Effect of areca on contraction of colonic muscle strips in rats

Dong-Ping Xie, Wei Li, Song-Yi Qu, Tian-Zhen Zheng, Ying-Li Yang, Yong-Hui Ding, Yu-Ling Wei, Lian-Bi Chen

Dong-Ping Xie, Lian-Bi Chen, Department of Physiology, Medical College, Shandong University, Jinan 250012, Shandong Province, China
Wei Li, Song-Yi Qu, Tian-Zhen Zheng, Department of Physiology, Lanzhou Medical College, Lanzhou 730000, Gansu Province, China
Ying-Li Yang, Northwest Normal University, Lanzhou 730070, Gansu Province, China
Yong-Hui Ding, Yu-Ling Wei, Drug Control Institute of Gansu Province, Lanzhou 730000, Gansu Province, China
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Correspondence to: Dong-Ping Xie, Department of Physiology, Medical College, Shandong University, Jinan 250012, Shandong Province, China, xiedping@sdu.edu.cn
Telephone: +86-531-2942037 Fax: +86-531-2942156 Received 2001-07-19 Accepted 2002-01-20

Abstract
AIM: To investigate the effects of areca on the contractile activity of isolated colonic muscle strips in rats and mechanism involved.

METHODS: Each strip (LMPC, longitudinal muscle of proximal colon; CMPC, circular muscle of proximal colon; LMDC, longitudinal muscle of distal colon; CMDC, circular muscle of distal colon) was suspended in a tissue chamber containing 5mL Krebs solution (37°C), bubbled continuously with 950mL·L⁻¹ O₂ and 50mL·L⁻¹ CO₂. The mean contractile amplitude (A), the resting tension (T), and the contractile frequency (F) were simultaneously recorded on recorders.

RESULTS: Areca dose dependently increased the mean contractile amplitude, the resting tension of proximal and distal colonic smooth muscle strips in rats (P<0.05). It also partly increased the contractile frequency of colonic smooth muscle strips in rats (P<0.05). The effects were partly inhibited by atropine (the resting tension of LMPC decreased from 0.44±0.12 to 0.17±0.03; the resting tension of LMDC decreased from 0.71±0.14 to 0.03±0.01; the mean contractile amplitude of LMPC increased from -45.8±7.2 to -30.5±2.9; the motility index of CMDC decreased from 86.6±17.3 to 32.8±9.3; P<0.05 vs areca), but the effects were not inhibited by hexamethonium (P>0.05).

CONCLUSION: Areca increased the motility of isolated colonic smooth muscle strips in rats. The stimulation of areca might be relevant with M receptor partly.

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INTRODUCTION
Areca (Areca catechu L.) had already been shown to relieve indigestion, unblocked stagnation of the circulation of vital energy. It had been used to treat abdominal distention and constipation, which were caused by stagnation of the circulation of vital energy in taste. But the actions and mechanisms of areca on the colonic smooth muscle motility are not reported. In this study, we observed the effect of areca on the different colonic smooth muscle strips in rats and investigated the mechanism involved.

MATERIALS AND METHODS

Animal preparation
Wistar rats of either sex (graded, purchased from Animal Center of Lanzhou Medical College), weighing 200-250g, were sacrificed, and the proximal colon and distal colon were removed. The segments of the colon were opened along the mesentery. Muscle strips (8×3mm) were cut, parallel to either the circular or the longitudinal fibers, and named circular muscle of proximal colon (CMPC), longitudinal muscle of proximal colon (LMPC), circular muscle of distal colon (CMDC), and longitudinal muscle of distal colon (LMDC). The mucosa on each strip was carefully removed.

Experiments
The muscle strip was suspended in a tissue chamber containing 5mL Krebs solution (37°C) and bubbled continuously with 950mL·L⁻¹ O₂ and 50mL·L⁻¹ CO₂. One end of the strip was fixed to a hook on the bottom of the chamber. The other end was connected to an external isometric force transducer (JZ-BK, BK). Motility of colonic strips (under an initial tension of 1g) in 4 tissue chambers were simultaneously recorded on ink-writing recorders (LMS-ZB, Cheng-Du). After 1h equilibration, areca(10,100,1000g·L⁻¹) was added in the tissue chamber to observe their effects on colon; atropine(0.1µmol·L⁻¹) or hexamethonium(10µmol·L⁻¹), given 3min before the administration of areca(100g·L⁻¹), was added separately to investigate whether the actions of areca were relevant with M receptor or N receptor. The resting tension, the frequency, and the mean contractile amplitude of LMPC, CMPC and LMDC, as well as the motility index of CMDC were measured. Motility index=∑(amplitude×duration).

Drugs preparation
Areca was broken into pieces, boiled, filtrated, and diluted to 1000g·L⁻¹ (the drug was appraised and prepared by Drug Control Institute of Gansu Province). The following agents were used: atropine (Pharmaceutical Factory in Yancheng, Jiangsu Province), hexamethonium (Sigma Chemical Company).

Data analysis
The results were presented as x±s, and statistically analyzed by paired t-test, P<0.05 was considered to be significant.

