Antihemorrhagic Effect of the Extract from *Blumea megacephala* (Randeria) Chang et Tseng on the Uterine Bleeding Model in Early Pregnancy Rats

Xixue NA[1,2△], Shenggao YIN[1△], Wentao ZHANG[1], Yuanfeng TAN[1], Wei WEI[1], Xiaoqing NING[1*]

1. Guangxi University of Chinese Medicine, Nanning 530200, China; 2. Guangxi Academy of Medical Sciences · the People's Hospital of Guangxi Zhuang Autonomous Region, Nanning 530016, China

Abstract [**Objectives**] To investigate the effect of extract A from *Blumea megacephala* (Randeria) Chang et Tseng on the hemostasis of postpartum uterine hemorrhage in early pregnancy rats. [**Methods**] 12 mg/kg of mifepristone and 120 μg/kg of misoprostol were used to establish the uterine bleeding model of early pregnancy rats, and the effects of the drugs on the amount of uterine bleeding, the contents of angiotensin II (Ang-II) and prostaglandin E_2 (PGE_2) in serum, the four factors of coagulation, platelet adhesion, platelet aggregation and platelet number were investigated. [**Results**] Extract A can shorten prothrombin time (PT) and activated partial thromboplastin time (APTT) in rats. It can reduce the amount of uterine bleeding in the model, reduce the contents of PGE_2 and Ang-II, reduce APTT and PT, increase the content of fibrinogen FIB, enhance platelet adhesion, enhance platelet aggregation and increase the number of platelets. [**Conclusions**] Extract A has obvious hemostatic effect on uterine bleeding model of early pregnancy rats. It may play a hemostatic role by affecting vasoconstriction-dilation, coagulation factors in the blood's internal and external coagulation system, platelet adhesion and aggregation, increasing FIB content, increasing platelet number, affecting uterine bleeding, *etc.*, showing the characteristics of multiple pathways and multiple targets.

Key words *Blumea megacephala* (Randeria) Chang et Tseng, Uterine hemorrhage model of early pregnancy rats, Hemostasis, Blood vessel, Blood

1 Introduction

It is from the aboveground part of *Blumea megacephala* (Randeria) Chang et Tseng, which is widely produced in Guangxi, Yunnan, Sichuan, Guizhou, Guangdong, southern Hunan, southern Jiangxi, Fujian, Taiwan and other regions. In addition, *B. megacephala* is also distributed in northern Vietnam[1]. *B. megacephala* is commonly used in Guangxi Zhuang folk medicine for the treatment of postpartum excessive bleeding through decoction and oral administration[2]. The preliminary experimental results of the research group indicated that extract A had a significant contractile effect on uterine smooth muscle of mice[3]. Therefore, this study investigated the hemostatic effect of extract A on uterine bleeding model in early pregnancy rats, providing scientific basis for its further research.

2 Materials and methods

2.1 Materials

2.1.1 Animals. 120 Wistar rats, (280 ± 20) g, SPF grade, half male and half female, purchased from Changsha Tianqin Biotechnology Co., Ltd., animal license No.: SCXK (Xiang) 2016-0011. Before the experiment, animals were adaptively fed for one week. The male and female experimental rats were housed in separate cages, with 5 rats per cage. They were allowed to drink water freely at room temperature of 20 - 25 ℃ and relative humidity of 45% - 65%.

2.1.2 Drugs and reagents. *B. megacephala* used in the experiment was collected from the suburbs of Nanning City, and it was identified by senior experimenter Zhu Yilin from the School of Pharmacy, Guangxi University of Chinese Medicine as the aboveground part of *B. megacephala*. Yunnan Baiyao, lot No.: ZKA1646; caffeic acid tablets, Dezhou Deyao Pharmaceutical Co., Ltd, lot No.: H37020537; carbazochrome tablets, Yabang Pharmaceutical; misoprostol tablets, Hubei Gedian Renfu Pharmaceutical Co., Ltd., lot No.: H20073696; mifepristone tablets, Hubei Gedian Renfu Pharmaceutical Co., Ltd., lot No.: H20033551; angiotensin II, Nanjing Jiancheng Bioengineering Institute, lot No.: 20180627; rat prostaglandin E_2, Nanjing Jiancheng Bioengineering Institute, lot No.: 20180827; chloral hydrate, Tianjin Damao Chemical Reagent Factory, lot No.: 302-17-0; bovine fibrinogen, Fibrinogen, lot No.: 9001-32-5; bovine serum albumin (BSA), Albumin Bovine, lot No.: 9048-46-8; adenosine diphosphate (ADP), Ruibio, lot No.: 16178-48-6; HEPES, Ruibio, lot No.: 7365-45-9; pNpp, Ruibio, lot No.: XP7171; PBS, Solarbio, lot No.: P1022.

