Effects of *Polygala fallax* Hemsl Water Extract on a Mouse Model of Gastric Motility Disorders

Liangyin ZHU[1], Xiaofeng HAO[1], Liuqi HUANG[1], Zongyuan CHEN[1], Wenfeng CHEN[1], Liu YANG[1], Bingchen HUANG[1], Liyuan LI[2], Aipeng LI[2], Suoyi HUANG[2,3,4*], Xiuzhen SU[2,4*]

1. School of Clinical Medicine, Youjiang Medical University for Nationalities, Baise 533000, China; 2. Key Laboratory of Guangxi Universities on National Medicine in Youjiang River, Youjiang Medical University for Nationalities, Baise 533000, China; 3. School of Pharmacy, Youjiang Medical University for Nationalities, Baise 533000, China; 4. Institute of Life Sciences, Youjiang Medical University for Nationalities, Baise 533000, China

Abstract [**Objectives**] To explore the effects of *Polygona fallax* Hemsl water extract on gastrointestinal motility in normal mice and gastric motility disorder model mice and approximate mechanism. [**Methods**] Using normal mice and mice with gastric motility disorders (modeled with atropine), the effects of different mass concentration groups of *P. fallax* Hemsl water extract (0.125, 0.250, 0.500 g/mL) and domperidone groups on gastric residual rate, small intestine propulsion rate, serum motilin (MLT), vasoactive intestinal peptide (VIP), and tissue morphology were studied. [**Results**] There was a highly significant difference ($P<0.01$) in the small intestine propulsion rate of liquid in normal mice among the different concentration groups of *P. fallax* Hemsl water extract compared to the blank group. The small intestine propulsion rate and gastric residue rate of semi-solid paste were statistically significant compared to the blank group ($P<0.05$). Among them, there was a highly significant difference between the high concentration group (67.75% ±7.65%, 46.5% ±10.62%) and the medium concentration group (60.90% ±5.87%, 59.27% ±7.82%) ($P<0.01$). There was statistical significance in normal mouse serum MLT content in the high concentration group ($P<0.05$). There was no effect on serum VIP levels in normal mice; no effect on the morphology of stomach and intestinal tissues of normal mice. The small intestine propulsion rate and gastric residue rate of liquid and semi-solid paste in mice with gastric motility disorders were statistically significant compared to the atropine group, with extremely significant differences ($P<0.01$). [**Conclusions**] *P. fallax* Hemsl water extract has a promoting effect on gastrointestinal motility. One of the specific mechanisms by which *P. fallax* Hemsl promotes gastrointestinal motility in normal mice may be related to the content of MLT in mouse serum. The mechanism of action in atropine induced gastric paresis mice may be related to the reactivation of M receptors, and the action mechanism of *P. fallax* Hemsl does not change the original histological basis. It can be inferred that *P. fallax* Hemsl water extract has a synergistic effect on promoting gastrointestinal motility through other mechanisms, but it is not fully understood and further in-depth research is needed.

Key words *Polygala fallax* Hemsl, Gastric motility, Mouse model, Gastric emptying, Gastric paresis, Motilin, Vasoactive intestinal peptide

1 Introduction

Polygala fallax Hemsl belongs to *Polygala* of Polygalaceae, and its dry roots are used for medicinal purposes. It has a mild qi and a slightly sweet or non sweet taste, and is a commonly used medicinal herb among ethnic minorities in Guangxi. It has the functional characteristics of tonifying and strengthening, strengthening the spleen and removing dampness, promoting blood circulation and dispersing blood stasis. Currently, it is clinically used for the treatment of hyperlipidemia and acute and chronic viral hepatitis[1-3]. It is also found that *P. fallax* Hemsl has anti damage and inhibitory effects on cell proliferation[4-6]. Its main chemical components include saponins, ketones, and sugars[7].

Functional dyspepsia (FD) is a type of functional gastrointestinal disease[8]. Its main symptoms include upper abdominal pain, upper abdominal distension, early satiety, belching, loss of appetite, nausea, vomiting, *etc*[9]. Currently, gastrointestinal motility promoting drugs are commonly used in clinical treatment[8,10]. This experiment explored the effects of *P. fallax* Hemsl water extract on gastrointestinal motility in normal mice and gastric motility disorder model mice and approximate mechanisms. Using atropine to create gastrointestinal dysfunction models, it opens up new ideas for clinical treatment of functional dyspepsia and provides reference for further research on the pharmacological effects of *P. fallax* Hemsl.

