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**THE EFFECT OF DRY EXTRACT OF *GERANIUM PALUSTRE* HERB ON
COAGULATION SYSTEM
ВПЛИВ СУХОГО ЕКСТРАКТУ ТРАВИ ГЕРАНІ БОЛОТНОЇ НА СИСТЕМУ
ЗСІДАННЯ КРОВІ**

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Abstract

The article is devoted to the studying of mechanism action on coagulation system the dry extract of *Geranium Palustre* herb. Established, those during 20-ty days of introduction the investigation extract increasing the activity of platelet's mechanism of hemostasis (increasing platelet's amount, their aggregation activity and retraction of blood clotting). On the background of introduction the investigation extract decreasing indicators of I and III phase of coagulation cascade (activated partial thromboplastin time, thrombin time), increasing prothrombin time and level of fibrinogen. Obtaining result suggest about active action the dry extract of *Geranium Palustre* herb on «external» way activation of hemocoagulation by possibility effect of accelerate the formation of thromboplastin, causing the hypercoagulation.

The mechanism of antihemorrhagic action of dry extract of *Geranium Palustre* herb due to the presence in the composition biological active substances (such as tannins, flavonoids, elagic, galic and ascorbinic organic acids) that acting complex on vascular-platelet and coagulation

hemostasis at the expense of increasing the strength and sealing vascular-tissue barriers, P-vitamin activity – it is ability to reduce capillary fragility and permeability and increasing their resistance.

Key words: dry extract of *Geranium Palustre* herb, platelets, coagulation, phenolic compounds.

Реферат

Стаття присвячена дослідженню механізму дії сухого екстракту трави герані болотної на систему зсідання крові. Встановлено, що протягом 20-ти денного введення досліджуваного екстракту підвищувалася активність тромбоцитарної ланки гемостазу (підвищувалася кількість тромбоцитів, їх агрегаційна здатність та ретракція кров'яного згустку). На фоні введення сухого екстракту трави герані болотної знижувалися показники I та III фази коагуляційного гемостазу (активованій частковий тромбопластиновий час, тромбіновий час), підвищувався протромбіновий час та рівень фібриногену. Отримані дані свідчать про вплив сухого екстракту трави герані болотної на «внутрішній» шлях активації зсідання крові за рахунок прискорення формування тромбопластину, що призводить до гіперкоагуляції.

Механізм антигеморагічної дії сухого екстракту трави герані болотної обумовлений наявністю у складі біологічно активних речовин (дубильних речовин, флавоноїдів, елагової, галової та аскорбінової органічних кислот), які діють комплексно як на судинно-тромбоцитарний, так і на коагуляційний гемостаз за рахунок ущільнення та збільшення міцності судинно-тканинних бар'єрів, Р-вітамінної активності – здатності зменшувати проникність та ламкість капілярів, підвищувати їх резистентність.

Ключові слова: сухий екстракт трави герані болотної, тромбоцити, зсідання крові, фенольні сполуки.

Реферат

ВЛИЯНИЕ СУХОГО ЭКСТРАКТА ТРАВЫ ГЕРАНИ БОЛОТНОЙ НА СИСТЕМУ СВЕРТЫВАНИЯ КРОВИ. Стаття посвящена исследованию механизма действия сухого экстракта травы герани болотной на систему свертывания крови. Установлено, что на протяжении 20-ти дневного введения исследуемого экстракта повышалась активность тромбоцитарного звена гемостаза (увеличивалось количество тромбоцитов, их агрегационная способность и ретракция кровяного сгустка). На фоне введения сухого экстракта травы герани болотной снижались показатели I и III фазы коагуляционного гемостаза (активированное частичное тромбопластиновое время, тромбиновое время), повышалось протромбиновое время и уровень фибриногена. Полученные данные

свидетельствуют о влиянии сухого экстракта травы герани болотной на «внутренний» путь активации свертывания крови за счет ускорения формирования тромбопластина, что приводит к гиперкоагуляции.

Механизм антигеморрагического действия сухого экстракта травы герани болотной обусловлен наличием в составе биологически активных соединений (дубильных веществ, флавоноидов, эллаговой, галловой и аскорбиновой органических кислот), которые действуют комплексно как на сосудисто-тромбоцитарный, так и на коагуляционный гемостаз за счет уплотнения и увеличения прочности сосудисто-тканевых барьеров, Р-витаминной активности – способности уменьшать проницаемость и ломкость капилляров, повышать их резистентность.

Ключевые слова: сухой экстракт травы герани болотной, тромбоциты, свертывание крови, фенольные соединения.

