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• *BRIEF REPORTS* •

Effects of rhubarb on isolated gastric muscle strips of guinea pigs

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Abstract

AIM: To study the effects of rhubarb (dried root of *Rheum officinale* Baill.) on contractile activity of isolated gastric muscle strips of guinea pigs and its possible mechanism.

METHODS: A total of 48 guinea pigs were killed to remove the whole stomach. Then, the stomach was opened and the mucosal layer was removed. Parallel to the circular fibers, muscle strips were cut from the body. Each isolated gastric muscle strip was suspended in a tissue chamber containing 5 mL Krebs solution, constantly warmed by water jacket at 37 ℃ and bubbled continuously with a mixed gas of 950 mL/L O_2 and 50 mL/L CO_2. After being incubated for 1 h with 1 g tension, rhubarb of varied concentrations (1%, 2%, 7%, 20% and 70%) was added cumulatively into the tissue chamber at intervals of 2 min. Atropine (10^{-6} mol/L) or isoptin (5×10^{-8} mol/L) or hexamethonium (10^{-5} mol/L) was given 2 min before the administration of rhubarb. The isometrical response was measured with an ink-writing recorder.

RESULTS: Rhubarb dose dependently increased the resting tension of gastric body circular muscle (CM) (r = 0.726, P<0.05). Atropine (r = 0.829, P<0.05), isoptin (r = 0.764, P<0.05) and hexamethonium (r = 0.797, P<0.05) did not affect its action in a dose-related manner. Atropine apparently reduced the increasing action of 1%, 3%, 10%, 30% and 100% rhubarb on the resting tension of gastric body CM. Isoptin inhibited the effect of 10%, 30% and 100% rhubarb on the resting tension of gastric body CM. Hexamethonium reduced the increasing action of 1%, 10%, 30% and 100% rhubarb on the resting tension of gastric body CM. Rhubarb increased the contractile frequency of CM of body. While atropine, isoptin and hexamethonium did not inhibit the contractile frequency of gastric body CM in comparison with rhubarb at the same concentration, rhubarb at the highest concentration (100%) decreased the mean contractile amplitude of gastric body CM. Atropine, isoptin and hexamethonium did not affect the mean contractile amplitude of gastric body CM compared to rhubarb at the same concentration.

CONCLUSION: Rhubarb has exciting actions on isolated gastric smooth muscle strips of guinea pig. The exciting action of rhubarb is partly mediated via cholinergic M receptor, cholinergic N receptor and L-type calcium channel.

Key words: Rhubarb; Stomach; Smooth muscle; Muscle contraction; Cholinergic receptor; Calcium channel; Guinea pigs

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INTRODUCTION

Recently, close attention has been paid to the Chinese drugs that affect the alimentary tract and are used to treat gastrointestinal motility disorder. Rhubarb is the root of *Rheum palmatum* L. or *Rheum officinale* Baill. or *Rheum tanguticum* Maxim. et Regel. of polygonaceae. The roots of *Rheum palmatum* L. and *Rheum officinale* Baill. have a long tradition as laxative and it is well known that they can increase the emptying movement of large intestine. So it is used to treat constipation, intestinal tympanies, intestinal obstruction, *etc.* Recently, the effects of rhubarb decoction on co-ordinating and promoting the gastrointestinal motility *in vivo* have been reported[1]. But the effects of rhubarb on isolated gastric muscle strips of guinea pigs have not been reported, so we studied the action of rhubarb on gastric smooth muscle of guinea pigs and the possible mechanism involved. *Rheum officinale* Baill. was used in this study.

MATERIALS AND METHODS

Materials

Rhubarb was ground into coarse powder, boiled in distilled water, filtered and made into 100% (1 000 g/L) extract solution (the drug was made and identified by Gansu Institute for Drug Control). The 100% rhubarb extract solution was dispensed at the concentration of 1%, 2%, 7%, 20% and

Table 1 Effect of rhubarb and antagonists plus rhubarb on the resting tension of gastric body CM of guinea pigs (mean±SE, n = 12)

Group	0	1%	3%	10%	30%	100%
Rhubarb	1.00	1.04±0.02[a]	1.15±0.05[a]	1.42±0.08[b]	1.75±0.08[b]	1.88±0.08[b]
Atropine (10^{-6}mol/L)+rhubarb	1.00	1.00[c]	1.02±0.01[c]	1.08±0.02[b,d]	1.19±0.03[b,d]	1.43±0.06[b,d]
Isoptin (5×10^{-8}mol/L)+rhubarb	1.00	1.01±0.01	1.03±0.02	1.09±0.04[a,d]	1.23±0.05[b,d]	1.42±0.06[b,d]
Hexamethonium (10^{-5}mol/L)+rhubarb	1.00	1.00[c]	1.05±0.02[a]	1.10±0.02[b,d]	1.24±0.05[b,d]	1.39±0.04[b,d]

[a]P<0.05, [b]P<0.01 *vs* control; [c]P<0.05, [d]P<0.01 *vs* rhubarb in the same concentration.