Preparation of extract A: 1.5 kg of dried medicinal herb *B. megacephala* was taken, and water was added for ultrasonic extraction. Then, it was filtered. After concentrating the filtrate, ethanol was added to make the alcohol content around 80%, and let it stand. It was filtered. After the filtrate was dried, 150 g of extract was obtained[4].

2.1.3 Instruments. Microscope, OLYMPUS, lot No.: SZX9; electronic balance, Sartorius Scientific Instruments (Beijing) Co., Ltd., lot No.: SQP; DHG, Shanghai Hongdu Electronic

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△These authors contributed equally to this this work.
Xixue NA, master's degree, Shenggao YIN, master's degree. * Corresponding author. Xiaoqing NING, senior experimentalist, master's degree.

Technology Co., Ltd., lot No.: DHG-914OA; microplate reader (TECAN), Tecan Austria GmbH Untersbergstr, lot No.: 30050303; incubator, Shanghai Hongdu Electronic Technology Co., Ltd., lot No.: DHG-914OA; pipette, Dalong Instrument, lot No.: 7111110; high-speed freezing centrifuge, Shanghai Anting Scientific Instrument Factory, lot No.: TG16-WS; electronic analytical balance, Sartorius Germany, lot No.: JA1003B; fully automatic blood coagulation analyzer, Sysmex, lot No.: CA1500; cell counting board, Shanghai Qiujing Biochemical Reagent Instrument Co., Ltd., lot No.: 02270113; Coag Dx animal blood coagulation analyzer, USA IDEXX.

2.2 Methods

2.2.1 Establishment of postpartum uterine bleeding rat model. Referring to Wang Xiaodong's method[5], female and male rats were put in the same cage in a 1∶1 ratio, and vaginal smear experiment was conducted in the next morning. The presence of sperm or vaginal plugs observed under a microscope was considered pregnancy (D1). Ten non pregnant rats were selected as the blank control group, and 50 successfully pregnant rats were randomly divided into five groups, with 10 rats in each group, namely model group, positive group, high (9.4 g/kg), medium (4.7 g/kg), and low (2.4 g/kg) dose groups of *B. megacephala*. Each group was administered mifepristone solution (12 mg/kg) by gavage at 08:00 and misoprostol solution (120 μg/kg) by gavage at 18:00 on the 7th d of pregnancy (D7), creating an incomplete miscarriage uterine bleeding model in early pregnancy rats. They were administered continuously until the 14th day. One cotton ball was placed in the vagina of rats every day, and was taken out at 08:00 and 18:00 the next day. The cotton ball was sealed and refrigerated for future use, and was replaced with a new cotton ball.

2.2.2 Medication. Ten non pregnant rats were selected as the blank group (physiological saline), and 50 pregnant rats were randomly divided into five groups: model group, positive control group (10 mg/kg of caffeic acid tablet group converted from dosage of human and experimental Wistar rats), high-dose extract A group (9.4 g/kg), medium-dose extract A group (4.7 g/kg), and low-dose extract A group (2.4 g/kg), with 10 rats in each group. On the 8th day of pregnancy, the blank group, model group, and high, medium, and low dose groups were orally administered once a day for continuous 7 d starting from the 8th d after modeling.

