

## MEDICINAL PLANTS WITH ANTITHROMBOTIC PROPERTY IN MAINTAINING HUMAN HEALTH (MINI REVIEW)

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Hypercoagulability can be the result of hemostasis imbalance, leading to incorrect blood clot and Thrombosis. Thromboembolic manifestations in vital organs such as brain, heart, lung and liver can be overwhelming and even may lead to death. Hence, appropriate therapeutic approaches play a critical role for the prevention and treatment of abnormal blood clots such as pulmonary emboli, deep vein thrombosis, strokes and heart attacks [1, 24]. Anticoagulants are chemical compounds that target different coagulation cascade, interacting with formation of coagulation factors [4]. Although anticoagulant drugs such as heparin and vitamin K antagonists for more than five decades have been developed and known as accepted treatment, they are mostly accompanied by life-threatening side effects. For instance, hemorrhage is the most important side effect of heparins, warfarin, Factor X inhibitors, direct thrombin inhibitors (DTIs) and fibrinolytics [13]. Therefore, discovery of safer, cheaper and more available herbal anticoagulants with less toxicity and fewer side effects is a research interest. The role of medicinal plants as a compatible source of phytochemicals with anticoagulant properties has been well documented [16]. Importance of phytochemicals derived from plants in modern medicine has been discussed in various investigations. According to chemical structure there are some well-known phytochemicals such as alkaloids, tannins, saponins, phenolics, terpenoids, steroids, cardiac glycosides, flavonoids, coumarins, lignans, xanthenes and anthraquinones. These phytochemicals possess different pharmacological activities, representing cardioprotective property, anti-inflammatory, immunomodulatory, antibiotic, anti-helminthic, cytoprotective, hepatoprotective,

antidiabetic and antioxidant activity, reducing the risk of developing certain types of cancer [14]. Alikhani Pour et al. (2017) using cheminformatics methods and based on *in vitro* coagulation tests such as prothrombin time (PT) and activated partial thromboplastin time (aPTT) listed some anticoagulant compounds and plants with anticoagulant bioactivity. Plants *Terminalia bellirica* Roxb. that contains tannins, *Origanum vulgare* L. including Caryophyllene, Spathulenol, Germacrene,  $\alpha$ -Caryophyllene and Astragalusarbusculinus (with non-available major chemical compounds) showed significant changes in aPTT and anticoagulant effect, although they didn't exhibit any notable effect on PT. Moreover, Dioscin, Resveratrol, Konjacglucmannan, Ginkgolide B, Cedrol, Polycarpol, Quercitrin, Ajoene and Tanshinone IIA are some registered anticoagulant compounds of plant origin [1, 2].

*Crassocephalum crepidioides* Benth S. Moore is a wide spread medicinal plant in many tropical and subtropical areas [4, 5, 18]. Both hexan (non-polar) and methanol (polar) fractions of *C. crepidioides* leaf extract significantly increase PT and PTT and concentration-dependent clotting time of healthy human blood samples. Hexane fraction of *C. crepidioides* leaf extract contains various biological active substances including Benzofuranone, Benzofuran (coumarin-related compounds), Thujone, Eugenol and 9,12,15-Octadecatrienoic acid ( $\alpha$ -linolenic acid) represent Antiplatelet aggregation property, inhibiting thrombus formation [4].

Hyperaggregability of platelets in pathological conditions may lead to formation of thrombus, increasing the risk of myocardial infarction and stroke [19]. Essential oils are one of the bioactive products obtained from raw plant material, which main-

ly contain low molecular terpenes (monoterpenes, sesquiterpenes). The potential of essential oils and their compounds in the management of cardiovascular diseases targeting major related risk factors has been reported. Several studies assessed hypotensive and vasorelaxant effects of essential oils through different mechanism [9, 3, 10]. Also, anti-diabetic and Anti-Dyslipidemic essential Oils have been demonstrated in different researches [25, 15]. Alves-Silva and co-authors (2021) collected some *in vitro* results about essential oil antiplatelet aggregation capacity. *Artemisia dracuncululus* L. contains Estragole which in a dose dependent manner inhibits platelet aggregation [22, 3]. *Foeniculum vulgare* Mill. contains trans-anethole and estragole which prevent adenosinediphosphate (ADP), arachidonic acid (AA) and 4 $\beta$ -phorbol-12-myristate-13-acetate (PMA) induced platelet aggregation. Geraniol, Linalool, Carvacrol, thymol and p-Cymene are major essential oil of plants *Monarda didyma* L., *Ocimum basilicum* L., *Origanum vulgare* L. and *Thymus vulgaris* L. which decrease arachidonic acid induced platelet aggregation in Guinea pig and rat plasma [23, 3]. Moreover, a few *in vivo* studies in thromboembolism animal models have evaluated the capability of some extracts to decrease paralysis events preventing death [23, 6, 11].