70% respectively. Atropine was purchased from Shanghai Harvest Pharmaceutical Co., Ltd. Isoptin and hexamethonium were from Sigma (St. Louis, MO, USA). Krebs buffer solution contained (mmol/L) NaCl 120.6, KCl 5.9, NaH_2PO_4 1.2, $MgCl_2$ 1.2, $NaHCO_3$ 15.4, $CaCl_2$ 2.5 and $C_6H_{12}O_6$ 11.5.

JZ-BK external isometric force transducer was from BK Company. LMS-ZB two channels recorder was purchased from Chengdu Equipment Factory.

Guinea pigs, weighing 350-450 g, were provided by the Animal Center of Lanzhou Medical College.

Methods

Guinea pigs, weighing 350-450 g, were fasted with free access to water for 24 h. Then they were hit to lose consciousness and the whole stomach was removed. The stomach was opened along the greater curvature, and rinsed with Krebs solution. The stomach was pinned on a wax block with the mucosa side up, and the mucosal layer was gently removed with a pair of scissors. Parallel to circular fibers of the body, muscle strips (8 mm×2 mm) were cut and named as circular muscle (CM) of the body[2,3].

Each strip with mucosa removed was suspended in a tissue chamber containing 5 mL Krebs solution, constantly warmed by circulating water jacket at 37 ℃ and supplied with a mixed gas of 950 mL/L O_2 and 50 mL/L CO_2. One end of the strip was fixed to a hook on the bottom of the chamber, while a thread was used to connect JZ-BK at the top and the other end. Preparation was subjected to 1 g load tension and washed with 5 mL Krebs solution every 20 min. The contractions of the gastric body CM in tissue chambers were simultaneously recorded on LMS-ZB. After being incubated for 1 h, rhubarb (1%, 2%, 7%, 20% and 70%) was added into the 5 mL tissue chamber continuously at intervals of 2 min, so that its cumulative concentration reached 1%, 3%, 10%, 30% and 100%. Atropine (10^{-6} mol/L) or isoptin (5×10^{-8} mol/L) or hexamethonium (10^{-5} mol/L) was given 2 min before administration of rhubarb[2-6].

Statistical analysis

We measured the resting tension and the mean contractile amplitude of gastric body CM. Frequency of contractions was calculated by counting the contraction waves per minute. Values of the results were presented as mean±SE. The data were analyzed with Student's t test, and the correlation coefficients were calculated, P<0.05 was considered statistically significant.

RESULTS

Effect of rhubarb on the resting tension of gastric body CM

Rhubarb dose dependently increased the resting tension of gastric body CM (r = 0.726, P<0.05). Atropine (r = 0.829, P<0.05), isoptin (r = 0.764, P<0.05) and hexamethonium (r = 0.797, P<0.05) did not affect its action in a dose-related manner. Atropine apparently reduced the increasing action of 1% (P<0.05), 3% (P<0.05), 10% (P<0.01), 30% (P<0.01) and 100% (P<0.01) rhubarb on the resting tension of gastric body CM. Isoptin inhibited the effect of 10% (P<0.01), 30% (P<0.01) and 100% (P<0.01) rhubarb on the resting tension of gastric body CM. Hexamethonium reduced the increasing action of 1% (P<0.05), 10% (P<0.01), 30% (P<0.01) and 100% (P<0.01) rhubarb on the resting tension of gastric body CM (Table 1 and Figure 1).

Effect of rhubarb on the contractile frequency of gastric body CM

Rhubarb increased the contractile frequency of gastric body CM (P<0.05), while atropine, isoptin and hexamethonium did not inhibit the contractile frequency of gastric body CM in comparison with rhubarb at the same concentration (Table 2).

Effect of rhubarb on the mean contractile amplitude of gastric body CM

Rhubarb at the highest concentration (100%) decreased the mean contractile amplitude of gastric body CM (P<0.05).

