Effects of rhubarb on isolated gastric muscle strips of guinea pigs

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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 a water jacket at 37 °C and bubbled continuously with a mixed gas of 95% O<sub>2</sub> and 5% CO<sub>2</sub>. 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<sup>-6</sup> mol/L) or isoptin (5×10<sup>-6</sup> mol/L) or hexamethonium (10<sup>-6</sup> mol/L) was given 2 min before the administration of rhubarb. The isometric 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.

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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[3]. 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...
Rhubarb at the highest concentration (100%) decreased the mean contractile amplitude of gastric body CM (P<0.05).

**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) 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 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±0.02a| 1.15±0.05a| 1.42±0.06a| 1.75±0.08a| 1.88±0.08a|
| Atropine (10⁻⁶ mol/L)+rhubarb | 1.00| 1.00a| 1.02±0.01a| 1.08±0.02a| 1.19±0.03a| 1.43±0.06a|
| Isoptin (5×10⁻⁶ mol/L)+rhubarb | 1.00| 1.01±0.01| 1.03±0.02| 1.09±0.04a| 1.23±0.05a| 1.42±0.06a|
| Hexamethonium (10⁻⁵ mol/L)+rhubarb | 1.00| 1.00a| 1.05±0.02a| 1.10±0.02a| 1.24±0.05a| 1.39±0.04a|

*P<0.05, *P<0.01 vs control; **P<0.05, ***P<0.01 vs rhubarb in the same concentration.

### 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±0.11a| 5.60±0.09a| 5.73±0.10a|
| 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 (5×10⁻⁶ 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±0.17a|
| Hexamethonium (10⁻⁵ mol/L)+rhubarb | 5.43±0.05| 5.48±0.04| 5.48±0.05| 5.48±0.04| 5.53±0.04a| 5.61±0.06a|

*P<0.05, *P<0.01 vs control.
Atropine, isoptin and hexamethonium did not affect the mean contractile amplitude of gastric body CM compared to rhubarb at the same concentration.

**DISCUSSION**

Many diseases are caused by gastrointestinal motility or accompany gastrointestinal motility abnormality, such as gastroparesis, gastroesophageal reflux, gastric dysrhythmias, gastric ulcer[11-13]. 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[10,11]. But it 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[16,14]. 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.

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