2.2.3 Measurement of uterine bleeding volume. 20 μL of rat tail vein blood was taken, and 4 mL of 5% NaOH solution was added to mix well. The absorbance *A* of tail vein blood was measured at an *OD* value of 546 nm using an enzyme-linked immunosorbent assay (ELISA) reader. Each collected uterine bleeding cotton ball was placed in a beaker, and an appropriate amount of 5% NaOH was added according to the amount of bleeding. The cotton ball was wash, and the liquid was filtered, namely the uterine infusion. Under the same absorbance conditions, A value of the uterine bleeding was measured, and the vaginal bleeding volume was calculated.

Vaginal bleeding volume (mL) = [(Tail vein blood flow × *A* value of uterine infusion V_2)/A value of tail vein blood V_1 (4 mL)]

where V_1 is the volume of 50 g/L of NaOH used for diluting the tail vein blood (4 mL); V_2 is the volume of 50 g/L NaOH used for soaking uterine blood.

2.2.4 Blood collection by anesthesia. In 30 min after administration of 14 d (D14), anesthesia was administered via intraperitoneal injection of 0.3 mL/100 g of 10% chloral hydrate. Three blood tubes were collected from the abdominal aorta and set in 5 mL of regular blood collection tube, 2 mL of EDTA blood collection tube, and 2 mL of 3.2% sodium citrate blood collection tube.

2.2.5 Determination of angiotensin II (Ang-II) and prostaglandin E_2 (PGE_2) contents. The serum was isolated from ordinary blood collection tubes, and the levels of PGE_2 and Ang-II were detected by Nanjing Jiancheng Bioengineering Institute.

2.2.6 Determination of four coagulation parameters. 3.2% sodium citrate blood collection tubes were used to separate plasma, and Sysmex fully automatic blood coagulation analyzer was used to detect indicators such as PT (prothrombin time), APTT (activated partial thromboplastin time), TT (thrombin time), and FIB (fibrinogen time).

2.2.7 Platelet adhesion assay. Using the method of Zhong Peiru[6], Buffer A (NaCl 8.47 g, KCl 0.37 g, HEPES 2.38 g, Na_2HPO_4 0.18 g, glucose 1.19 g, BSA 2 g, diluted with distilled water to 1 000 mL, pH 7.4), Buffer B ($CaCl_2$ 0.03 g, $MgSO_4$ 0.07 g, diluted with Buffer A to 100 mL), 15 μmol/L of ADP solution (ADP 25 mg, diluted with Buffer B to 100 mL, as a reserve liquid. 176.7 μL of reserve liquid was taken and diluted with Buffer B to 25 mL), pNpp solution (pNpp 0.05 g, $C_6H_8O_7 \cdot H_2O$ 0.13 g, $Na_3C_6H_5O_7 \cdot 2H_2O$ 0.55 g, TritonX-100 25 μL, diluted to 25 mL, pH 5.4), and 2 mol/L of NaOH solution (method *Chinese Pharmacopoeia*) were prepared. 3.2% sodium citrate blood collection tube was used to separate plasma, and platelets were diluted with Buffer A to 5×10^7/mL of platelet suspension. Platelet cells were counted, and the formula was as below:

5×10^7/mL = [(Total number of cells in the four major grids of the hemocytometer × 10^6)/N]

where *N* is the added volume of Buffer A, thus preparing a platelet suspension with a concentration of 5×10^7/mL for future use.

25 μL of ADP was added to each well of the microreactor plate, and the plate was incubated in a 37 ℃ of water bath. 50 μL of platelet suspension was added to each well, and it was incubated at 37 ℃ for 60 min. The microreactor plate was rinsed twice with PBS solution, and 150 μL of pNpp solution was added to each well to incubate in a greenhouse for 60 min. 100 μL of 2 mol/L NaOH solution was added, to terminate the reaction, and the *OD* value was read at 405 nm.

2.2.8 Platelet aggregation measurement. 3.2% sodium citrate blood collection tube was used to separate plasma, and 100 μL of ADP and 200 μL of platelet suspension were added to each well.

After incubated at 37 ℃ for 60 min, the *OD* value was read at 620 nm.

