

Study Of Specific Activity Of The Hemostat Liquid Extract

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ABSTRACT

Our studies have suggested that the mechanism of action of the sum of flavonoids (liquid extract "Hemostat") from pylori, pylori, nettle and nettle in a ratio of 1: 1: 1 on the blood coagulation process is associated with its effect on the number, adhesion and platelet aggregation, as well as the retractive ability of platelets. It was revealed that the liquid extract "Hemostat" has a pronounced hemostatic effect and in this respect it is noticeably superior to the known preparation of the liquid extract of the shepherd's bag.

KEY WORDS: *Polygonum aviculare L., Polygonum hydropiper L., Urtica dioica L., galenic preparations, flavonoid compound, tannins, astringent, anti-inflammatory, antimicrobial.*

1. INTRODUCTION

Bleeding is one of the formidable complications in various diseases and conditions of the body, especially in surgery, obstetric pathology, otolaryngology, infectious diseases, overdose of anticoagulants, as well as wounds and disseminated intravascular coagulation. Recently, the incidence of acute gastroduodenal bleeding has significantly increased, which is observed in 71.3% of patients with peptic ulcer. According to some reports, 7-15% of patients entering the pulmonary department suffer from hemoptysis. With cirrhosis of the liver, bleeding is observed in 90% of patients. The frequency of pathological bleeding in patients with infectious hepatitis ranges from 2.5-30% [3].

Bleeding caused by drugs, an overdose of anticoagulants, and the simultaneous administration of anticoagulants and salicylates, sulfonamides and antibiotics are observed in 3.9-10% of patients. Acute hemorrhage is one of the main causes of the development of terminal conditions during pain injury [5].

Relevance of the study. The drugs used to stop bleeding do not always satisfy the requirements of clinicians and patients. The main drugs used to stop bleeding of various origins are imported synthetic drugs and have various side effects [10,13,16]. Based on this, the search, study and implementation of hemostatic drugs from local plant materials is extremely relevant.

In view of the foregoing, we studied the specific hemostatic activity of the liquid extract from the herbs of the mountaineer, avian, pepper and nettle in a ratio of 1: 1: 1 under the name "Hemostat". For comparison, a well-known hemostatic preparation used in medical practice, a liquid extract of a shepherd's bag was taken.

According to the literature, traditional herbs have long been widely used medicinal herbs of mountaineer (*Polygonum aviculare L.*), mountaineer (*Polygonum hydropiper L.*) and nettle (*Urtica dioica L.*). They have astringent, diuretic, anti-inflammatory and antimicrobial

effects. In particular, folk medicine, galenical preparations from the herbs of the mountaineer, pepper, and nettle in the form of infusion, decoction are used for diseases of the liver, kidneys, bladder, uterus, stomach ulcer and hemorrhoids as anti-inflammatory, diuretic and hemostatic agents [1,2,4 8,11,15,18,19]. Preparations of avian highlander, pepper mountain and nettle due to the content of flavonoid compounds (avicularin, quercetin, isoramnetin, myricetin, kempferol, luteolin), flavonol derivatives (ramnazine, hyperoside), tannins, phylloquinone, vitamins B2, B6 , K, carotene, pantothenic acid, coumarins, chlorophyll, as well as essential oils, mucus, fats, sugars, silicic acid compounds, a significant amount of trace elements-iron, copper, vanadium, calcium, magnesium and silver have an astringent, anti-inflammatory and antimicrobial effect [7,12,15,20,21,22].

Shepherd's bag is a famous medicinal plant. The shepherd's bag contains a large amount of vitamins B, C, provitamin A, risnoglycoside gisopen, tannins, flavonoids, phenolic glycosides [9,13].

Preparations of a shepherd's bag have many medicinal properties. They have a pronounced hemostatic effect, especially with hemorrhages with a due to insufficient formation of fibrin. In addition, they enhance the contractility of the smooth muscles of the uterus, which is explained by the presence of essential oil and other compounds in the plant, as well as, apparently, the action of acetylcholine. The leaves of the shepherd's bag have a high phytoncide activity. Plant preparations increase intestinal motility. Aqueous and alcoholic extracts of grass plants have hypotensive, choleric, diuretic properties. There is a high efficiency of the grass of the shepherd's purse in case of renal bleeding in those cases when the previously used hemostatic agents did not give a positive result. The grass of the shepherd's bag is part of the official hemostatic collection [14,18].

