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Anticoagulant activities of several active compounds from medicinal plants: A review

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Abstract

Anticoagulants are classified as pharmaceutical agents that inhibit the development and expansion of clots. Despite its well-documented safety profile and extensive therapeutic efficacy against a wide range of diseases, this medication does possess perilous adverse effects. As a result, medicinal plants can be utilized as an alternative to anticoagulants due to their ability to mitigate potentially harmful side effects. A review of anticoagulant-active compounds derived from a variety of medicinal plants is the subject of this study. The anticoagulant properties of compounds derived from medicinal plants were assessed, including kaempferol, curkumin, luteolin, catechin, quercetin, andrographolide, and piperine. Multiple research studies have provided evidence that these compounds possess the ability to impede blood clotting via diverse mechanisms of action. The implications of these results for the development of novel anticoagulants derived from medicinal plants are significant.

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Introduction

At present, there are a multitude of diseases that pose a global menace, with particular emphasis on those associated with the circulatory system or thrombotic disorders. These include venous thrombosis, pulmonary embolism, ischemic stroke, hypercoagulable states, strokes, and heart attacks, all of which rank among the leading causes of morbidity and mortality in numerous developed nations [1,2]. Consequently, anticoagulants assume a critical role in both the prevention and treatment of thromboembolic disorders. Anticoagulants are medications that inhibit the clotting mechanism of the body. For the treatment of conditions that cause blood clotting, this medication is administered as a blood thinner [3]. Nonetheless, there are numerous reports at present of adverse effects linked to the administration of anticoagulant medications. One of the unavoidable complications associated with the use of this medication is bleeding [4]. Therefore, it is essential to seek alternative anticoagulant therapies that minimize the occurrence of hazardous side effects [5]. Globally, the utilization of medicinal plants to treat a variety of ailments has increased due to their reputation for being considerably safer than synthetic drugs [6,7]. Researchers are still trying to come up with new anticoagulant drugs that come from natural ingredients. One way they are doing this is by looking into active compounds that are extracted from natural ingredients, especially medicinal plants that have been used for a long time to treat heart problems in many countries [8,9]. The objective is to identify novel anticoagulant compounds characterized by minimal toxicity and mild side effects, so as to prevent harm to patients [10,11]. Therefore, this review article presents to examine the potential anticoagulant properties of active compounds derived from a variety of medicinal plants.

Kaempferol: Kaempferol (3,4' 5, 5,7-tetrahydroxyflavone) is an abundant flavonoid derivative and natural flavonol that can be found in kale, nuts, tea, spinach, broccoli, and nuts, among other plant and food sources [12,15]. When administered in doses of 1, 2, 3, and 4 µg, kaempferol inhibits the activity of activated factor X (FXa) enzymes and thrombin. Additionally, between 1 and 30 µg of kaempferol can inhibit the formation of fibrin clots and fibrin polymers. Conversely, it has been documented that kaempferol (15-30 µg) degrades blood clots and inhibits platelet activation in a manner that is dependent on the dosage [16].

Curcumin: urcumin, which is 1,7-bis (4'hydroxy-3-methoxyphenyl) 1,6-heptadiene, 3,5-dione, is mostly found in Curcuma longa and Curcuma zanthorrhiza, but it can also be found in other plants. In many nations, curcumin is

frequently employed as a component of traditional medicines and remedies for a wide range of ailments [17, 18]. Curcumin is known to possess a variety of pharmacological activities, including hepatoprotective, antibacterial, anti-inflammatory, and antioxidant properties [11]. It has been reported that the administration of curcumin at a dosage of 100 mg/kg increased the duration of bleeding in a mouse tail transection model [19]. It has also been said that curcumin at a concentration of 50 M can greatly increase the activated partial thromboplastin time (aPTT) and prothrombin time (PT) in studies done in vitro. At a concentration of 100 M, curcumin is also reported to inhibit the activation of thrombin and FXa [19].

Luteolin: Luteolin (3',4',5,7-tetrahydroxyflavone) is a prevalent flavonoid that is present in medicinal plants, herbs, and vegetables, among others [20]. Luteolin has been documented to possess a variety of pharmacological activities, such as antioxidant, anti-cancer, anti-diabetic, and anti-microbial properties [21]. It has been reported that the administration of luteolin at a dosage of 10 mg/kg resulted in an extended duration of bleeding in a mouse tail transection model [22]. In addition, in tests carried out in vitro, luteolin is reported to inhibit FXa at a concentration of 20 µg. Luteolin has also been reported to significantly prolong activated partial thromboplastin time (aPTT) and prothrombin time (PT) at concentrations of 2, 5, and 10 µg [22].