Received: May 2, 2024 Accepted: July 25, 2024
Supported by 2022 National College Student Innovation and Entrepreneurship Training Program (202210599004).
* Corresponding author. E-mail: huangsuoyi@ymun.edu.cn; 00874@ymun.edu.cn

2 Materials and methods

2.1 Experimental reagents *P. fallax* Hemsl used traditional Chinese medicine powder and was purchased from Rongye Trading Co., Ltd. in Yulin City of Guangxi. Motilium Domperidone Tablets, Xian Janssen Pharmaceutical Co., Ltd., lot No.: H1091003; specifications: 10 mg × 30 sheets/plate. Physiological sodium chloride solution, Sichuan Kelun Pharmaceutical Co., Ltd., lot No.: L218042204; specifications: 500 mL/bottle. 98.5% atropine sulfate powder was bought from Shanghai McLean Biochemical Technology Co., Ltd., lot No.: C14360040; specifications: 1 g/bottle. Whole fat sweet milk powder, Yunnan Eurasian Dairy Co., Ltd., specifications: 20 g/bag. Soluble starch, Tianjin Damao Chemical Reagent Factory, lot No.: 20220410; lot No.: 500 g/bottle. Sodium carboxymethyl cellulose, Tianjin Bodi Chemical Co., Ltd., standard No.: Jin Q/HG 3361-99; specifications: 500 g/bag. Anhydrous glucose, Chengdu Kelong Chemical Reagent Factory, lot No.: Q/C 5411196-9; specifications:

500 g/bottle. Activated carbon powder. Carbon ink.

2.2 Experimental animals and equipment SPF-level Kunming mice, male, weight: 20 – 30 g. They were provided by Experimental Animal Center of Youjiang Medical University for Nationalities, and bought from Beijing Weitonglihua Experimental Animal Technology Co., Ltd. License key: SCXK (Jing) 2021-0011. Electric heating sleeve, Shanghai Biaohe Instrument Co., Ltd. Electronic balance, Hangzhou Youheng Weighing Equipment Co., Ltd., model No.: ZN-10002. FA1204B analytical balance, Shanghai Tianmei Balance Instrument Co., Ltd. High-speed desktop centrifuge, model No.: Anting TGL-15B. Mithras LB 943 multifunctional enzyme-linked immunosorbent assay (ELISA) reader, Germany Berthold Company.

2.3 Preparation of medicinal liquid

2.3.1 Preparation of *P. fallax* Hemsl water extract. After weighing, *P. fallax* Hemsl was ground evenly to prepare the medicinal solution. 5 times volume of distilled water was added to *P. fallax* Hemsl powder, and it was heated with a heating sleeve until it was boiled. Keeping it boiling for 1.5 h, the first batch of medicinal liquid was obtained. After filtering with filter paper, the filtrate was collected. Then, 5 times volume of distilled water was added, and it was heated and boiled for 1.5 h. After that, it continued to extract. Finally, all the filtrates were merged. After filtering, a multi-stage flash evaporator was used to evaporate and concentrate. After cooling, distilled water was added to prepare the medicinal solution with a final mass concentration of 0.5 g/mL (0.5 g of raw medicine per milliliter). The obtained medicinal solution was diluted with distilled water to 0.25 and 0.125 g/mL, and they were prepared as the high concentration (0.5 g/mL), medium concentration (0.25 g/mL), and low concentration (0.125 g/mL) of *P. fallax* Hemsl water extract, respectively. After preparation, all water extracts should be stored in a refrigerator at 4 ℃ for later use. Before gavage, it should be equilibrated at the room temperature for 15 min.

2.3.2 Preparation of atropine injection. 0.050 8 g of atropine sulfate was weighed using an analytical balance, and it was dissolved in 500 mL of physiological saline. The concentration of atropine sulfate was approximately 0.1 mg/mL. After preparation, the obtained solution was placed in a refrigerator at 4 ℃ for later use. Before intraperitoneal injection, it should be equilibrated at room temperature for 1 h.

2.3.3 Preparation of nutritious semi-solid paste. 10 g of carboxymethyl cellulose sodium was dissolved in 250 mL of distilled water, and 16 g of milk powder, 8 g of glucose, and 8 g of starch were added to stir well, and a semi-solid paste of about 300 mL was prepared. It was put in a refrigerator at 4 ℃ for later use, and was equilibrated at room temperature for 1 h before gavage.

2.3.4 Preparation of domperidone solution. 20 domperidone tablets were ground and dissolved in 100 mL of distilled water, with a domperidone concentration of 2 mg/mL. After preparation, all water extracts were stored in a refrigerator at 4 ℃ for later use, and were equilibrated at room temperature for 15 min before gavage.