The purpose of the scientific work is to study the effect of the Hemostat liquid extract on blood coagulation processes and the effect of the studied drug on capillary permeability.

2. MATERIALS AND METHODS

1-Experiment: In this series of experiments, we studied the effect of the sum of the flavonoids of the liquid extract from the mountaineer, pylori and nettle on the time of bleeding and on the amount of blood loss. The experiments were carried out on 18 rats weighing 160-185 g, both sexes. This test reflects the vascular-platelet mechanism of hemostasis and is determined by the number and state of platelets by their ability to adhesion and aggregation [6,18].

The results are shown in table -1.

Table 1. The bleeding time and the amount of blood loss in rats 60 minutes after administration of the hemostat liquid extract (M ± m; n = 6)

№	The studied drugs and their doses	Bleeding time			Blood loss time		
		Seconds	%	P	Mg	%	P
1.	Control	320±20	100	-	407±24	100	-
2.	Liquid extract "Hemostat": 2 mg / kg	177±14	55	<0,01	140±12	34	<0,01
3.	Liquid extract "Hemostat": 4 mg / kg	143±11	45	<0,01	100±10	25	<0,01
4.	Shepherd's Bag Liquid Extract 4 mg / kg	211,6±13,94	66	<0,05	170±13,93	41,76	<0,01

P <0.01 with respect to control

2-Experiment: In this series of experiments, we studied the effect of the sum of flavonoids isolated from avian mountaineer, mountaineer perennial and nettle (ie, liquid extract "Hemostat") on the process of blood coagulation of rabbits.

The general orientation of the coagulation process was judged by the records of thromboelastograms performed on a thromboelastograph - Thrombus-2.

Thromboelastography makes it possible to draw a conclusion about the general direction of changes in the blood coagulation process, changes in the phases of prothrombinase, thrombin and fibrin formation, and diagnose acute fibrinolysis [6].

The results are shown in table -2.

Table 2. The effect of flavonoids from the liquid extract "Hemostat" on the indicators of thromboelastograms (TEG) of rabbits with a single oral administration, a dose of 0.5 ml / kg (M ± m; n = 6)

* TEG indicators	Research time, from the moment of drug administration, minutes.			
	Исход	30	60	120
R, mm	45±4,0	10±1,0	20±2,0*	28±2,0*
K, mm	27±1,7	7±0,6*	7±0,4*	14±1,0*
R+K, mm	72±5,2	17±1,3*	27±2,0*	42±3,0
R/K	1,7±0,1	1,40,1	2,9±0,2*	2,0±0,2
MA, mm	45±1,0	47±1,4	48±1,0	45±1,0*
t, mm	100±10	100±10	100±10	120±10
S, mm	130±11	107±10*	107±10*	134±12
T, mm	185±15	117±10*	127±12*	162±14
Ci	0,82±0,05	2,8±0,2*	1,8±0,1*	1,1±0,1*
E	82±6	89±6	92±8*	82±6*
ITP	0,63±0,04	0,84±0,06	0,86±0,06*	0,61±0,04*

P <0.01 with respect to control

3-Experiment: In this series of experiments, the liquid extract and the dry extract from the herbs of the mountaineer, pylori, and nettle "Hemostat" have a similar effect
The results are shown in table-4.

Table 4. The influence of the liquid extract "Hemostat" on indicators thromboelastogram (TEG) of rabbits with a single oral administration, dose of 0.5 ml / kg (M ± m; n = 6)

TEG indicators	Research time, from the moment of drug administration, minutes.			
	Outcome	30	60	120
R, mm	20±2,0	8±0,5	7±0,5*	45±3,0
K, mm	12±1,0	10±2,6	10±1,0	25±2,0
R+K, mm	32±2,2	18±6,0*	17±1,0*	70±5,2*
R/K	1,7±0,1	0,8±0,1	0,7±0,2	1,8±0,1
MA, mm	48±1,0	54±1,4	49±1,0*	43±1,0
t, mm	110±10	110±10	110±10	120±11
S, mm	122±11	120±11	110±11	145±13
T, mm	135±12	128±11	117±11	190±16

* P <0.05 with respect to control.

4-Experiment: In this series of experiments, we studied the effect on the number and on the functional activity of platelets in rabbits in order to identify the mechanism of action of the hemostatic effect of the studied drug “Hemostat”

The Hemostat liquid extract was administered intravenously at a dose of 0.5 ml / kg, which was previously diluted 5 times. The drug was studied in dynamics: baseline, after 30, 60, 120 minutes from the start of drug administration. The results are shown in table-4.