Catechin: Catechin (2R,3S)-2-(3,4-dihydroxyphenyl)-3,4-dihydro-2H-chromene-3,5,7-triol) is the main bioactive compound found in green tea (Camellia sinensis) [23]. Catechin is reported to have several pharmacological activities, including antioxidant, antimicrobial, anti-inflammatory, antiviral, anticancer, and anti-allergic properties [24]. Administration of catechin at a dose of 100 mg/kg is reported to prolong bleeding time in a mouse tail transection model [25]. Apart from that, in tests carried out in vitro, catechin is reported to inhibit collagen, thrombin, ADP, and platelet aggregation with IC50 values of 0.64, 0.52, 0.63, and 0.03 mg/mL, respectively [26]. Catechin has also been reported to significantly prolong activated partial thromboplastin time (aPTT), prothrombin time (PT), and thrombin time (TT) at a concentration of 1 mg/mL [25].

Quercetin: Quercetin (2-(3,4-dihydroxyphenyl)-3,5,7-trihydroxy-4H-1-benzopyran-4-one; 3,3',4',5,6-pentahydroxyfl avone) is one of the important bioflavonoids. It is present in more than twenty plant materials and is known to have anti-inflammatory, anti-hypertensive, vasodilator, anti-obesity, anti-hypercholesterolemic, and anti-atherosclerotic effects [27]. In a mouse model of acute thromboembolism caused by human thrombin, quercetin at doses of 10 and 20 mg/kg is shown to help prevent blood clots [28]. In addition, in tests carried out in vitro, quercetin is reported to inhibit the formation of fibrin clots at a concentration of 30 µg, inhibit the formation of fibrin polymer in the concentration range of 5-50 µg, reduce blood clots at a concentration of 200 µg, inhibit the enzymatic activity of human FXa with concentrations of 2 and 5 µg, and significantly prolong activated partial thromboplastin time (aPTT), prothrombin time (PT), and thrombin time (TT) with a concentration of 50 µg [28].

Andrographolide: Andrographolide (3-[2-[Decahydro-6-hydroxy-5-(hydroxymethyl)- 5,8a-dimethyl-2-methylene-1-napthalenyl]ethylidene] dihydro-4- hydroxy-2(3H)-furanone) is a diterpene lactone compound isolated from the plant Andrographis paniculata (Burm. F) Nees, commonly known as the "king of bitters" [29]. Andrographolide has been reported to have several pharmacological activities, such as anti-inflammatory, anti-tumor, antidiabetic, and hepatoprotective [30]. Administration of andrographolide is reported to inhibit platelet aggregation, reduce TXB2 levels, and activate antithrombin III (AT-III) in a mouse model induced by platelet-rich plasma and arachidonic acid with an ED50 of 386.9 mg/kg [31].

Piperine: There is a main amide compound called piperine (1-[5-(1,3-benzodioxol-5-yl)-1-oxo-2,4-pentadienyl] piperidine) that is found in the fruit of Piper chaba Hunt, Piper nigrum L., and Piper longum L [32, 33]. Piperine has been proven to have several pharmacological activities, such as antioxidant, anticancer, antidepressant, hepatoprotective, antiasthmatic, antipyretic, anti-inflammatory, analgesic, and anticonvulsant [11]. Administration of piperine at a dose of 8.25 µg is reported to prolong bleeding time in the mouse tail transection model [34]. Piperine is also found to extend the activated partial thromboplastin time (aPTT) and prothrombin time (PT) in tests done in vitro at 20 and 30 µM concentrations. Piperine is also reported to be able to directly inhibit thrombin activity at concentrations of 10, 20, and 30 µM and inhibit FXa activity at concentrations of 10 and 100 µM [34].

Conclusion

Anticoagulant activity has been scientifically demonstrated for each of these isolates; however, the specific mechanism by which each compound inhibits blood clotting is distinct. Nevertheless, additional investigation is required to ascertain the efficacy of this compound as an anticoagulant, thereby enabling its application in the management of blood clots that have demonstrated hazardous side effects to date.

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