2.2.9 Platelet number (PLT) measurement. Platelet counting experiment was conducted using two methods. One used the blood samples of EDTA blood collection tube, to measure the number of cells by a fully automatic blood cell counter. The other method was to use the blood samples of sodium citrate blood collection tube. Using a hemocytometer, 10 μL of blood was added each time, covered with a glass cover, and the number of platelet cells was calculated under a microscope. Each calculation was repeated 3 times, and the average value was taken as the number of platelet cells.

2.2.10 Statistical processing. The data was represented by $\bar{x} \pm s$ and processed using SPSS 22.0 software. One-way analysis of variance was used, and pairwise comparisons between samples were conducted using *t*-test. $P < 0.05$ was considered statistically significant.

3 Results and analysis

3.1 Effects on uterine bleeding volume and body weight of early pregnancy rats As shown in Table 1, compared with the model group, the bleeding volume of each dose group of extract A was significantly reduced ($^{*}P < 0.05$). As shown in Table 2, the weight gain rate of non pregnant rats in the blank group was the highest, and the weight gain of rats in the treated group was consistent with that of the model group, without statistical significance.

Table 1 Measurement of uterine bleeding volume in Wistar rats ($n = 10$, $\bar{x} \pm s$)

Group	Dosage	Bleeding volume//L
Blank	–	49.90 ± 4.64
Model	–	706.68 ± 14.33$^{\#}$
Caffeic acid tablet	10.0 mg/kg	522.12 ± 12.49*
High dose	9.4 g/kg	667.76 ± 14.53*
Medium dose	4.7 g/kg	585.06 ± 7.31*
Low dose	2.4 g/kg	590.50 ± 12.00*

NOTE Compared with blank group, $^{\#}$ showed $P < 0.05$, and $^{\#\#}$ showed $P < 0.01$; compared with model group, * showed $P < 0.05$, and ** showed $P < 0.01$. The same in Tables 3 – 5.

Table 2 Effect of extract A on body weight of Wistar rats with early pregnancy hemorrhage ($n = 10$, $\bar{x} \pm s$)

Group	Dosage	Body weight		
		D7//g	D14//g	Weight gain//%
Blank	–	251.2 ± 5.1	281.8 ± 10.2	15.6
Model	–	251.8 ± 11.9	274.2 ± 12.7	8.1
Positive	10.0 mg/kg	255.0 ± 10.2	282.4 ± 12.6	9.7
High dose	9.4 g/kg	251.5 ± 9.8	271.2 ± 18.7	7.3
Medium dose	4.7 g/kg	257.9 ± 15.4	284.6 ± 9.9	9.4
Low dose	2.4 g/kg	247.3 ± 21.2	274.2 ± 32.5	9.8

NOTE Compared with model group, $P > 0.05$.

3.2 Effects on the contents of Ang-II and PGE_2 As shown in Table 3, compared with the blank group, the model group showed an increase in Ang-II content, $P < 0.01$. Compared with the model group, the Ang-II contents of the positive control group and each dose group were lower than that of the model group. Compared with the model group, $P < 0.05$ and $P < 0.01$ were in the positive control group, medium-dose group, and low-dose group, with statistical significance. $P > 0.05$ was in the high-dose group, without statistical significance. Compared with the blank group, the model group showed an increase in PGE_2 content, $P < 0.01$. Compared with the model group, PGE_2 contents of the positive control group and each dose group were all lower than that of the model group. Compared with the model group, $P < 0.05$ was in the positive control group and high-dose group, and $P < 0.01$ was in the low-dose group. $P > 0.05$ was in the medium-dose group, without statistical significance.

Table 3 Determination of Ang-II and PGE_2 content ($\bar{x} \pm s$)

Group	Dosage	Ang-II content//ng/L	PGE_2 content//ng/L
Blank	–	311.13 ± 47.71	279.17 ± 19.36
Model	–	367.72 ± 22.08$^{\#\#}$	300.50 ± 15.92$^{\#\#}$
Caffeic acid tablet	10.0 mg/kg	318.85 ± 45.53*	288.37 ± 13.58*
High dose	9.4 g/kg	311.47 ± 28.17*	270.96 ± 18.68*
Medium dose	4.7 g/kg	321.00 ± 15.06*	278.82 ± 15.55*
Low dose	2.4 g/kg	337.05 ± 12.20**	289.13 ± 10.43**

