The investigation of anticoagulant effects of *Fumaria officinalis* hydroalcoholic extracts in rabbits

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**Key words**

*Fumaria officinalis*, hydroalcoholic extract, platelet, coagulation tests, rabbits.

**Background:** Herbal medicines are extensively used in several diseases treatment throughout the world, which the *Fumaria officinalis* is one of them.

**Objective:** In this study the anticoagulant effects of *Fumaria officinalis* hydroalcoholic extracts in New Zealand rabbits was investigated.

**Methods:** The effects of hydroalcoholic extracts of *Fumaria officinalis* on platelet and coagulation tests in rabbits during 28 days oral administration of the doses of 200 and 400 mg/kg body weight were investigated. The parameters evaluated include platelet count, prothrombin time (PT), partial thromboplastin time (PTT), clot time (coagulation time) (CT) and bleeding time (BT).

**Results:** The results showed that the *Fumaria officinalis* hydroalcoholic extract administration decreases platelet count, and increases PT, PTT, CT and BT in rabbits.

**Conclusion:** The hydroalcoholic extract of *Fumaria officinalis* has negative coagulating activities which should be considered in the management of blood coagulation, also can be used in coagulation system disorders treatment but needs to more investigations.

**Introduction**

The usage of herbal medicine has been common in all over the world since ancient times which may have toxic effect during consumption for a long term.

A number of herbs have inhibitory effects on platelet activity and coagulation factors with various mechanisms. The diagnosis of anticoagulation effects of different medical plants and their mechanisms are important to use as a preventive or therapeutics agents. Although, some of them are used as coagula-

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important in herbal anticoagulant effects. Therefore, the use of herbal medicinal products may present potential risk to human health (De Smet, 1995); but, some toxic herbal medicines have been proven to have beneficial effects at very low doses.

To protect public health, it is necessary to make sure from the safety, quality and efficacy criteria of herbal medicine as any other licensed medicine. Seven species of the annual plants of genus Fumaria grow in Iran. However, Fumaria officinalis is the medicinal species of this genus which don’t grow in Iran (Khalilighi - Sigaroodi, 2005).

This study was conducted to determine the anticoagulant effects of Fumaria officinalis hydroalcoholic extract in New Zealand rabbits.

Materials and Methods

Animals

This experimental study was carried out on 30 New Zealand white male rabbits with six-month old and 1.5-2 kg Weight. The rabbits were obtained from Razi Institute Centre of Shiraz, Shiraz, Iran. After transferring into laboratory, no experiment was done on them for two weeks in order to avoid stress and to let them for adaptation with the environment. The rabbits were kept in separate cages at the temperature of 20 ± 2 ºC with the 12:12 h light – dark cycle. The rabbits were kept at animal house of Kazerun Branch of Islamic Azad University, Kazerun, Iran and were fed with ready formulated pallet which is especially for laboratory animals, and also the animals were given water ad libitum.

Extract preparation

The herb was purchased from a local herbal shop in Shiraz city and authenticated in the Shiraz Agriculture Faculty, Shiraz, Iran. Its aerial parts were then cleaned and powdered by electric blender and the powder was extracted with 70% alcohol for 72 hours using macerated method.

The mixture was filtered with Whatman No 1 filter paper. The solvent of the filtrate was evaporated at ambient temperature and the extracted powder (13.1% of leaf powder) was kept at 4°C until used and was solvent in water before administration.

Extract administration

Thirty male rabbits were distributed into three quintets, randomly. The control group (group 1) rabbits didn’t receive Fumaria officinalis hydroalcoholic extract. The groups 2 and 3 (experimental groups) received 200 and 400mg/kg of Fumaria officinalis hydroalcoholic extracts based on their weight, for 28 days, respectively.

Administration of the extract was done orally by polyethylene canola. The animals didn’t represent any clinical, toxic, or medicinal symptoms or signs throughout the study period.

Blood sampling

After 24 h the last extract administration, all animals were weighed and blood samples were collected from the heart and transferred into citrated tubule. The platelet count and coagulation tests were done immediately after sampling. Prothrombin time (PT) and activated partial thromboplastin time (APTT) were measured by coagulometric method using Dade Behring kits (Dade Behring kit, Marburg, Germany), and four-channel-coagulometer set (Stago Diagnostic, Asnieres sur Seine, France).