Numerous investigations suggest a potential antithrombotic role for flavonoids. Flavonoids are compounds with antioxidant property. Antiaggregatory effect of polyphenols-flavonoids in prevention of thrombus formation has been of interest. It is obvious that activity of flavonoids is highly related to their chemical structure and lipophilicity. Also, both aglycone and flavonoid glycoside structure inhibit platelet aggregation. Flavonoids inhibit *in vitro* ADP-induced platelet aggregation by stabilizing platelet membrane that leads to decrease in the number of receptors [8]. Interestingly, Bojić and group (2012) for the first time reported proaggregatory activity of flavonoids that is correlated to antioxidant effect of flavonoids, stimulating chemical modification of prostaglandin (PG) G<sub>2</sub> to PG H<sub>2</sub>.

The last is additionally converted to thromboxane A<sub>2</sub> (by thromboxane A<sub>2</sub> synthase), causing platelet aggregation [7]. It is notable that antiplatelet aggregatory effect of ingested flavonoid quercetin and its metabolites have been documented by Stainer et al. (2019); therefore, quercetin supplementation may prevent thrombus formation and contribute to protective effects against cardiovascular disease [20]. Mira and co-authors (2017) suggest that quercetin and kaempferol may cause prolongation of PT, aPTT and thrombin time (TT) by inhibiting thrombin and coagulation factor X. Also these flavonoids suppress ADP and AA induced platelet aggregation [17].

Ginkgolide B is one of the ginkgolides have been extracted from leaves and root bark of the Chinese tree *Ginkgo biloba*, was known the most potent ginkgolide to be specific and selective antagonist of platelet activating factor (PAF) by competitively combining PAF receptors, presenting valuable effects on different PAF-related diseases [26]. Also, Ge et al. (2014) overviewed herb-warfarin interaction, highlighting clinical findings and corresponding mechanisms of interactions. Ginkgo was identified to cause severe interaction with warfarin [12].

It is noteworthy that according to Taki and colleagues (2012) *Ginkgo biloba* extract (GBE) affects warfarin anticoagulation via herb-drug interaction. They suggested that GBE and ginkgolide B don't cause blood coagulation *in vivo*, and GBE diminishes the anticoagulation action of warfarin through induction of hepatic cytochromes (CYPs) by bilobalide [21].

The findings from these studies testify that plants contain bioactive substances which hold anticoagulant activity with great capability in the development of novel anticoagulant drugs for prevention and treatment of cardiovascular diseases in one hand. On the other hand, patients should be aware of synergistic effect of simultaneously using these medicinal plants and chemical anticoagulant. Although more *in vivo* verification and clinical trials seems necessary.

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## MEDICINAL PLANTS WITH ANTITHROMBOTIC PROPERTY IN MAINTAINING HUMAN HEALTH (MINI REVIEW)

**Key word:** phytochemical, anticoagulant, antithrombotic, warfarin, essential oils, flavonoids.

Hypercoagulability can be the result of hemostasis imbalance, leading to incorrect blood clot and Thrombosis. Although anticoagulant drugs such as heparin and vitamin K antagonists for more than five decades have been developed and known as accepted treatment, they are mostly accompanied by life-threatening side effects. Therefore, discovery of safer, cheaper and more available herbal anticoagulants with less toxicity and fewer side effects is a research interest. Information of present review is collected from peer-reviewed journal articles to discuss about antithrombotic effects of various phytochemicals such as essential oils, flavonoids and Ginkgolide B. The findings from these studies testify that plants contain bioactive substances with great capability in the development of novel anticoagulant drugs for prevention and treatment of cardiovascular diseases. Also, specialist should be aware of synergistic effect of simultaneously

using these medicinal plants and chemical anticoagulant.