3.3 Effects on the four coagulation factors As shown in Table 4, compared with the model group, PT, APTT, and TT were shortened, and FIB was increased in the caffeic acid tablet group and each dose group. Compared with the model group, APTT showed $P < 0.05$, $P < 0.01$ in the caffeic acid tablet group and each dose group. Compared with the blank group, the model group showed $P < 0.05$. Compared with the model group, PT in the coffee acid tablet group, high and low dose groups had $P < 0.05$, and PT in the medium dose group had $P > 0.05$. Compared with model group, TT had no statistically significant difference ($P > 0.05$). Compared with the model group, FIB showed $P < 0.05$ in the caffeic acid tablet, high and medium dose groups, and $P > 0.05$ in the low-dose group.

3.4 Effects on platelet function As shown in Table 5, compared with the model group, the platelet adhesion values in the caffeic acid tablet and all dose groups were higher that in the model group, $P < 0.05$, $P < 0.01$. Compared with the blank group, the platelet adhesion value in the model group showed $P < 0.01$. Compared with the model group, the platelet aggregation values in the caffeic acid tablet and all dose groups were higher than that of the model group, with $P < 0.05$ in the caffeic acid tablet group, $P < 0.05$ in the medium-dose group, and $P < 0.01$ in the low-dose group. Compared with the blank group, the platelet aggregation value in the model group showed $P < 0.05$. Compared with the model group, the platelet number (PLT) of EDTA blood collection tubes in the caffeic acid tablet and various dose groups was higher than that in the model group, with $P < 0.05$ in the caffeic acid tablet group and $P > 0.05$ for the rest, indicating no statistical significance. Compared with the model group, the platelet

Table 4 Effects of extract A on four factors of coagulation in rats with early pregnancy hemorrhage ($\bar{x} \pm s$)

Group	Dosage	PT//s	APTT//s	TT//s	FIB//mg/L
Blank	–	9.99 ± 0.37	17.77 ± 1.61	41.74 ± 3.02	1.77 ± 0.18
Model	–	10.17 ± 0.38$^{\#}$	19.04 ± 1.31$^{\#}$	46.55 ± 3.93	1.67 ± 0.13$^{\#}$
Caffeic acid tablet	10.0 mg/kg	10.14 ± 0.18*	18.17 ± 1.18*	45.58 ± 3.41	1.81 ± 0.14*
High dose	9.4 g/kg	10.12 ± 0.28*	17.89 ± 1.23**	45.30 ± 3.54	2.54 ± 0.21*
Medium dose	4.7 g/kg	10.12 ± 0.24	18.40 ± 1.86*	45.07 ± 2.39	1.83 ± 0.24*
Low dose	2.4 g/kg	10.06 ± 0.31*	18.50 ± 1.72*	45.69 ± 2.47	1.80 ± 0.25

Table 5 Effects on platelet function ($\bar{x} \pm s$)

Group	Dosage	Platelet adhesion OD 405 nm	Platelet aggregation OD 620 nm	PLT EDTA//10^9/L	PLT sodium citrate//10^9/L
Blank	–	0.414 ± 0.041	0.120 0 ± 0.010 0	1 157.29 ± 95.89	664.17 ± 69.38
Model	–	0.353 ± 0.049$^{\#\#}$	0.093 4 ± 0.023 3$^{\#}$	1 128.14 ± 76.68	607.50 ± 79.07$^{\#\#}$
Caffeic acid tablet	10.0 mg/kg	0.435 ± 0.078*	0.097 5 ± 0.021 8*	1 295.56 ± 100.75*	775.00 ± 139.21**
High dose	9.4 g/kg	0.430 ± 0.059**	0.101 5 ± 0.022 6	1 168.43 ± 239.37	713.29 ± 70.88**
Medium dose	4.7 g/kg	0.566 ± 0.033*	0.104 7 ± 0.015 2*	1 167.11 ± 91.26	692.25 ± 149.51
Low dose	2.4 g/kg	0.367 ± 0.052**	0.138 1 ± 0.025 5**	1 216.83 ± 160.60	867.17 ± 146.53**

number (PLT) of sodium citrate blood collection tubes in the caffeic acid tablet and various dose groups was higher than that in the model group, with $P < 0.01$ in the caffeic acid tablet, high and low dose groups, and $P > 0.05$ in the medium-dose group, without statistical significance. Compared with the blank group, the platelet number in the model group showed $P < 0.01$.