Table 4. The influence of the studied preparation from the herbs of the mountaineer, bird's, mountaineer and nettle - “Hemostat” on the number and functional activity of platelets with a single intravenous administration to rabbits at a dose of 1 mg / kg ($M \pm m$; $n = 6$)

№	Indicators in %	Time since drug administration, minutes			
		Outcome	30	60	120
1.	Platelets, $10^9 / L\%$	$\frac{400 \pm 12}{100}$	$\frac{550 \pm 20}{138}^*$	$\frac{800 \pm 16}{200}^*$	$\frac{850 \pm 15}{212}^*$
2.	Clot retraction, min%	$\frac{13 \pm 0,8}{100}$	$\frac{9 \pm 0,6}{75}^*$	$\frac{7 \pm 0,4}{58}^*$	$\frac{6 \pm 0,4}{50}^*$
3.	Platelet adhesion,%	$\frac{20 \pm 1,0}{100}$	$\frac{28 \pm 3,0}{140}^*$	$\frac{38 \pm 4,0}{190}^*$	$\frac{45 \pm 2,4}{225}^*$
4.	Spontaneous aggregation in%	$\frac{25 \pm 1,4}{100}$	$\frac{36 \pm 2,6}{144}^*$	$\frac{44 \pm 2,4}{176}^*$	$\frac{35 \pm 2,4}{140}^*$

5-Experiment: In this series of experiments, capillary permeability disorders were studied. A model of capillary permeability disturbance was called by the methods of Yu.N. Nuraliev and G.A. Mednik [6, 16, 17].

The experiments were performed on 60 white mice of both sexes weighing 20 ± 2 g. For a quantitative study of changes in capillary reactivity, a method based on recording the time of development of disturbances in the capillary permeability of the skin of white mice when a standard p-xylene agent was applied to it. The Hemostat liquid extract was administered orally once at a dose of 0.15 ml / kg 60 minutes before the administration of trypan blue. The liquid extract was previously diluted with distilled water 10 times. The control group was injected with 0.5 ml. water-alcohol solution diluted in a similar way. Taking into account the fact that quercetin is formed from avicularin flavone glycoside by hydrolysis, vitamin P and rutin (close to quercetin) were taken at a dose of 3 and 5 mg / kg, respectively.

3. RESULTS AND DISCUSSION

1. As can be seen from table-1, the blood coagulation time after 60 minutes after the intraperitoneal injection of the sum of flavonoids of the liquid extract of the studied plants of the mountaineer, mountaineer perennial and nettle decreased in doses of 2 and 4 mg / kg, respectively, from 320 ± 20 sec to 177 ± 14 that is, 1.8-2.2 times. Under similar conditions, the liquid extract of the shepherd's bag at a dose of 4 mg / kg reduced the bleeding time to 211.6 ± 13.94 seconds, that is, 1.5 times.

A similar picture is observed when studying the amount of blood loss. So, in the control, this indicator was 407 ± 24 , and in doses of 2 and 4 mg / kg under the influence of the studied drug was 140 ± 12 and 100 ± 10 mg, respectively. With the introduction of 4 mg / kg of liquid extract of the shepherd's bag, this indicator was 170 ± 13.93 mg.

The studied drug “Hemostat” significantly reduces the bleeding time and the amount of blood loss in rats. A similar effect was noted with the introduction of the liquid extract of

the shepherd's bag, but they were relatively less pronounced than the studied liquid extract "Hemostat".

2. As can be seen from table -2, the sum of flavonoids obtained from bird highlander, mountaineer list and nettle at a dose of 1 mg / kg after 30 minutes lengthened the reaction time by 4.5 times by 4.5 times - K from 454.0 to 101.0 mm. It characterizes the 1st phase of blood coagulation, and reflects the rate of thromboplastin formation. After 60 minutes, this figure was 202.0 mm, and 2.3 times less than in the outcome. After 120 minutes, the K-reaction time was 282.0 mm, and was 38% shorter.

Similarly, after 30-60 minutes, the clot formation time indicator, K, which depends on the concentration of thrombin formed and the amount of fibrinogen, decreased from 271, 7 to 70.6 mm, or by 74%. After 120 minutes, this figure was 141.0 mm and was 48% shorter than the outcome.