2.4 Effects of *P. fallax* Hemsl water extract on the small intestine propulsion rate of liquid, gastric emptying rate of semi-solid paste, and small intestine propulsion rate of semi-solid paste in normal mice 50 male mice (20 – 30 g) were randomly divided into a blank group, high concentration, medium concentration, and low concentration groups of *P. fallax* Hemsl water extract, and a domperidone group, with 10 mice in each group. After 5 d of adaptive feeding, each group was given distilled water by gavage, corresponding concentration of *P. fallax* Hemsl water extract and 0.2% domperidone solution at a concentration of 10 mL/kg. Continuous gavage was lasted for 3 d, and fasting but drinking was conducted for 24 h before the last gavage. Liquid experiment part: 30 min after the last administration, 0.4 mL of carbon ink was orally administered to each group. After 15 min, the animals were euthanized by cervical dislocation. A laparotomy was performed, and the complete stomach was removed from the cardia to the pylorus, while the complete small intestine was removed from the pylorus to the ileocecal region. It should try not to pull the intestinal segment as much as possible, and the small intestine propulsion rate of liquid in normal mice was calculated. Solid experiment part: 30 min after the last administration, 0.5 mL (approximately 0.5 g) of semi-solid paste was orally administered to each group. After 25 min, the animals were euthanized by cervical dislocation. Laparotomy was performed, and the complete stomach was taken out from the cardia to the pylorus, and was weighed. The stomach was cut along the greater curvature of the stomach. The stomach contents were rinsed with physiological saline, and then dried with filter paper. The weight of the stomach was measured again to calculate the gastric residual rate of semi-solid paste in normal mice. The complete small intestine was removed from the pylorus to the ileocecal region, and the small intestine propulsion rate of semi-solid paste in normal mice was calculated.

2.5 Effects of *P. fallax* Hemsl water extract on serum motilin (MLT) and vasoactive intestinal peptide (VIP) levels in normal mice 100 male mice (20 – 30 g) were randomly divided into a blank group, high concentration, medium concentration, and low concentration groups of *P. fallax* Hemsl water extract, and a domperidone group, with 20 mice in each group. After 5 d of adaptive feeding, each group was given distilled water by gavage, corresponding concentration of *P. fallax* Hemsl water extract and 0.2% domperidone solution at a concentration of 10 mL/kg. Continuous gavage was lasted for 3 d, and fasting but drinking for 24 h was conducted before the last gavage. 45 min after the last administration, the eyeball was removed and blood was collected. The blood naturally coagulated at room temperature for 15 min, and was centrifuged for 20 min (2 500 rpm). The supernatant was carefully collected, and then mouse motilin (MLT) and vasoactive intestinal peptide (VIP) enzyme-linked immunosorbent assay (ELISA) kits were used to determine the MLT

and VIP levels in the obtained serum.

2.6 Effects of *P. fallax* Hemsl water extract on the small intestine propulsion rate of liquid, gastric emptying rate of semi-solid paste, and small intestine propulsion rate of semi-solid paste in a mouse model of gastric motility disorders 60 male mice (20 – 30 g) were randomly divided into a blank group, high concentration, medium concentration, and low concentration groups of *P. fallax* Hemsl water extract, domperidone group, and atropine group, with 10 mice in each group. After 5 d of adaptive feeding, the blank group and atropine group were given distilled water by gavage, and the *P. fallax* Hemsl group was given *P. fallax* Hemsl water extract of corresponding concentration by gavage, and the domperidone group was given 0.2% domperidone solution of 10 mL/kg by gavage. Continuous gavage was lasted for 3 d, and fasting but drinking for 24 h was conducted before the last gavage. 30 min after the last administration, the blank group was injected with physiological saline intraperitoneally, and the remaining groups were injected with 0.1 mL/10 g atropine sulfate solution intraperitoneally. Liquid experiment part: 20 min later, 0.4 mL of carbon ink was orally administered. 15 min later, the animals were euthanized by cervical dislocation. Laparotomy was performed, and the complete stomach was removed from the cardia to the pylorus, while the complete small intestine was removed from the pylorus to the ileocecal region. It should try not to pull the intestinal segment as much as possible, and the small intestine advancement rate of liquid was calculated. Experimental part of semi-solid paste: after 20 min, each group was given 0.5 mL (approximately 0.5 g) of semi-solid paste by gavage. After 25 min, the animals were euthanized by cervical dislocation. Laparotomy was performed, and the complete stomach was taken out from the cardia to the pylorus, and was weighed. The stomach was cut along the greater curvature of the stomach. The stomach contents were rinsed with physiological saline, and then dried with filter paper. The weight of the stomach was measured again to calculate the gastric emptying rate of semi-solid paste. The complete small intestine was removed from the pylorus to the ileocecal region, and the small intestine advancement rate of semi-solid paste was calculated.