4 Discussion

Postpartum bleeding" refers to vaginal bleeding exceeding 500 mL within 24 h after delivery, and it is the leading cause of maternal mortality in China and even globally[7]. Traditional Chinese medicine believes that postpartum hemorrhage mostly belongs to the syndrome of massive postpartum vaginal bleeding, and its basic pathological causes are: qi deficiency, blood stasis, and blood heat[8]. In the Zhuang ethnic group, the Zhuang medicine *B. megacephala* is commonly used to treat postpartum hemorrhage. Therefore, it is very meaningful to conduct research on hemostatic efficacy of *B. megacephala*, and investigate the hemostatic effect of extract A from *B. megacephala*, and its effects on the uterus, blood vessels, and blood of a rat uterine bleeding model, in order to provide a basis for whether it can become a new source of hemostatic drugs.

4.1 Effects of extract A on model blood vessels Angiotensin II (Ang-II) is the main component of the circulating renin-angiotensin system (RAS), which is mainly converted from angiotensin I (Ang-I) produced by the action of renin secreted by the periglomerular apparatus by angiotensin-converting enzyme (ACE) acting on angiotensinogen produced by the liver. It is an active polypeptide composed of 8 amino acids, and has effects on vascular smooth muscle, such as strong contraction of blood vessels, promotion of endothelial and vascular smooth muscle cell proliferation[9]. In the area of vascular injury, Ang-II can promote vascular contraction and spasm, aggravate vascular damage[10-11], and affect the occurrence and development of diseases. In the uterine bleeding model group of the experiment, the content of Ang-II was increased. This was due to the administration of mifepristone and misoprostol, which excited and contracted the uterus, promoting embryo expulsion. During the process, the endometrium was compressed, leading to local tissue necrosis and damage to endometrial blood vessels, the inability of local endometrial tissue to function normally. After treatment with a positive control group with hemostatic effect and different concentrations of extract A groups, the content of Ang-II was significantly reduced, reducing damage to blood vessels and indicating the recovery of vascular barrier function, thus achieving the goal of hemostasis. Prostaglandin E_2 (PGE_2) is an important cell growth and regulatory factor, which is a metabolite of arachidonic acid cyclooxygenase and an unsaturated fatty acid of 20 carbons. It is a type of prostaglandin (PG). Its function is to dilate blood vessels and increase organ blood flow. In the uterine bleeding model group of the experiment, the content of PGE_2 was increased due to misoprostol metabolizing a series of PGE derivatives, including PGE_2, which caused organ damage and increased bleeding after vasodilation. After treatment with positive control group and different concentrations of extract A, the content of PGE_2 was decreased, reducing damage to blood vessels. Therefore, extract A may reduce uterine bleeding and achieve hemostasis by adjusting the pathways of Ang-II and PGE_2.

4.2 Effects on blood The coagulation process is complex, and the waterfall theory is commonly used in medicine to explain the coagulation mechanism[12]. The test results of extract A on four coagulation parameters in rats after modeling showed that it could shorten PT, APTT, and TT, and add FIB. According to the research results of Zhang Qinghua *et al.*[13], the effect of fibrinogen in model rats may be related to the collective secretion metabolism during pregnancy, and the hemostatic effect of model rats may be mainly influenced by APTT and PT, achieving hemostatic effects through exogenous and endogenous coagulation pathways.

Platelets are a key component in the normal coagulation mechanism of the body, mainly involved in the formation of coagulation blocks and playing a role in hemostasis. The platelet count statistics of EDTA and sodium citrate blood collection tubes in this experiment showed that extract A promoted an increase in platelet

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loosely arranged after radiation injury, the oocytes showed nuclear condensation and nuclear lysis, and the necrosis of granulosa cells was seen in the follicle cavity. Serological detection of FSH increased, and the levels of LH and E_2 decreased significantly, which was related to the apoptosis of granulosa cells caused by radiation and the impact on the energy supply of oocytes.