Table 2 Effect of rhubarb and antagonists plus rhubarb on the contractile frequency of gastric body CM of guinea pigs (mean±SE, n = 12)

Group	0	1%	3%	10%	30%	100%
Rhubarb	5.40±0.08	5.48±0.10	5.45±0.09	5.61±0.11[a]	5.60±0.09[a]	5.73±0.10[b]
Atropine (10^{-6}mol/L)+rhubarb	5.40±0.10	5.43±0.12	5.42±0.12	5.46±0.15	5.53±0.16	5.59±0.12
Isoptin (5×10^{-8}mol/L)+rhubarb	5.35±0.11	5.32±0.10	5.38±0.09	5.36±0.10	5.47±0.09	5.63±0.17[a]
Hexamethonium (10^{-5}mol/L)+rhubarb	5.43±0.05	5.48±0.04	5.48±0.05	5.48±0.04	5.53±0.04[a]	5.61±0.06[a]

[a]P<0.05, [b]P<0.01 *vs* control.

Table 3 Effect of rhubarb and antagonists plus rhubarb on the mean contractile amplitude of gastric body CM of guinea pigs (mean±SE, n = 12)

Group	0	1%	3%	10%	30%	100%
Rhubarb	0.59±0.10	0.59±0.11	0.64±0.11	0.51±0.09	0.47±0.10	0.36±0.07[b]
Atropine (10^{-6}mol/L)+rhubarb	0.57±0.10	0.55±0.10	0.51±0.09[a]	0.48±0.10[a]	0.44±0.10[a]	0.33±0.07[a]
Isoptin (5×10^{-8}mol/L)+rhubarb	0.59±0.09	0.53±0.08	0.49±0.07[b]	0.44±0.07[a]	0.56±0.12	0.53±0.10
Hexamethonium (10^{-5}mol/L)+rhubarb	0.59±0.12	0.55±0.12[a]	0.54±0.11[a]	0.52±0.11[a]	0.48±0.10[a]	0.42±0.09[a]

[a]P<0.05, [b]P<0.01 *vs* control.

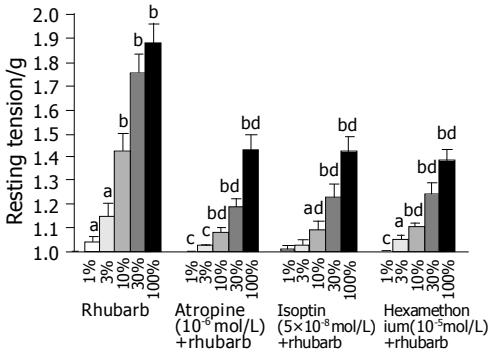

Figure 1 Effect of rhubarb and antagonists plus rhubarb on the resting tension of gastric body CM of guinea pigs. [a]P<0.05, [b]P<0.01 *vs* control; [c]P<0.05, [d]P<0.01 *vs* rhubarb at the same concentration.

Atropine, isoptin and hexamethonium did not affect the mean contractile amplitude of gastric body CM compared to rhubarb at the same concentration (Table 3).

DISCUSSION

Many diseases are caused by gastrointestinal motility or accompany gastrointestinal motility abnormality, such as gastroparesis, gastroesophageal reflux, gastric dysrhythmias, gastric ulcer[7-9]. There are some reports on the study of normal gastrointestinal motility and gastric diseases that are connected with gastric motility[8,9]. The studies on how to treat the diseases that are caused by gastric motility disorder have also been reported[7,10]. But it still needs a long time for us to recognize gastric motility completely.

Recently, the effects of Chinese herbs on the gastrointestinal motility have been reported[11-13]. Rhubarb has been used to treat constipation, intestinal tympanies, intestinal obstruction, *etc*. The present study revealed that rhubarb increased the resting tension and the contractile frequency of gastric body CM. Rhubarb at low and middle concentrations did not affect the mean contractile amplitude of gastric body CM. Rhubarb at the highest concentration (100%) decreased the mean contractile amplitude of gastric body CM, suggesting that rhubarb has a promoting action on the isolated strips of gastric body of guinea pigs.

All smooth muscles are involuntary and the nerves in the gastrointestinal tract are controlled both by extrinsic autonomic nerves and by intrinsic neural plexus. These plexus extensively interact with each other and are out of extrinsic neural control. Many local neurogenic reflexes in the gut occur in these plexus, and play an important role in regulating the gastrointestinal motility. Cholinergic N-receptor exists on the membrane of nerve ganglion cells of cholinergic M receptor on the membrane of gastric smooth muscles. Our experiment showed that atropine (muscarinic cholinergic antagonist) could partly block the increased action of rhubarb on the isolated strips of gastric body of guinea pigs. Isoptin (L-type calcium channel blocker) and hexamethonium (nicotinic cholinergic antagonist) had the same effect on gastric body, suggesting that effect of rhubarb can be partly mediated via cholinergic M receptor, cholinergic N receptor and L-type calcium channel.

