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• BASIC RESEARCH •

Effect of areca on contraction of colonic muscle strips in rats

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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℃), bubbled continuously with 950mL·L^{-1} O_2 and 50mL·L^{-1} CO_2. 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 stimulated 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 (gradeI, purchased from Animal Center of Lanzhou Medical College), weighing 200-250g, were sacrificed, and the proximal colon and distal colon were removed[1]. 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℃) and bubbled continuously with 950mL·L^{-1} O_2 and 50mL·L^{-1} CO_2[2]. 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(0.01μmol·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= Σ(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 $x\pm s$, 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.

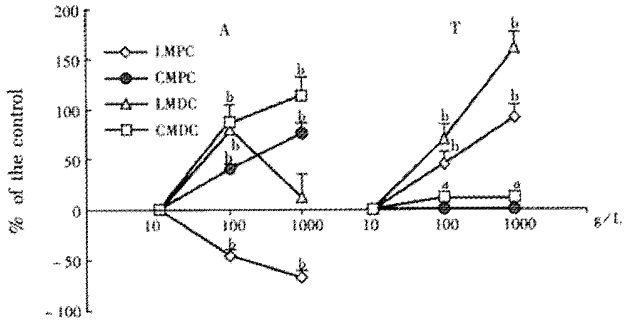

Figure 1 Effect of areca on the mean contractile (the motility index of CMDC) and the resting tension ($\bar{x}\pm s$, n=12)
LMPC: longitudinal muscle of proximal colon; CMPC: circular muscle of proximal colon; LMDC: longitudinal muscle of distal colon; CMDC: circular muscle of distal colon. A, the mean contractile amplitude; T, the resting tension. $^aP<0.05$, $^bP<0.01$ *vs* control.

Table 1 Effect of areca on the contractile frequency of colonic contractile in rats ($\bar{x}\pm s$, waves·min^{-1}, n=12)

	Areca (g·L^{-1})					
	0	10	0	100	0	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^a	1.6±0.1	2.3±0.1^b
LMDC	1.3±0.1	1.3±0.1	1.5±0.1	2.3±0.2^a	1.5±0.2	2.7±0.5^b
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

LMPC: longitudinal muscle of proximal colon; CMPC: circular muscle of proximal colon; LMDC: longitudinal muscle of distal colon; CMDC: circular muscle of distal colon. $^aP<0.05$, $^bP<0.01$ *vs* control (0).

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 motilityindex of distal colon after atropine pretreatment in rats ($\bar{x}\pm s$, n=12)

	LMPC		CMPC		LMDC		CMDC	
	T/g	A/mm	T/g	A/mm	T/g	A/mm	T/g	MI/mm·s^{-1}
Areca	0.44.± 0.12^b	-45.8± 7.2^b	0	40.0± 3.5^b	0.71± 0.14^b	79.7± 12.8^b	0.11± 0.05^a	86.6± 17.3^b
Atropine	0	0.1± 0.1	0	0.6± 1.4	0	1.3± 3.0	0	0.9± 1.3
Atropine +Areca	0.17± 0.03^{bc}	-30.5± 2.9	0	36.9± 2.5^b	0.03± 0.01^{ab}	70.9± 13.6^b	0.03± 0.02	32.± 98.3^{bc}

T, the resting tension; A, the mean contractile amplitude; MI, the motility index. $^aP<0.05$, $^bP<0.001$ *vs* control. $^cP<0.05$, $^dP<0.001$ *vs* areca.

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[3-11]. There are some reports on the study of normal colonic motility and intestinal diseases that are connected with colonic motility[12-25]. The studies on how to treat the diseases that are caused by colonic motility disorder have also been reported[26-35]. But it still needs a long time for us to recognize the colonic motility completely.

Recently, the effects of Chinese herbals on the gastrointestinal motility have been reported[36-46]. 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[47-49]. 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 Ca^{2+} channel was opened, which will cause the influx of extracellular Ca^{2+} and then cause the contraction of smooth muscle[50]. Areca might stimulate M receptor and then cause the concentration of intracellular Ca^{2+} increased, areca might also act on the Ca^{2+} 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.