After treatment with Zuogui Pill, the body weight and hematopoietic function of rats gradually recovered, and the number of peripheral blood cells increased, and the Zuogui Pill high dose group was significantly better than Progynova group and the Zuogui Pill low dose group. The number of secondary oocytes in the ovaries increases, immune function is restored, the spleen index increases, and serum inflammatory pro-inflammatory factors decrease. This study shows that the mechanism of POF caused by radiotherapy may be related to "blood stasis", so promoting blood circulation and removing blood stasis is a means of treating POF.

References

[1] SUN P, WANG ZH, ZHANG Q, *et al*. Prevention and treatment of chemotherapy-induced premature ovarian failure with traditional Chinese and western medicine[J]. Journal of Basic Chinese Medicine, 2021, 27(11): 1838 - 1842. (in Chinese).

[2] GAO MZ, XU WH, WANG TQ, *et al*. Exploration of Chinese medicine etiology of acute radiation injury[J]. Journal of Traditional Chinese Medicine, 2016, 57(6): 454 - 457. (in Chinese).

[3] BI HZ. Theory of fire pathomechanism of electromagnetic radiation damage[J]. Journal of Basic Chinese Medicine, 2011, 17(5): 576 - 578. (in Chinese).

[4] ZHANG JB (LI JM, collated). Jingyue Quanshu[M]. Beijing: People's Medical Publishing House, 2007: 1283. (in Chinese).

[5] SHANG YJ, CHEN Y, LU S. Systematic review and meta-analysis of Bushen Huoxue Chinese medicine in the treatment of premature ovarian failure[J]. Journal of Traditional Chinese Medicine, 2018, 59(15): 1295 - 1299. (in Chinese).

[6] XIONG XL, WANG QY, ZENG XX, *et al*. Efficacy of Shibuwan Jiawei in treating premature ovarian failure with syndrome of yang deficiency of spleen and kidney and its mechanism[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2018, 24(7): 223 - 227. (in Chinese).

[7] XIA LJ, XIA YB. Clinical research and the effect mechanism on premature ovarian failure treated with acupuncture in recent 20 years[J]. Chinese Acupuncture & Moxibustion, 2018, 38(5): 565 - 570. (in Chinese).

[8] WANG ZX, LIANG XL, LI G, *et al*. Progress on traditional Chinese medicine research of electromagnetic radiation injury[J]. Occupation and Health, 2021, 37(5): 707 - 709. (in Chinese).

[9] WINSHIP AL, STRINGER JM, LIEW SH, *et al*. The importance of DNA repair for maintaining oocyte quality in response to anti-cancer treatments, environmental toxins and maternal ageing[J]. Human Reproduction Update, 2018, 24(2): 119 - 134.

[10] QUAN N, HARRIS LR, HALDER R, *et al*. Differential sensitivity of inbred mouse strains to ovarian damage in response to low-dose total body irradiation[J]. Biology of Reproduction, 2020, 102(1): 133 - 144.

[11] BERTOLDO MJ, DUFFARD N, BERNARD J, *et al*. Effects of bone morphogenetic protein 4 (BMP4) supplementation during culture of the sheep ovarian cortex[J]. Animal Reproduction Science, 2014, 149(3/4): 124 - 134.

[12] LUN BS, LI D, LIU JP, *et al*. Anti-radiation traditional Chinese medicine and natural products: Research advances[J]. Journal of International Pharmaceutical Research, 2015, 42(4): 453 - 462. (in Chinese).

[13] JIN Y L, WU J Y, LU Y, *et al*. Dynamic detection of 6.0 Gy X-irradiation induced the hematopoietic system damage in BALB/c mice[J]. China Medical Herald, 2017, 14(13): 13 - 16. (in Chinese)

[14] WU BY, WANG X, WANG JL, *et al*. Effects of anti-tumor function and survival time of RPS on tumor-bearing mice[J]. Information on Traditional Chinese Medicine, 2012, 29(6): 19 - 21. (in Chinese).