2.7 Effects of *P. fallax* Hemsl water extract and domperidone solution on the morphology of stomach and small intestine in normal mice Normal mice were taken from the high, medium, and low concentration groups of *P. fallax* Hemsl water extract, the domperidone solution group, and the blank group. After mice were euthanized by cervical dislocation, laparotomy was performed, and the stomach (middle section of the stomach) and small intestine tissue (clean area 5 – 10 cm below the pylorus) were taken. After the contents were rinsed with physiological saline, they were fixed in 10% formalin solution, and embed in paraffin. After slicing, HE staining was performed, and the morphological changes of the tissue were observed under a microscope.

2.8 Observation indicators Small intestine propulsion rates of liquid and semi-solid paste in normal mice and gastric paresis mice; gastric residual rates of semi-solid paste in normal mice and gastric paresis mice; the effects of different drugs on serum motilin (MLT) and vasoactive intestinal peptide (VIP) levels in normal mice; morphological changes of stomach and small intestine tissues in normal mice under different medications.

$$\text{Small intestine propulsion rate} = [\text{Ink in the small intestine}/\text{Advance distance of semi-solid paste}]/\text{Total length of small intestine} \times 100\% \quad (1)$$

$$\text{Gastric residual rate} = [\text{Total weight of stomach} - \text{Gastric net weight}]/\text{Weight of filled semi-solid paste} \times 100\% \quad (2)$$

2.9 Statistical methods SPSS 26.0 statistical software was used, and one-way ANOVA was used for inter group comparison. $P < 0.05$ showed that the difference was statistically significant; $P < 0.01$ showed extremely significant differences.

3 Resultss and analysis

3.1 Effects of *P. fallax* Hemsl water extract on the small intestine propulsion rate of liquid, gastric emptying rate of semi-solid paste, and small intestine propulsion rate of semi-solid paste in normal mice Seen from Table 1, the small intestine propulsion speed of liquid was significantly accelerated in the high, medium, and low concentration groups of *P. fallax* Hemsl water extract, as well as the domperidone group, and the small intestine propulsion rate of liquid was significantly improved. Compared with the blank group, there was a highly significant difference. Under the condition of $P < 0.01$, there were statistically significant differences in the small intestine propulsion rate of liquid among the groups of normal mice. The high, medium, and low concentration groups of *P. fallax* Hemsl water extract, as well as the domperidone group, showed a significant increase in the small intestine propulsion speed of semi-solid paste, and a significant increase in the small intestine propulsion rate of semi-solid paste. Compared with the blank group, there was a significant difference, with extremely significant differences observed in the medium and high concentration groups and domperidone group. Under the condition of $P < 0.05$, there were statistically significant differences in the small intestine propulsion rate of semi-solid paste between the high concentration group and the low, medium concentration groups, as well as the domperidone group in normal mice. The gastric residual rate of semi-solid paste in the non blank group was significantly reduced, with significant differences compared to the blank group. There were extremely significant differences in the medium concentration, high concentration, and domperidone groups. Under the condition of $P < 0.01$, there were statistically significant differences in the small intestine propulsion rate of semi-solid paste in normal mice between the domperidone group, high concentration group, and medium, low concentration groups.

Table 1 Small intestine propulsion rate of liquid, gastric residue rate of semi-solid paste, small intestine propulsion rate of semi-solid paste in normal mice ($n=10$)

Group	Dosage g · Raw medicine/kg	Small intestine propulsion rate of liquid//%	Small intestine propulsion rate of semi-solid paste//%	Gastric residue rate of semi-solid paste//%
Blank	–	35.53 ± 2.82	46.95 ± 4.29	82.50 ± 12.02
High concentration	5.00	60.70 ± 3.96**	67.75 ± 7.65**	46.50 ± 10.62**
Medium concentration	2.50	51.51 ± 3.01**	60.90 ± 5.87**	59.27 ± 7.82**
Low concentration	1.25	40.44 ± 2.02**	54.14 ± 11.18*	68.50 ± 12.43*
Domperidone	0.02	44.48 ± 3.66**	55.52 ± 4.64*	37.50 ± 12.02**

NOTE Compared with blank group, * showed $P<0.05$, ** showed $P<0.01$. The same below.