REFERENCES

1 Xie DP, Li W, Qu SY, Zheng TZ, Yang YL, Ding YH, Wei YL. Effects of ranitidine and cimetidine on the contractile activity of colonic smooth muscle strips in rats. *Zhongguo Yaolixue Yu Dulixue Zazhi* 2001;15:12-16
2 Qu SY, Zheng TZ, Li W. Comparative study of ranitidine and cimetidine on contractile activity of isolated gastric muscle strips in rats. *Xin Xiaohuabingxue Zazhi* 1997;5:75-76
3 Rajapakse R, Warman J, Korelitz BI. Colchicine for persistent constipation after total abdominal colectomy with ileorectostomy for colonic inertia. *J Clin Gastroenterol* 2001;33:81-84
4 O'Sullivan MA, O'Morain CA. Bacterial supplementation in the irritable bowel syndrome. A randomised double-blind placebo-controlled crossover study. *Dig Liver Dis* 2000;32:294-301
5 Chey WY, Jin HO, Lee MH, Sun SW, Lee KY. Colonic motility abnormality in patients with irritable bowel syndrome exhibiting abdominal pain and diarrhea. *Am J Gastroenterol* 2001;96:1499-1506
6 Coulie B, Camilleri M, Bharucha AE, Sandborn WJ, Burton D. Colonic motility in chronic ulcerative proctosigmoiditis and the effects of nicotine on colonic motility in patients and healthy subjects. *Aliment Pharmacol Ther* 2001;15:653-663
7 Bonapace ES, Maurer AH, Davidoff S, Krevsky B, Fisher RS, Parkman HP. Whole gut transit scintigraphy in the clinical evaluation of patients with upper and lower gastrointestinal symptoms. *Am J Gastroenterol* 2000;95:2838-2847
8 Borum ML. Irritable bowel syndrome. *Prim Care* 2001;28:523-538
9 Knowles CH, Scott SM, Lunniss PJ. Slow transit constipation: a disorder of pelvic autonomic nerves *Dig Dis Sci* 2001;46:389-401
10 Knowles CH, Nickols CD, Scott SM, Bennett NI, de Oliveira RB, Chimelli L, Feakins R, Williams NS, Martin JE. Smooth muscle inclusion bodies in slow transit constipation. *J Pathol* 2001;193:390-397
11 Ringel Y, Sperber AD, Drossman DA. Irritable bowel syndrome. *Annu Rev Med* 2001;52:319-338
12 Eglen RM. Muscarinic receptors and gastrointestinal tract smooth muscle function. *Life Sci* 2001;68:2573-2578
13 Plattner V, Leray V, Leclair MD, Aube AC, Cherbut C, Galmiche JP. Interleukin-8 increases acetylcholine response of rat intestinal segments. *Aliment Pharmacol Ther* 2001;15:1227-1232