R / K is the constant of the use of prothrombin, it expresses the ratio of the rate of generation of thromboplastin (K) to the amount of thrombin formed (K). The decrease in the constant is affected not so much by an excess of thrombin, but by the rate of its formation, and by an increase, there is more activity and less speed. From table b it can be seen that after 30 minutes the rate of thrombin formation increased by 18%, and after 60 minutes the thrombin activity increased by 71% with respect to the outcome. After 120 minutes, this indicator did not differ from the outcome.

R + K is a non-specific coagulation constant that expresses the total duration of blood coagulation. It has approximately the same clinical significance as the determination of plasma tolerance to heparin and reflects the content of antithrombin III. In our studies, the maximum reduction in this indicator occurs in 30 minutes (76%) and amounts to 171.3 mm (outcome 72 ± 5.2 mm). After 60 minutes it is 272.0 mm, and after 120 - 423.0 mm.

The hypercoagulant effect of the sum of flavonoids from avian mountaineer, mountaineer list and nettle on the blood of intact rabbits confirms, and an increase in the index of hypercoagulation Ci 3.4-2.2 times after 30-60 minutes from the time of administration of the drug.

The maximum amplitude of MA and the elasticity of clot E varied within the initial parameters.

3. As can be seen in table-3, the maximum effect of the sum of flavanoids from the highlander, bird highlander and nettle occurs after 30 minutes. Duration of action is more than 120 minutes. The drug affects the first and second phases of blood coagulation — thromboplastin formation, increases the rate of formation and activity of thrombin, and possibly affects the plasma tolerance to heparin.

In this series of experiments, the liquid extract and the dry extract from the herbs of the mountaineer, bird's mountain, and nettle have a similar effect.

4. As can be seen in table -4, intravenous administration of the studied drug at a dose of 1 mg / kg caused within 30-120 min, an increase in the number of platelets in peripheral blood by 38-112%. Moreover, the maximum increase in platelet count occurred in 120 minutes from the start of drug administration and amounted to $850 \pm 25 * 109 / l$, respectively.

Under the influence of the sum of flavonoids of the Hemostat liquid extract, there are platelets in the blood with increased functional activity. Moreover, after 60 minutes adhesion increased from $20 \pm 2.0\%$ to $38 \pm 3.0\%$ or 90%. The maximum increase in adhesion was observed after 120 minutes from $20 \pm 1.0\%$ to $45 \pm 4.0\%$ or 123%. The drug after 30 minutes changed spontaneous platelet aggregation from 25 ± 1.4 to 36 ± 2.6 or by 44%. After 60 and 120 minutes, he increased by 44 ± 2.4 and 35 ± 2.4 , respectively, or by 76% and 40%.

The effect of the liquid extract on the platelet retractivity is indicated by a reduction in clot retraction time after 30 minutes from 13 ± 0.8 minutes to 9 ± 0.6 minutes or by 25%,

after 60 to 7 ± 0.4 minutes or by 42% and after 120 minutes to 6 ± 0.4 minutes or 50%.5. The results of the experiments showed that the liquid extract “Hemostat” at a dose of 0.5 ml / kg increases the time of staining of the skin of mice from 5.8 ± 0.25 to 8.9 ± 0.8 minutes or the resistance of capillaries increased by 53%.

Vitamin P in the studied doses increases the staining time of the skin of mice from 6.8 ± 0.5 to 10.0 ± 1.0 and 8.9 ± 0.9 minutes or by 47 and 30%, respectively. Rutin at a dose of 3 and 5 mg / kg increased the staining time of the skin of mice from 6.8 ± 0.5 to 8.6 ± 0.5 and 9.5 ± 0.6 , or by 26% and 40%.

Thus, the “hemostat” liquid extract, one hour after administration, lowers the permeability of capillaries of the skin of mice by 1.5 times and surpasses the action of vitamin P and rutin in activity.

4. CONCLUSION

Thus, our studies have suggested that the mechanism of action of the sum of flavonoids (liquid extract “Hemostat”) from pylori, pylori and nettle in a ratio of 1: 1: 1 on the blood coagulation process is associated with its effect on the quantity, adhesion and platelet aggregation, as well as the retractive ability of platelets. Therefore, the studied liquid extract “Hemostat” has a pronounced hemostatic effect and in this respect it is noticeably superior to the known preparation of the liquid extract of the shepherd’s bag. Based on the results of our experiments, we can conclude that the expansion of the arsenal of hemostatic agents of plant origin is very important, since herbal preparations are more easily absorbed by the body and practically do not have side effects.

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