There are many studies on gastrointestinal motility in recent years[10,14]. The effects of some Western medicines on modulating gastric motility have already been accepted, for example the medicines of promoting gastric motility have already been accepted, such as cisapride, erythromycin[15-17]. Because of their high price and side effects, they are limited in clinical application. Chinese herbs that can modulate gastrointestinal motility have been studied. We should further study single Chinese herbs, and search for safe, valid and cheap Chinese herbs that can modulate gastrointestinal motility.

REFERENCES

1 **Chen X**, Ran R. Rhubarb decoction prevents intestinal bacterial translocation during necrotic pancreatitis. *Huaxi Yike Daxue Xuebao* 1996; **27**: 418-421
2 **Wang F**, Luo JQ, Zhen TZ, Qu SY, Li W, He DY. Effect of oxytocin on the contractile activity of gastric strips of rats *in vitro*. *Zhongguo Yaolixue Yu Dulixue Zazhi* 1999; **13**: 285-287
3 **Li W**, Zhen TZ, Zhang YF, Qu SY, Ding YH, Wei YL. Effect of Dangshen and Zhishi on contractile activity of isolated gastric muscle strips in rats. *Zhongguo Zhongyi Jichu Yixue Zazhi* 2001; **7**: 31-33
4 **Li W**, Zheng TZ, Qu SY, Ding YH, Wei YL. Effect of Cangzhu on isolated gastric muscle strips in rats. *Zhongyao Yaoli Yu Linchuang* 1999; **15**: 29-30
5 **Zheng TZ**, Li W, Qu SY, Ding YH, Wei YL. Effect of Radix Astragali on contractile activity of gastric muscle strips in rats. *Zhongyao Yaoli Yu Linchuang* 1999; **15**: 22-24
6 **Li W**, Zheng TZ, Qu SY, Zhang YF, Tian ZF, Ding YH, Wei YL. Effect of Peilan on contractile activity of gastric muscle strips in rats. *Lanzhou Yi Xueyuan Xuebao* 2000; **26**: 3-4
7 **Horowitz M**, Su YC, Rayner CK, Jones KL. Gastroparesis: prevalence, clinical significance and treatment. *Can J Gastroenterol* 2001; **15**: 805-813
8 **Estevao-Costa J**, Campos M, Dias JA, Trindade E, Medina AM, Carvalho JL. Delayed gastric emptying and gastroesophageal reflux: a pathophysiologic relationship. *J Pediatr Gastroenterol Nutr* 2001; **32**: 471-474
9 **Pfaffenbach B**, Adamek RJ, Bartholomaus C, Wegener M. Gastric dysrhythmias and delayed gastric emptying in

patients with functional dyspepsia. *Dig Dis Sci* 1997; **42**: 2094-2099
10 **Washabau RJ**. Gastrointestinal motility disorders and gastrointestinal prokinetic therapy. *Vet Clin North Am Small Anim Pract* 2003; **33**: 1007-1028, vi
11 **Qi QH**, Wang J, Hui JF. Effect of dachengqi granule on human gastrointestinal motility. *Zhongguo Zhongxiyi Jiehe Zazhi* 2004; **24**: 21-24
12 **Zhang HQ**, Xu ZX, Wu YQ, Zhou CH. Effect of Compound Rhubarb Mixture on contraction of isolated small intestinal smooth muscle of rabbit. *Zhongxiyi Jiehe Xuebao* 2004; **2**: 210-212
13 **Zhou CH**, Wu YQ, Xu ZX, Zhang HQ. Effect and mechanism of emodin on small intestine. *Zhongguo Yaolixue Tongbao* 2003; **19**: 1421-1424
14 **Monnikes H**, Tebbe JJ, Hildebrandt M, Arck P, Osmanoglou E, Rose M, Klapp B, Wiedenmann B, Heymann-Monnikes I. Role of stress in functional gastrointestinal disorders. Evidence for stress-induced alterations in gastrointestinal motility and sensitivity. *Dig Dis* 2001; **19**: 201-211
15 **MacLaren R**, Patrick WD, Hall RI, Rocker GM, Whelan GJ, Lima JJ. Comparison of cisapride and metoclopramide for facilitating gastric emptying and improving tolerance to intragastric enteral nutrition in critically III, mechanically ventilated adults. *Clin Ther* 2001; **23**: 1855-1866
16 **Boivin MA**, Carey MC, Levy H. Erythromycin accelerates gastric emptying in a dose-response manner in healthy subjects. *Pharmacotherapy* 2003; **23**: 5-8
17 **Berne JD**, Norwood SH, McAuley CE, Vallina VL, Villareal D, Weston J, McClarty J. Erythromycin reduces delayed gastric emptying in critically ill trauma patients: a randomized, controlled trial. *J Trauma* 2002; **53**: 422-425

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