14 Percy WH, Brunz JT, Burgers RE, Fromm TH, Merkwan CL, van Dis J. Interrelationship between colonic muscularis mucosae activity and changes in transmucosal potential difference. *Am J Physiol Gastrointest Liver Physiol* 2001;281:G479-G489
15 Lin VW, Hsiao I, Goodwin D, Perkash I. Functional magnetic stimulation facilitates colonic transit in rats. *Arch Phys Med Rehabil* 2001;82: 969-972
16 Shafik A, El-Sibai O, Ahmed A. Study of the mechanism underlying the difference in motility between the large and small intestine: the "single" and "multiple" pacemaker theory. *Front Biosci* 2001; 6:B1-B5
17 Onori L, Aggio A, Taddei G, Ciccocioppo R, Severi C, Carnicelli V, Tonini M. Contribution of NK3 tachykinin receptors to propulsion in the rabbit isolated distal colon. *Neurogastroenterol Motil* 2001;13:211-219
18 Herve S, Leroi AM, Mathiex-Fortunet H, Garnier P, Karoui S, Menard JF, Ducrotte P, Denis P. Effects of polyethylene glycol 4000 on 24-h manometric recordings of left colonic motor activity. *Eur J Gastroenterol Hepatol* 2001;13:647-654
19 Al-Saffar A, Hellstrom PM. Contractile responses to natural tachykinins and selective tachykinin analogs in normal and inflamed ileal and colonic muscle. *Scand J Gastroenterol* 2001;36:485-493
20 Sun WM, Hasler WL, Lien HC, Montague J, Owyang C. Nizatidine enhances the gastrocolonic response and the colonic peristaltic reflex in humans. *J Pharmacol Exp Ther* 2001;299:159-163
21 Portincasa P, Moschetta A, Giampaolo M, Palasciano G. Diffuse gastrointestinal dysmotility by ultrasonography, manometry and breath tests in colonic inertia. *Eur Rev Med Pharmacol Sci* 2000;4:81-87
22 Carini F, Lecci A, Tramontana M, Giuliani S, Maggi CA. Tachykinin NK(2) receptors and enhancement of cholinergic transmission in the inflamed rat colon: an *in vivo* motility study. *Br J Pharmacol* 2001;133: 1107-1113
23 Ye JH, Ponnudurai R, Schaefer R. Ondansetron: a selective 5-HT(3) receptor antagonist and its applications in CNS-related disorders. *CNS Drug Rev* 2001;7:199-213
24 Lecci A, Carini F, Tramontana M, D'Aranno V, Marinoni E, Crea A, Bueno L, Fioramonti J, Criscuoli M, Giuliani S, Maggi CA. Nepadutant pharmacokinetics and dose-effect relationships as tachykinin nk(2) receptor antagonist are altered by intestinal inflammation in rodent models. *J Pharmacol Exp Ther* 2001;299:247-254
25 Bassotti G, Fratini M. Of tubes and men: studying manometrically the effects of laxatives on colonic motility. *Eur J Gastroenterol Hepatol* 2001;13:631-633
26 Crowell MD. The role of serotonin in the pathophysiology of irritable bowel syndrome. *Am J Manag Care* 2001;7:S252-S260
27 Menzies JR, McKee R, Corbett AD. Differential alterations in tachykinin NK(2) receptors in isolated colonic circular smooth muscle in inflammatory bowel disease and idiopathic chronic constipation. *Egul Pept* 2001;99:151-156
28 Schwartz D, Stollman N. University of Miami Division of Clinical Pharmacology therapeutic rounds: irritable bowel syndrome-pathophysiology, diagnosis, and treatment. *Am J Ther* 2000;7:265-272
29 Talley NJ. Drug therapy options for patients with irritable bowel syndrome. *Am J Manag Care* 2001;7:S261-S267
30 Niedzielin K, Kordecki H, Birkenfeld B. A controlled, double-blind, randomized study on the efficacy of Lactobacillus plantarum 299V in patients with irritable bowel syndrome. *Eur J Gastroenterol Hepatol* 2001;13:1143-1147
31 Villanueva A, Dominguez-Munoz JE, Mearin F. Update in the therapeutic management of irritable bowel syndrome. *Dig Dis* 2001;19:244-250
32 Beglinger C. Tegaserod a novel, selective 5-HT4 receptor partial agonist for irritable bowel syndrome. *Int J Clin Pract* 2002;56:47-51
33 De Ponti F, Tonini M. Irritable bowel syndrome: new agents targeting serotonin receptor subtypes. *Drugs* 2001;61:317-332
34 De Schryver AM, Samsom M. New developments in the treatment of irritable bowel syndrome. *Scand J Gastroenterol* 2000; 232:38-42
35 Bouras EP, Camilleri M, Burton DD, Thomforde G, McKinzie S, Zinsmeister AR. Prucalopride accelerates gastrointestinal and colonic transit in patients with constipation without a rectal evacuation disorder. *Gastroenterology* 2001;120:354-360
36 Tian XL, Mourelle M, Li YL, Guarner F, Malagelada JR. The role of Chinese herbal medicines in a rat model of chronic *coli*tis. *World J Gastroenterol* 2000;6:40
37 Zheng BJ. Understanding of gastrointestinal prokinetic Chinese drugs. *Zhongyi Zazhi* 1996; 37:697-698
38 Yang YL, Zheng TZ, Qu SY, Li W, Xie DP. Action of Binglang on contractile activity of isolated small intestinal strips in rats. *Lanzhou Daxue Xuebao* 2000;36:43-46
39 Yang YL, Zheng TZ, Qu SY, Li W, Xie DP, Ding YH, Wei YL. Action of Zhishi on the smooth muscle of isolated small intestine in rats. *Xibei Shifan Daxue Xuebao* 1998;34:69-72
40 Xie DP, Li W, Qu SY, Zheng TZ, Yang YL, Ding YH, Wei YL,Zhang MY. Effect of Fructus Aurantii Immaturus on contractile activity of colonic muscle strips in rats. *Shandong Yike Daxue Xuebao* 2001;39:437-438
41 Xie DP, Li W, Qu SY, Zheng TZ, Yang YL, Ding YH, Wei YL. Effect of Qing Pi on contractile of colonic muscle strips in rats. *Lanzhou Yixueyuan Xuebao* 1998;24:1-3
42 Song YJ. Treatment of chronic *coli*tis by integration of traditional and western medicine method in 92 cases. *Huaren Xiaohua Zazhi* 1998;6:454
43 Li Y, Sun SY, Zhou Z. Effect of Chinese herbal medicines Xiaoshixingqi on gastrointestinal motility in mice. *Xin Xiaohuabingxue Zazhi* 1997;5:153
44 Chen RS, Zhang YF, Deng LM, Guo DQ. The Influences of Jiechang-Kangtai on the Movement Function of Intestine. *Zhongguo Zhongxiyi Jiehe Piwei Zazhi* 1998;6:157-159
45 Zhang HX, Ren P, Huang X, Li Y. Regulation of Chinese herbal on gastrointestinal hormones and gastrointestinal motility. *Shijie Huaren Xiaohua Zazhi* 2000;8:1141-1144
46 Dou DP, Cai G. Regulation of gastric motility. *Shijie Huaren Xiaohua Zazhi* 1999;7:353-354
47 Zhao XP, Zhang BL. Therapy of qingfutongchangchongji for 46 patients with intestinal disorder after abdomen operated. *Shanxi Zhongyi* 1999;20: 57-58
48 Qin ZD. Abstracts about therapy of muxiangbinglangwan for patients with rectostenosis in 23 cases. *Guangxi Zhongyiyao* 1999;22:33
49 Xiao ChQ, Huo GQ. Therapy of simowubeitang for 60 patients with non-ulcer dyspepsia. *Shijie Huaren Xiaohua Zazhi* 2000;8:98
50 Zhou L,Ke MY. Textbook of Gastrointestinal Motility-Basic and Clinical Aspects. Beijing: *Science Press* 1999:202

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