Platelets were counted by manual method with using of hemacytometry lam. Clotting and bleeding time were measured by capillary and duke methods, respectively.

Statistical analysis

The data were expressed in SI units and were analyzed by one way ANOVA method and Duncan’s multiple range tests was used to detect significant difference at the $P < 0.05$ level among the means using SPSS/PC software (Norusis, 1993). All values were expressed as mean and standard error (SE).

Results

The effects of oral consumption of Fumaria officinalis hydroalcoholic extracts on platelet count, PT, PTT, BT and CT in all the groups are shown in Table 1. The significant differences between each parameter in the experimental groups compared to control group are shown in Table 2.
Table 1: Mean ± SE of platelet count, prothrombin time, partial thromboplastin time, clotting time and bleeding time in the studied rabbits.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameter</th>
<th>Plt (1000/μL)</th>
<th>PT (Sec)</th>
<th>PTT (Sec)</th>
<th>CT (Sec)</th>
<th>BT (Sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control Group (Group 1)</td>
<td></td>
<td>205 ± 44.5</td>
<td>7.5 ± 1.5</td>
<td>22.5 ± 1.5</td>
<td>100 ± 4</td>
<td>3.9 ± 0.41</td>
</tr>
<tr>
<td>Group 2</td>
<td></td>
<td>352.3 ± 33.7</td>
<td>9.1 ± 1.3</td>
<td>19.9 ± 0.5</td>
<td>185 ± 29</td>
<td>4.0 ± 2.0</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td>407.7 ± 38.5</td>
<td>9.3 ± 1.4</td>
<td>19.7 ± 0.5</td>
<td>150 ± 15</td>
<td>4.9 ± 3.4</td>
</tr>
</tbody>
</table>

SE  Standard error; Sec second; Plt Platelet; PT prothrombin time; PTT partial thromboplastin time; CT clotting time; BT bleeding time. Groups 2 and 3 (experimental groups) received 200 and 400mg/kg of Fumaria officinalis hydroalcoholic extracts based on their weight, for 28 days, respectively.

Table 2: The Significant differences between platelet count, prothrombin time, partial thromboplastin time, clotting time and bleeding time in control group compared to the experimental groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Parameters</th>
<th>Plt</th>
<th>PT</th>
<th>PTT</th>
<th>CT</th>
<th>BT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 2</td>
<td></td>
<td>0.023</td>
<td>0.002</td>
<td>0.477</td>
<td>0.028</td>
<td>0.004</td>
</tr>
<tr>
<td>Group 3</td>
<td></td>
<td>0.036</td>
<td>0.001</td>
<td>0.702</td>
<td>0.037</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Plt Platelet; PT prothrombin time; PTT partial thromboplastin time; CT clotting time; BT bleeding time. Groups 2 and 3 (experimental groups) received 200 and 400mg/kg of Fumaria officinalis hydroalcoholic extracts based on their weight, for 28 days, respectively.

The results of this study showed that the Fumaria officinalis hydroalcoholic extracts led to increase in PT, BT, platelet and CT in experimental groups; and also, there was significant statistical difference between these parameters in experimental groups compared to control group. There was no statistical significant difference concerning the PTT among all the groups.

Discussion

In this study, the mean of platelets count increased after the orally administration of Fumaria officinalis hydroalcoholic extracts, and there were significant differences between this parameter in experimental groups in comparison to control group, also this plant extracts affected the bleeding time, clotting time and prothrombin time and were observed significant differences between these parameters in experimental groups compared to control group. Bleeding time (BT) is an indicator that can be affected by platelets count and their activity, due to significant increasing in BT despite increasing in platelets count can resulted from the Fumaria officinalis hydroalcoholic extract which decrease platelets activity despite their increased count. It seems, consumption of Fumaria officinalis extract stimulates bone marrow platelet releasing but these platelets are ineffective.

According to the results of current study, the Fumaria officinalis hydroalcoholic extracts did not affect the partial thromboplastin time, due to no observed considerable changes in PTT in different
groups. There are significant differences between the mean times of PT and CT in two experimental groups in comparison to control group. So, these findings showed that the *Fumaria officinalis* hydroalcoholic extracts did not affect intrinsic coagulation factors, but this plant extracts affect extrinsic coagulation factors due severity increase observed in PT and CT.

