaertn.) | Scrophulariac eae | dried roots | antiplatelet | furan derivatives | Antiplatelet aggregation | [87] |
| Spiraea japonica L. | Rosaceae | roots | antiplatelet | atisine-type diterpenoid alkaloids | Antiplatelet aggregation | [88] |
| Scutellaria baicalensis Georgi. | Lamiaceae | root | anti-platelet, anticoagulant | Baicalin | Antiplatelet aggregation | [89] |
| Spatholobus suberectus Dunn. | Leguminosae | stem | antiplatelet | daidzein and genistein | Antiplatelet aggregation | [90] |
| Sophora japonica L. | Fabaceae | plant | antiplatelet | flavonoids | Inhibited fibrin polymerization and platelet | [91] |
| Salvia prattii | Lamiaceae antiplatelet | Flower | Antiplatelet, antithrombotic | Cc 11,12-seco-abietane diterpenes | Antiplatelet aggregation | [92] |
| Selaginella tamariscina (P. Beauv.) Spring | Selaginellacea e | herb | anti-coagulant | dihydrocaffeic acid & amentof-lavone | Inhibition of fibrinogen binding | [93] |
| Sparganium stoloniferum Buch. | Typhaceae | plant | antiplatelet, antithrombotic | flavonoids | Antiplatelet aggregation | [94] |
| Salvia miltiorrhiza | Labiateae | Root | antiplatelet | 15,16-dihydrotanshinone I, Tanshinone I, Tanshinone IIA | Inhibit platelet aggregation | [95] |
| Sapindus mukorossi Gaertn. | Sapindaceae | Galls | antiplatelet | Sapinmusaponins F-J; Sapinmu- saponins Q and R (1–50 µM) respectively | Antiplatelet aggregation | [96] |
| Silybum marianum (L.) Gaertn. | Asteraceae | Seeds,fruits | antiplatelet activity | Silymarin( flavonolignans) | Antiplatelet aggregation | [97] |
| Spiraea japonica L. | Rosaceae | roots | antiplatelet | spiramine C1 | Antiplatelet aggregation | [98] |
| Viola yedoensis Makino | Violaceae | whole plants | anticoagulant | dicoumarins: dimeresculetin, euphorbetin, esculetin | Prolonged aPTT, PT | [99] |
| Veratrum dahuricum (Turcz.) O.Loes. | Melanthiaceae | rhizomes | antiplatelet | Veratroylgermine-steroidal alkaloid | Inhibit AA-induced platelet aggregation | [100] |
| Zingiber officinale Roscoe | Zingiberaceae | rhizome | antiplatelet | Gingerol, paradol | Antiplatelet aggregation | [101] |

## VII. Conclusion

Potential benefits of herbal medicines for clotting problems, emphasizing their advantage over synthetic coagulants due to reduced side effects. It highlights the importance of herbal medicines, mechanism of action, focusing on their anti-platelet and anti-coagulant effects. The review covers a wide range of bioactive compounds found in various plants and shows their potential to prevent thrombosis and hemostasis. Overall, the goal is to document the effects of natural anticoagulants and provide a comprehensive overview of the field. This review may be beneficial for further study perspective.

## Abbreviations

WHO: World Health Organization; CAD: Coronary Artery Disease; NHANES: National Health and Nutrition Examination Survey; COVID 19: Corona Virus Disease 2019; DVP: Deep Vein Thrombosis; CHF: Congestive Heart Failure; cAMP: Cyclic Adenosine Monophosphate; TXA2: Thromboxane A2.

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