[15] ZHANG R, LUO B, LI F, *et al*. Discussion on the pathogenesis of traditional Chinese medicine of ionizing radiation injury from the theory of pathogenic toxins[J]. Journal of Beijing University of Traditional Chinese Medicine, 2007, 30(9): 595 - 596. (in Chinese).

[16] FENG J, WANG YG, XU CY, *et al*. Study on the mechanism of clearing heat and detoxication and cooling blood method to improve blood coagulation and microcirculation in rats with acute radiation injury[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2019, 34(1): 355 - 358. (in Chinese).

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count; the results of platelet adhesion experiments suggested that extract A can enhance platelet adhesion ability; the results of platelet aggregation experiments showed that extract A can induce platelet adhesion in a rat model. Therefore, extract A can increase the number of platelets, produce platelet adhesion, cause platelet aggregation, and lead to platelet thrombus formation, playing a hemostatic role.

In summary, extract A had hemostatic effects and a significant hemostatic effect on uterine bleeding model of early pregnancy rat. Its function may be induced by affecting blood vessel contraction-relaxation; coagulation factors of the internal and external coagulation systems in the blood; the adhesion and aggregation of platelets, as well as the increase in platelet count, the amount of uterine bleeding, thereby displaying the characteristics of multiple pathways and multi-target effects.

References

[1] Editorial Committee of Flora of China, Chinese Academy of Sciences. Flora of China (Volume 75)[M]. Beijing: Science Press, 1979: 11 - 13. (in Chinese).

[2] FANG D, YIN JY, TAO YP, *et al*. Selected Folk Medicines of the Zhuang Ethnic Group[M]. Nanning: Guangxi Nationalities Publishing House, 1985: 74. (in Chinese).

[3] NA XY, NING XQ, ZHANG WT, *et al*. Determination of caffeic acid in Zhuang medicine Blumea megacephala (Randeria) Chang et Tseng extract and its effect on uterine smooth muscle[J]. Pharmacology and Clinics of Chinese Materia Medica, 2019, 35(3): 71 - 74. (in Chinese).

[4] NING XQ, LU RM, CHEN WW, *et al*. An extract of Blumea riparia and its preparation method and application: China, ZL20171190576.9[P]. 2021 - 01 - 15. (in Chinese).

[5] WANG XD, ZHAO JN, ZHANG BJ, *et al*. Establishment of uterine bleeding model by mifepristoneand misoprostol in eralypregnancy rats[J]. Chinese Pharmacological Bulletin, 1999(2): 90 - 92. (in Chinese).

[6] ZHONG PR. The effect of Danshen injection on the platelet function in the normal and blood stasis rats[D]. Tianjin: Tianjin Medical University, 2005. (in Chinese).

[7] SUN QW, WU JX, WU MF. Medical Physiology, 5th Edition[M]. Beijing: Peking University Medical Press, 2014: 8. (in Chinese).

[8] LIU HQ. Gynecology of Traditional Chinese Medicine[M]. Beijing: Science Press, 2004: 138. (in Chinese).

[9] LIN SY. Renin-angiotensin system and clinical practice[J]. Clinical Focus, 1989, 5(4): 228 - 233. (in Chinese).

[10] LIU J, XU CB. Angiotensin II and its receptors and cardiac ischemia-reperfusion injury[J]. Advances in Cardiovascular Diseases, 1999, 20(3): 18 - 21. (in Chinese).

[11] INAGAMI T, EGUCHI S, NUMAGUCHI K, *et al*. Cross-talk between angiotensin II receptors and the tyrosine kinases and phosphatases[J]. Journal of the American Society of Nephrology, 1999, 10 (Suppl 11): 57 - 61.

[12] XU DY, MA CZ, CHEN PD, *et al*. Experimental study on the hemostatic mechanism of Imperatae Rhizoma Carbonisata[J]. Chinese Traditional Patent Medicine, 2010, 12(32): 2114 - 2117. (in Chinese).

[13] ZHANG QH, ZHANG T, YAO LY. Correlation analysis between plasma fibrinogen and D-dimer levels and missed abortion[J]. Maternal and Child Health Care of China, 2019, 34(4): 881 - 883. (in Chinese).