3.2 Effects of *P. fallax* Hemsl water extract on serum motilin (MLT) and vasoactive intestinal peptide (VIP) levels in normal mice Seen from Table 2, the MLT content increased in the high concentration group of *P. fallax* Hemsl water extract; when compared with blank group, there was a significant difference. There was no statistically significant difference in VIP content between the different concentration groups of *P. fallax* Hemsl, the domperidone group and the blank group under the condition of $P<0.05$. According to the standard substance, the linear regression equations of serum MLT and VIP enzyme-linked immunosorbent assay kits in normal mice were shown in Fig. 1.

Table 2 Serum MLT and VIP levels in normal mice ($n=10$, pg/mL)

Group	MLT content	VIP content
Blank	27.54 ± 4.76	89.29 ± 6.86
High concentration	33.75 ± 4.73*	92.75 ± 7.84
Medium concentration	26.25 ± 5.74	96.38 ± 8.87
Low concentration	25.75 ± 4.48	83.83 ± 16.17
Domperidone	23.88 ± 7.22	92.20 ± 30.10

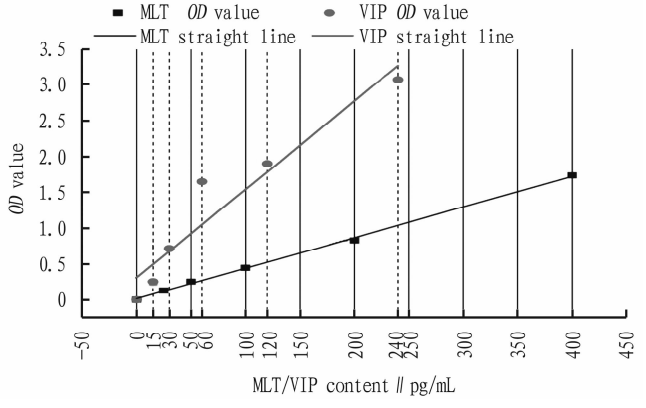


Fig. 1 Linear regression equation of serum MLT and VIP in normal mice

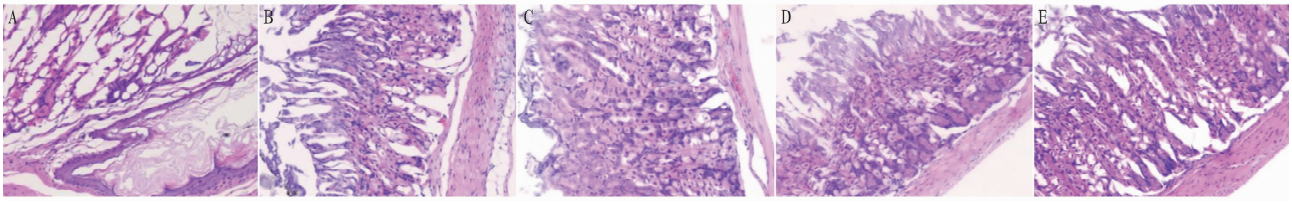
3.3 Effects of *P. fallax* Hemsl water extract on the small intestine propulsion rate of liquid, gastric emptying rate of semi-solid paste, and small intestine propulsion rate of semi-solid paste in a mouse model of gastric motility disorders Seen from Table 3, the small intestine propulsion rate of liquid in the atropine group was lower than that of the other groups, while the small intestine propulsion rate of liquid in the low concentration group of *P. fallax* Hemsl water extract and the domperidone group was significantly accelerated when compared to the blank group, and the small intestine propulsion rate of liquid was significantly improved. When compared with blank group, there was a highly significant difference. Under the condition of $P<0.01$, there were statistically significant differences in the small intestine propulsion rate of liquid between the low concentration group and other groups in the gastric motility disorder model mice. The blank group, the high, medium, and low concentration groups of *P. fallax* Hemsl water extract, and the domperidone group showed a significant increase in the small intestine propulsion speed of semi-solid paste, and a significant improvement in the small intestine propulsion rate of semi-solid paste. When compared with atropine group, there was an extremely significant difference. Under the condition of $P<0.05$, there was no statistically significant difference in the small intestine propulsion rate of semi-solid paste between the non atropine groups. The gastric residual rate of semi-solid paste in the atropine group was significantly increased, and there was a highly significant difference compared to other groups. There was a highly significant difference between the high concentration group and the blank group. Under the condition of $P<0.01$, there were statistically significant differences in the gastric residual rate of semi-solid paste between the high, medium and low concentration groups in mice with gastric motility disorders.