Introduction. Hemostasis – it is a complex of functional-morphological and biochemical mechanism that promote the stoppage of bleeding when these vessels are damage and support blood in a liquid state inside the vessels. The components of coagulation system are: vessel's wall, blood cells and plasma factors. Each of them carries activators and inhibitors of coagulation and fibrinolysis. Depending of the size of injury vessels release 2 mechanisms of blood clotting: vascular-platelet (primary) and coagulation (secondary) [1]. Primary hemostasis is based on adhesion and aggregation functions of platelets, secondary (coagulation hemostasis) – it is multistep enzymatic process where sequentially procoagulants transform to the active form [2, 3]. Disturbance of the balance in one of these mechanisms leads to bleeding. That pathological process requires correction by destination of hemostatic drugs [4]. One of the main problem in modern pharmacology – it is development a new medications that can allows complex impact on the course of pathological process, would be effective and safety during long introduction. The most perspective direction for solving this problem – it is searching and synthesis the hemostatic drugs by plant's origin. In this case on the pharmacognosy department of National University of Pharmacy has been studied and found that flowering herb of *Geranium Palustre* content plenty biological active substances (tannins, flavonoids, ascorbinic, elagic and galic organic acids) which exhibit antihemorrhagic action.

The researches are realized according to the plan of Scientific Researches Work of the

National University of Pharmacy «Pharmacological studying of biological active substances and medicine drugs by synthetic and natural origin, their using in practical medicine» (Registration №0103U000478).

The aim of our research – it is establishing the possible mechanism action on the coagulation system the dry extract of *Geranium Palustre* herb.

Materials and methods. Experiments conducted on white non-linear rats mass 170, 0 – 200, 0g. All animals were divided into 2 groups (6 animals in every group): 1 group – intact animals which were prepared distillate water in volume 1 ml; 2 group – animals which administrated the dry extract of *Geranium Palustre* herb during 20-ty days in effective dose 3 mg/kg intragastrically as water solution, stabilized by tween-80.

For established the possible mechanisms action of dry extract of *Geranium Palustre* herb on the vascular-platelet hemostasis studied the following indicators: amount of platelets, their aggregation activity and retraction of clot formation. Counting of platelets performed by method G. F. Berezaycevoy and M. G. Shubich (1958) used microscopy «Carson Advanced 400-1600 x» (USA). The aggregation activity of platelets was determinate by express-method of visual assessment (method A. S. Shitikova, 1984). Retraction of blood clotting was determinate by method that based on definition serum volume which realized during retraction of blood clot against to plasma volume of investigation blood [5, 6].

The main indicators that characterize coagulation hemostasis are: activated partial thromboplastin time (APTT), prothrombin time (PT), thrombin time (TT) and level of fibrinogen [7]. This indicators studied in blood plasma which received by mixed with 3,8 % sodium citrate (9:1), centrifugation during 10 min with speed 150 g. For investigation the indicators of secondary hemostasis used analytical 4-channels coagulometer RT-2204 C (USA) with reagent of company «RENAM» (Russia) [8, 9].

During experiment with animals was followed the International codec's of medical ethics (Venice, 1983), «European convention about protection of spine bone animals, which using with experimental and others scientific purpose» (Strasbourg, 1986), Directive 2010/63/EU of European Parliament and Council on the protection of animals used for scientific purposes.

Results of researches processed using descriptive statistics. Statistics credibility evaluated with univariate analysis of variance ANOVA [10].

Results and discussion. During studied the effect of dry extract of *Geranium Palustre* herb on primary hemostasis established that platelet's amount in peripheral blood increasing in 1,08 and 1,10 times after 14th and 20th days of introduction (Fig. 1).

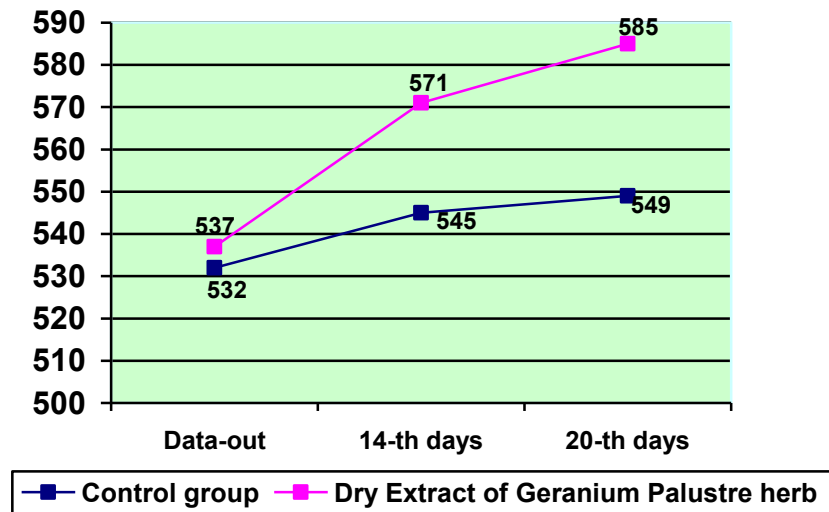


Figure 1. The effect of dry extract of *Geranium Palustre* herb on platelet's amount in peripheral blood

After 14th and 20th days of introduction the dry extract of *Geranium Palustre* herb established increasing the platelets aggregation in 1,53 and 3,2 times against to intact animals (fig. 2).