Herbal medicines can participate to unexplained surgical bleeding in the absence of other causative factors; it would therefore be beneficial to include an enquiry about the taking of herbal remedies at the history-taking stage for dental and maxillofacial surgical procedures (Gray and West, 2012). Danshen is an herbal medicine often used for various complaints, particularly cardiovascular, in the Chinese community. A case of Danshen-induced over coagulation has been reported with severe and dangerous abnormalities of clotting in a patient with rheumatic heart disease (Yu et al., 1997).

The non-dialyzable fraction of the ammonia extract from *Pulmonaria officinalis* contains the anticoagulant glycopeptide. It reducing total coagulation activity of the blood 4-5 fold, but does not change the animals’ behavior; hypocoagulemia remains at a high level up to 6 h after intravenous administration of the anticoagulant, and diminishes only after 24 h. The anticoagulant can reduce the death rate of the animals with exogenous thromboplastinemia by suppressing the blood coagulation activity. The inhibitor effect is realized mainly at the stage of fibrinogen conversions (Byshevskii et al., 1990).

The oral administration of Huang-lien-chieh-tu-tang (HLCT) extract rise the plasma concentration of factor VIII from less than 1 to 41% during 1 h in a patient with severe hemophilia A. APTT also decreases from 102.0 to 70.9 s. In vitro experiments, HLCT shows factor VIII, IX and X biological activity at concentrations around 0.08%. There is no factor - VIII - antigen - related activity in HLCT (Adachihara, 1983).

The garlic administration decreases serum cholesterol and increases clotting time and fibrinolytic activity. Hence, garlic may be a useful agent in prevention of thromboembolic phenomenon (Gadkari and Joshi, 1991).

The aqueous extract of Herba Lamiophlomis Rotata (HLRE) orally administered in rats can increase the contents of fibrinogen and shorten thromboplastin time. The short PT is found after treated with high dose for a long time. Hemostatic effect of HLRE has a dose-effect and time-effect relationship (Li et al., 2006).

PGE2-1(polysaccharide 2-1 from Gastrodia elata) may be the main component of the isolation from *Gastrodia elata* in the field of antithrombosis, due its remarkable anticoagulant and antithrombotic effects (Ding et al., 2007).

Raw Agi can play its role in hemostasis and coagulation by affecting the intrinsic pathway of coagulation and fibrinolytic system. These effects are enhanced after processing drugs; moreover, the charred Agi could increase fibrinogen (Zhong et al., 2011).

The hydroalcoholic extracts of *Boswellia serrata*’s gum resin as a good source for lead/therapeutic compounds have antioxidant, antiplatelet and anticoagulant activities (Kokkiripati et al., 2011).

Mishra et al. (2012) reported the use of *Hibiscus rosa sinensis* whereas may not cause any adverse effect on animals, Bougainvillea spectabilis is to be consumed with care as its chronic use may induce anemia.

Adeneye (2008) concluded the folkloric use of methanol seed extract of *Citrus paradisi Macfad* can be useful in the treatment of blood deficiency.

Plants in the Cucurbitaceae family, especially *Telfaria occidentalis* have also been recognized to have hematonic effect and have proven to be of therapeutic value in conditions of anemia (Alada, 2000; Dina et al., 2000).

Saba et al. (2009) showed the prolonged administration of extract of *Lagenaria breviflora* causes electrolyte imbalance but it is not hemotoxic, rather, it acts as erythropoiesis stimulator and enhance immunity especially the cell-mediated immunity.

The result of Ozogwu (2011) study indicated that *Allium sativum* extracts induce positive hematological activities in rats which should warrant its consideration in the management of anemia and immunity dependent disorders such as AIDS.

**Conclusion**

In this study the increase in PT, CT and BT in experimental groups suggest the use of *Fumaria officinalis* hydroalcoholic extracts in long term should be done with cautious, because this plant can be have anticoagulant effects by early platelet
releasing stimulating and produce ineffect platelet and decrease in extrinsic coagulation factors.

References