Table 3 Small intestine propulsion rate of liquid in gastric motility disorder model mice ($n=10$)

Group	Dosage g · Raw medicine/kg	Small intestine propulsion rate of liquid//%	Small intestine propulsion rate of semi-solid paste//%	Gastric residual rate of semi-solid paste//%
Blank	–	41.57 ± 7.22##	45.73 ± 2.34##	58.18 ± 14.49##
High concentration	5.00	45.33 ± 2.65##	42.00 ± 5.68##	68.39 ± 3.01**##
Medium concentration	2.50	40.31 ± 5.52##	43.68 ± 13.07##	67.64 ± 8.52##
Low concentration	1.25	57.46 ± 5.36**##	43.11 ± 9.23##	55.64 ± 8.27##
Domperidone	0.02	49.81 ± 3.12**##	39.82 ± 3.25##	62.55 ± 5.37##
Atropine	–	31.89 ± 3.61**	27.00 ± 4.59	82.80 ± 6.48

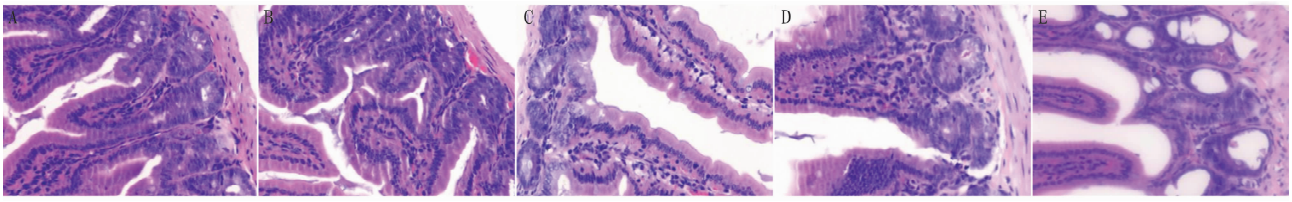
NOTE Compared with blank group, * showed $P<0.05$, ** showed $P<0.01$; compared with atropine group, # showed $P<0.05$, ## showed $P<0.01$.

3.4 Effects of *P. fallax* Hemsl water extract and domperidone solution on the morphology of stomach and small intestine tissues in normal mice No significant lesions were observed in the gastric mucosa and small intestine mucosa of each group of experiments. The specific experimental results were shown in Fig. 2 – 3.



NOTE A. Low concentration group of *P. fallax* Hemsl; B. Medium concentration group of *P. fallax* Hemsl; C. High concentration group of *P. fallax* Hemsl; D. Blank group; E. Domperidone group.

Fig. 2 Morphology of gastric mucosal tissue in normal mice (HE, ×200)



NOTE A. Low concentration group of *P. fallax* Hemsl; B. Medium concentration group of *P. fallax* Hemsl; C. High concentration group of *P. fallax* Hemsl; D. Blank group; E. Domperidone group.

Fig. 3 Morphology of small intestinal mucosal tissue in normal mice (HE, ×400)

4 Discussion

Research has shown that the various pathogenesis of FD are not completely independent, but rather interact with each other[11-12]. Currently, research has found that cholinergic M receptors, adrenaline α receptors and β receptors, histamine receptors, and various gastrointestinal hormone receptors mainly exist in the gastrointestinal tract. The M receptor is mainly distributed in effector cells innervated by the parasympathetic nervous system, sweat glands innervated by the sympathetic nervous system, and smooth muscle cell membranes in skeletal muscle blood vessels. When the M receptor is excited, the gastrointestinal tract produces a parasympathetic nerve excitation effect: contraction of gastrointestinal smooth muscles. α receptor is one of the receptors that can bind to the norepinephrine and adrenaline released by the sympathetic postganglionic fibers. When combined with norepinephrine and adrenaline, they can inhibit the smooth muscle of the small intestine and cause it to relax. β receptor has weaker gastrointestinal forces. D2 receptor in dopamine receptors is mainly concentrated in the gastrointestinal tissue and has a significant impact on the gastrointestinal tract. When dopamine acts on the D2 receptor, it can inhibit the peristalsis and tension recovery of the upper gastrointestinal tract, inhibit gastric emptying, reduce the movement of the gastric antrum and duodenum, and also weaken the peristalsis of the esophagus and the tension of the lower esophageal sphincter. Motilin (MTL) is a type of gastrointestinal hormone and a contraction related indicator. It is mostly secreted by mucosal cells in the duodenum and jejunum, which can accelerate gastric emptying and improve small intestine peristalsis.