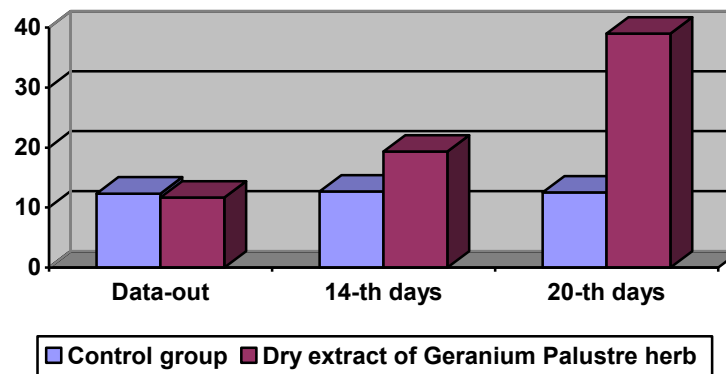


Figure 2. The effect of dry extract of *Geranium Palustre* herb on platelets aggregation activity

The retraction of blood clotting characterizes the amount of active platelets and content 32 % against to control group.

In the study of coagulation hemostasis during introduction the dry extract of *Geranium Palustre* herb was established the presence a moderate-severe hypercoagulation in 14th days of experiment that observed during the whole investigation period.

As we known, APTT – it is one of the most informative test that characterize the condition of hemostasis «internal» cascade: activity of factors XII, XI, IX, VIII, X, V, I, II, high molecular kininogen (HMK) and prekallikrein. In group that received the dry extract of *Geranium Palustre*

herb observed decreasing APTT level in 1,3 time against to control group.

Table 1

Indicators of coagulation phase of hemostasis during introduction the dry extract of *Geranium Palustre* herb

Indicator	Control group	The dry extract of <i>Geranium Palustre</i> herb, ED ₅₀ =3 mg/kg
Activated partial thromboplastin time, s	23,6±0,45	18,6±0,8*
Prothrombin time, s	12,17±0,48	12,82±0,26
Thrombin time, s	32,60±1,24	30,80±1,42
Fibrinogen, g/l	2,55±0,39	2,81±0,22

Note. * - $p \leq 0,001$ against to control group

The indicator of II phase of hemocoagulation is PT. During the introduction the dry extract of *Geranium Palustre* herb PT increasing on 0,55 second against to intact animals. That indicates on effect of investigation extract on II phase of hemostasis – it is accelerating of transition prothrombin in thrombin. Since the level of PT not increased greatly this suggests about absence of risk thrombosis.

TT characterizes the III phase of coagulation – transformation fibrinogen in fibrin. The level TT decreasing in 1,06 time during introduction the dry extract of *Geranium Palustre* herb against to control group.

The level of fibrinogen increasing in 0,9 time against to control group. That, possibility, balances the hemostasis system and don't effected on posthemorrhagic state of coagulation. Also, the moderate hyperfibrinogenemia can be precursor for further hypercoagulation shift.

Obtaining result suggests about effect the dry extract of *Geranium Palustre* herb on «external» way activation of hemocoagulation by possibility effect of accelerate the formation of thromboplastin, causing the hypercoagulation.

The effect of dry extract of *Geranium Palustre* herb due to the presence in the composition biological active substances – phenolic compounds (tannins, flavonoids, organic acids). The mechanism of antihemorrhagic action of phenolic compounds caused by compaction and increase strength of vascular tissue barriers, possess P-vitamin activity – can reduce permeability and fragility of capillaries, improve their resistance, due to a decrease of hyaluronidase, preventing oxidation of ascorbic acid and epinephrine.

Conclusion

1. During intragastrically introduction the dry extract of *Geranium Palustre* herb in effective dose 3 mg/kg on 14th and 20th days the amount of platelets increasing in 1,08 and 1,10 times; their

aggregation in 1,53 and 3,2 time against to control group. The retraction of blood clotting content 32%.

2. On the background of introduction the investigation extract decreasing indicators of I and III phase of coagulation cascade (activated partial thromboplastin time, thrombin time), increasing prothrombin time and level of fibrinogen. Obtaining result suggest about active action the dry extract of *Geranium Palustre* herb on «external» way of hemocoagulation.

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