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## ЛЕКАРСТВЕННЫЕ РАСТЕНИЯ КАК ИСТОЧНИК ПРИРОДНЫХ АНТИТРОМБОТИЧЕСКИХ СРЕДСТВ В КОРРЕКЦИИ ЗДОРОВЬЯ (ОБЗОР ЛИТЕРАТУРЫ)

**Ключевые слова:** фитохимическое вещество, антикоагулянт, антитромботик, варфарин, эфирное масло, флавоноиды.

Гиперкоагуляция может быть результатом дисбаланса гемостаза, что приводит к нарушению кровообращения и тромбозу. Хотя антикоагулянты, такие как гепарин и антагонисты витамина К, были разработаны более пяти десятилетий назад и известны как общепринятые методы лечения, они в большинстве случаев сопровождаются опасными для жизни побочными эффектами. Таким образом, открытие более безопасных, дешевых и доступных травяных антикоагулянтов с меньшей токсичностью и меньшим количеством побочных эффектов представляет собой исследовательский интерес. Информация для настоящего обзора собрана из ре-

цензуруемых статей для обсуждения антитромботических эффектов различных фитохимических веществ, таких как эфирные масла, флавоноиды и гинкголид Б. Результаты этих исследований свидетельствуют о том, что растения содержат биоактивные вещества, обладающие большим потенциалом для разработки новых антикоагулянтных препаратов для профилактики и лечения сердечно-сосудистых заболеваний. Также специалисты должны знать о синергетическом эффекте одновременного применения этих лекарственных растений и химического антикоагулянта.

Сепідех Парчамі Газас, Т.П. Гарник, В.А. Туманов, Е.В. Горова, Хамід Муртаза

## ЛІКАРСЬКІ РОСЛИНИ ЯК ДЖЕРЕЛО ПРИРОДНИХ АНТИТРОМБОТИЧНИХ ЗАСОБІВ У КОРЕКЦІЇ ЗДОРОВ'Я (ОГЛЯД ЛІТЕРАТУРИ)

**Ключові слова:** фітохімічна речовина, антикоагулянт, антитромботик, варфарин, ефірна олія, флавоноїди

Гіперкоагуляція може бути результатом дисбалансу гемостазу, що призводить до порушення кровообігу і тромбозу. Хоча антикоагулянти, такі як гепарин і антагоністи вітаміну К, були розроблені більше п'яти десятиліть тому і відомі як загальноприйняті методи лікування, вони в більшості випадків супроводжуються загрозовими для життя побічними ефектами. Таким чином, відкриття більш безпечних, дешевих та доступних трав'яних антикоагулянтів з меншою токсичністю і меншою кількістю побічних ефектів викликає зацікавлення дослідників. Інформація для даного огляду зібрана з переглянутих статей для обговорення антитромботичних ефектів різних фітохімічних речовин, таких як ефірні олії, флавоноїди і гинкголид Б. Результати цих досліджень свідчать, що рослини містять біоактивні речовини,

які володіють великим потенціалом для розробки нових антикоагулянтних препаратів для профілактики та лікування серцево-судинних захворювань. Також фахівці повинні знати про синергетичний ефект одночасного застосування цих лікарських рослин і хімічного антикоагулянта.

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## ІРИДОДІАГНОСТИКА У КЛІНІЧНІЙ ПРАКТИЦІ

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В основі іридодіагностики лежить клінічна інтерпретація змін, які виникають на райдужній оболонці ока. Іридологія як наука розглядає райдужку як екстерорецептивну зону, як складний генетичний маркер. При обстеженні проводиться аналіз іридознаків, які можуть бути вродженими чи набутими.

Райдужка відображає вроджені вади, закріплені в генотипі. Є дані, які свідчать, що вона відображає інформацію про дефекти до четвертого

покоління включно. За результатами численних досліджень Bourdiol (1975) виявив, що праве око чоловіків несе батьківський генотип, а ліве – материнський. У жінок – навпаки. На думку Вельхова (1992), передача локальних знаків від батьків становить 50%.

У практичній діяльності лікаря іридолога у 85% випадків зустрічаються пацієнти з поєднаною патологією органів шлунково-кишкового тракту, яка є причиною виникнення захворювань