Domperidone is a gastrointestinal motility promoting drug, and its pharmacological mechanism is specific binding to dopamine receptors, effectively blocking the inhibitory effect of the neurotransmitter dopamine on gastrointestinal smooth muscle, thereby promoting gastric emptying. Atropine is an M-receptor blocker that inhibits the binding of acetylcholine to choline receptors, slowing down the contraction of gastrointestinal smooth muscle and inhibiting gastric emptying. As a result, the residual amount in the model group's stomach is significantly higher than that in the blank group, causing gastric motility disorders. In similar experiments, scholars such as Qi Yue found that the mice in the 1 mg/kg atropine group had the highest residual amount of gastric contents. However, with the increase of atropine dosage, the residual amount of gastric contents in each group of mice decreased, and they exhibited varying degrees of excitement and irritability[13]. Therefore, we also chose a dose group of 1 mg/kg of atropine as the modeling dose for a mouse atropine gastric motility disorder model.

In the small intestine propulsion rate experiments of liquid and semi-solid paste in normal mice, the small intestine propulsion rates of the high, medium, and low concentration groups of *P. fallax* Hemsl and the domperidone group were higher than those of the blank group. Among them, the small intestine propulsion rates of the high and medium concentration groups of *P. fallax* Hemsl were better than the domperidone group, indicating that the *P. fallax* Hemsl water extract had the effect of accelerating small intestine movement in normal mice. In the residue rate experiment of semi-solid paste in normal mice, the gastric residue rates of the high, medium, and low concentration groups of *P. fallax* Hemsl and the domperidone group were lower than that of the blank group, indicating that *P. fallax* Hemsl water extract had the effect of accelerating gastric emptying in normal mice. Among them, the gastric residue rate of the domperidone group was lower than that of *P. fallax* Hemsl group. Compared with the domperidone group, the effect of *P. fallax* Hemsl water extract was more significant in the small intestine. In the experiment on the effects of different

drugs on serum motilin (MLT) and vasoactive intestinal peptide (VIP) levels in normal mice, only the serum MLT level in high concentration group of *P. fallax* Hemsl had statistical significance, indicating that the drug contained substances that stimulated MTL release, but the concentration needed to be at 0.5 g/mL of the raw material to take effect. However, the serum VIP content was not statistically significant, indicating that the effect of *P. fallax* Hemsl was not related to VIP. In the study on the effects of different drugs on the tissue morphology of the gastric and small intestinal mucosa in normal mice, no significant changes were observed in each group compared to the blank group. Therefore, it can be concluded that the mechanism of enhancing normal gastrointestinal motility by various concentrations of *P. fallax* Hemsl water solution and domperidone solution would not cause changes in tissue morphology.

In the small intestine propulsion rate experiments of liquid and semi-solid paste in gastric motility disorder model mice, the high, medium, and low concentration groups of *P. fallax* Hemsl, the domperidone group, and the blank group had higher small intestine propulsion rates than the atropine group. Among them, the low concentration group was the most significant, and it did not show a linear relationship with concentration. It can be inferred that there may be a substance concentration in the low concentration group that can reactivate the M receptor blocked by atropine, causing the low concentration of the drug to reverse the effect of atropine and result in enhanced small intestine motility. In the residue rate experiment of semi-solid paste in gastric motility disorder model mice, the gastric residue rate showed a similar situation to the small intestine propulsion rate. The gastric residue rates of the high, medium, and low concentration groups of *P. fallax* Hemsl, the domperidone group, and the blank group were lower than that of the atropine group, with the low concentration group showing the strongest performance. It can be inferred that the low concentration of this drug can reverse the effect of atropine and result in enhanced gastric motility.

In summary, *P. fallax* Hemsl water extract had a promoting effect on gastrointestinal motility. One of the specific mechanisms by which *P. fallax* Hemsl promoted gastrointestinal motility in normal mice may be related to the content of MLT in mouse serum. The mechanism of action in atropine induced gastric paresis mice may be related to the reactivation of M receptors, and the action mechanism of *P. fallax* Hemsl did not change the original histological basis. It can be inferred that there are other synergistic effects of *P. fallax* Hemsl water extract on gastrointestinal motility, but it is not fully understood and further in-depth research is needed.

References

[1] State Administration of Traditional Chinese Medicine. Chinese Materia Medica[M]. Shanghai: Shanghai Science and Technology Press, 1999. (in Chinese).

[2] HUANG SG, CHEN XY, LI ZW, *et al.* Clinical observation on 30 cases of hyperlipidaemia treated with *Polygala fallax* Hemsk[J]. Hunan Journal of Traditional Chinese Medicine,1999,15(3): 6-8. (in Chinese).

[3] LIANG JS, SHA XY, WANG L. Bailiang soup for the treatment of chronic hepatitis in 48 cases[J]. Journal of Chinese Medicinal Materials, 2000,23(8): 511-512. (in Chinese).