RESULTS

Effect of areca on the spontaneous contraction of colonic smooth muscle strips
Areca (10,100,1000g·L⁻¹) dose dependently increased the mean contractile amplitude of CMPC and LMDC, the motility index of CMDC, and the resting tension of LMPC, LMDC and CMDC; but it
decreased the mean contractile amplitude of LMPC (Figure 1). It increased the contractile frequency of CMPC and LMDC (Table 1). It had no significant effects on the resting tension of CMPC and the contractile frequency of LMPC and CMDC.

Figure 1  Effect of areca on the mean contractile (the motility index of CMDC) and the resting tension (T, n=12) of LMPC: longitudinal muscle of proximal colon; CMPC: circular muscle of proximal colon; LMDC: longitudinal muscle of distal colon; CMDC: circular muscle of distal colon. A, the mean contractile amplitude; T, the resting tension. *P<0.05, **P<0.01 vs control.

Table 1  Effect of areca on the contractile frequency of colonic contractile in rats (Tas, waves·min⁻¹, n=12)

| Areca (g·L⁻¹) | 0   | 10  | 100 | 1000 |
|--------------|-----|-----|-----|------|
| LMPC         | 1.8±0.2 | 1.9±0.2 | 2.2±0.2 | 2.5±0.3 | 1.8±0.2 | 1.8±0.4 |
| CMPC         | 1.5±0.1 | 1.5±0.1 | 1.6±0.1 | 2.1±0.2 | 1.6±0.1 | 2.3±0.1* |
| LMDC         | 1.3±0.1 | 1.3±0.1 | 1.5±0.1 | 2.3±0.2* | 1.5±0.2 | 2.7±0.5* |
| CMDC         | 0.7±0.1 | 0.7±0.1 | 0.6±0.1 | 0.6±0.1 | 0.6±0.1 | 0.6±0.1 |

Effect of atropine on the responses caused by areca
Atropine (0.01µmol·L⁻¹) itself had no significant effects on rat colon. But when given 3min before the administration of areca (100g·L⁻¹), it reduced the increasing action of areca on the resting tension of LMPC and LMDC, the motility index of CMDC, and the mean contractile amplitude of LMPC. It had no significant effects on the other action of areca (Table 2).

Table 2  Effect of areca on the mean contractile amplitude and the resting tension of colon, and the motility index of distal colon after atropine pre-treatment in rats (Tas, n=12)

| Areca (g·L⁻¹) | 0   | 10  | 100 | 1000 |
|--------------|-----|-----|-----|------|
| LMPC         | T/g  | A/mm | T/g | A/mm | T/g | MI/min×cm² |
| Areca        | 0.44± | -45.8± | 0 | 40.0± | 0.71± | 79.7± | 0.11± | 86.6± |
| Atropine 0.1µmol·L⁻¹ | 0.12± | 7.2± | 3.5± | 0.14± | 12.8± | 0.05± | 17.3± |
| Atropine 0.17µmol·L⁻¹ | 0.1± | 0.6± | 0 | 1.3± | 0 | 0.9± |
| +Areca 0.3µmol·L⁻¹ | 0.3± | 2.9 | 2.5± | 0.01± | 13.6± | 0.02 | 98.3± |

Effect of hexamethonium on the responses caused by areca
Hexamethonium (10µmol·L⁻¹) had no significant effect on the contractile activity of each colonic smooth muscle strip. Hexamethonium given 3 minute before administration of areca (100g·L⁻¹) had no significant effects on the action of areca.

DISCUSSION
There are many diseases which are caused by colonic motility disorder or accompany with colonic motility abnormality, such as constipation, diarrhea, irritable bowel syndrome and so on[10-11]. There are some reports on the study of normal colonic motility and intestinal diseases that are connected with colonic motility[12-20]. The studies on how to treat the diseases that are caused by colonic motility disorder have also been reported[28-30]. But it still needs a long time for us to recognize the colonic motility completely. Recently, the effects of Chinese herbas on the gastrointestinal motility have been reported[26-28]. Areca had been used to treat abdominal distention, constipation, abdominal pain and non-ulcer dyspepsia, which were considered to be connected with intestinal motility disorder[31-40]. Whether the clinical use is connected with its effects on colonic motility The present study revealed that areca dose dependently stimulated the contractions of proximal and distal colonic smooth muscle strips of rats. The exciting actions suggested that areca might caused the colonic contents to be mixed, stirred, promoted, and even excreted. These results can partly explained why areca was used to treat intestinal motility disorder. Areca has been showed to stimulate both cholinergic M and N receptors. Our results showed that the stimulating effects of areca were partly blocked by atropine but not by hexamethonium. Our results suggested that the stimulating effects of areca on rat colonic smooth muscle strips were relevant with M receptor but irrelevant with N receptor. When M receptor was stimulated, the potential sensitive Ca²⁺ channel was opened, which will cause the influx of extracellular Ca²⁺ and then cause the contraction of smooth muscle[30]. Areca might stimulate M receptor and then cause the concentration of intracellular Ca²⁺ increased, areca might also act on the Ca²⁺ channel receptor directly, which still need to be further studied. In conclusion, areca stimulates the contractile activity of colonic smooth muscle of rats in vitro. The effect of areca is partly relevant with M receptor, but irrelevant with N receptor.

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