[4] WANG M, LIU X, WANG M, *et al.* The extract of *Polygala fallax* Hemsl. Slows the progression of diabetic nephropathy by targeting TLR4 anti-inflammation and MMP-2/9-mediatanti-fibrosis in vitro[J]. Phytomedicine, 2022(104): 1-15.

[5] YAO ZR, LI Y, WANG ZW, *et al.* Research on anti-hepatocelllular carcinoma activity and mechanism of *Polygala fallax* Hemsk[J]. Journal of Ethnopharmacology, 2020, 260(5): 113062.

[6] CHAO SW, XU Q, DONG SN, *et al. Polygala fallax* Hemsl. combined with compound Sanqi granules relieves glomerulonephritisby regulating proliferation and apoptosis of glomerular mesangial cells[J]. Journal of International Medical Research, 2020, 48(1): 1-10.

[7] ZHANG CL, ZHANG KF, XU YR, *et al.* Progress of chemical composition and pharmacological activity of the *Polygala fallax* Hemsl[J]. China Pharmacy, 2017, 28(19): 2724-2728. (in Chinese).

[8] NONG M, WEI GY, LUO QS, *et al.* Study on the effect of auricular pressure bean on enteral nutrition feeding intolerance in neurocritical patients[J]. Journal of Youjiang Medical University for Nationalities, 2023, 45(1): 164-167. (in Chinese).

[9] POTTER M, TALLEY NJ. New insights into functional dyspepsia: Further evidence for postprandial distress syndrome as a distinct disease[J]. Lancet Gastroenterol Hepatol, 2018, 3(4): 217-218.

[10] MOAYYEDI P, SOO S, DEEKS J, *et al.* Pharmacological interventions for non-ulcer dyspepsia[J]. Cochrane Database of Systematic Reviews, 2004, 18(4): CD001960.

[11] DE LA ROCA-CHIAPAS JM, SOLÍS-ORTIZ S, FAJARDO-ARAUJO M, *et al.* Stress profile, coping style, anxiety, depression, and gastric emptying as predictors of functional dyspepsia: A case-control study[J]. Journal of Psychosomatic Research, 2010, 68(1): 73-81.

[12] DI STEFANO M, MICELI E, TANA P, *et al.* Fasting and postprandial gastric sensorimotor activity in functional dyspepsia: Postprandial distress vs. epigastric pain syndrome[J]. The American Journal of Gastroenterology, 2014, 109(10): 1631-1639.

[13] QI Y, JIANG H, WANG SH, *et al.* Effect of Zhongjing Wenwei granule on chronic atrophic gastritis rat model induced by ammonia water[J]. Journal of Liaoning University of Traditional Chinese Medicine, 2016, 18(5): 34-36. (in Chinese).

(From page 100)

[3] CHEN YP, XIAO BQ, ZHANG JH, *et al.* Establishment of new nonalcoholic fatty liver model and investigation of immune cell mechanism[J]. China Pharmacology Bulletin, 2018, 34(6): 882-886. (in Chinese).

[4] PAN L, ZHANG JB, CUI RG, *et al.* Establishment of a C57BL/6 mouse model of nonalcoholic fatty liver disease[J]. China Tissue Engineering Research, 2016, 20(40): 6054-6059. (in Chinese).

[5] DYSON JK, MCPHERSON S, ANSTEE QM. Republished: Non-alcoholic fatty liver disease: Non-invasive investigation and risk stratification [J]. Postgraduate Medical Journal, 2014, 90(1063): 254-266.

[6] WHITE DL, KANWAL F, EL-SERAG, *et al.* Association between nonalcoholic fatty liver disease and risk for hepatocellular cancer, based on systematic review[J]. Clinical Gastroenterology & Hepatology, 2012, 10(12): 1342-1359.

[7] CHI SC. Progress and perspectives in the pathogenesis of cirrhosis of nonalcoholic steatohepatitis[J]. Journal of Practical Liver Diseases, 2018, 21(2): 166-169.

[8] EUSEHWANDER-TETRI BA, CLARK JM, BASS NM, *et al.* Clinical, laboratory and histological associations in adults with nonalcoholic fatty liver disease[J]. Hepatology, 2010, 52(3): 913-924.

[9] QIU ZC, CHEN YX, ZHOU RL, *et al.* Experimental study of immune liver fibrosis in rats[J]. Chinese Medicinal Materials, 2010, 33(6): 974-976. (in Chinese).

[10] HA MH, HUANG ZM, TANG DX, *et al.* Efficacy observation of Shuanghuanglian combined with Xiaoyao Powder in the treatment of chronic hepatitis B[J]. Journal of Integrated Chinese and Western Medicine, 2016, 26(4): 222-223. (in Chinese).