

World Journal of *Gastroenterology*

World J Gastroenterol 2017 April 28; 23(16): 2819-3010



**EDITORIAL**

- 2819 High throughput RNA sequencing utility for diagnosis and prognosis in colon diseases
Gao M, Zhong A, Patel N, Alur C, Vyas D
- 2826 Transition of early-phase treatment for acute pancreatitis: An analysis of nationwide epidemiological survey
Hamada S, Masamune A, Shimosegawa T

DIAGNOSTICS ADVANCES

- 2832 Non-invasive evaluation of intestinal disorders: The role of elastographic techniques
Branchi F, Caprioli F, Orlando S, Conte D, Fraquelli M

REVIEW

- 2841 Oxidative stress, antioxidants and intestinal calcium absorption
Diaz de Barboza G, Guizzardi S, Moine L, Tolosa de Talamoni N
- 2854 Importance of antimicrobial susceptibility testing for the management of eradication in *Helicobacter pylori* infection
Arslan N, Yilmaz Ö, Demiray-Gürbüz E
- 2870 Strategies used by *helicobacter pylori* to establish persistent infection
Talebi Bezin Abadi A

MINIREVIEWS

- 2883 Magnetic anchor guidance for endoscopic submucosal dissection and other endoscopic procedures
Mortagy M, Mehta N, Parsi MA, Abe S, Stevens T, Vargo JJ, Saito Y, Bhatt A

ORIGINAL ARTICLE**Basic Study**

- 2891 Droplet digital PCR for quantification of *ITGA6* in a stool mRNA assay for the detection of colorectal cancers
Herring E, Kanaoka S, Tremblay E, Beaulieu JF
- 2899 Detection and characterization of murine colitis and carcinogenesis by molecularly targeted contrast-enhanced ultrasound
Brückner M, Heidemann J, Nowacki TM, Cordes F, Stypmann J, Lenz P, Gohar F, Lügering A, Bettenworth D

- 2912 *In vitro* and *in vivo* antioxidative and hepatoprotective activity of aqueous extract of Cortex Dictamni
Li L, Zhou YF, Li YL, Wang LL, Arai H, Xu Y

- 2928 Comparison of the analgesic effects between electro-acupuncture and moxibustion with visceral hypersensitivity rats in irritable bowel syndrome
Zhao JM, Li L, Chen L, Shi Y, Li YW, Shang HX, Wu LY, Weng ZJ, Bao CH, Wu HG

- 2940 Study of the effects of nesfatin-1 on gastric function in obese rats
Yang GT, Zhao HY, Kong Y, Sun NN, Dong AQ

Case Control Study

- 2948 Recent upper gastrointestinal panendoscopy increases the risk of pyogenic liver abscess
Tsai MJ, Lu CL, Huang YC, Liu CH, Huang WT, Cheng KY, Chen SCC

Retrospective Cohort Study

- 2957 Gutuo Jiejiu decoction improves survival of patients with severe alcoholic hepatitis: A retrospective cohort study
Mou HY, Nie HM, Hu XY

Retrospective Study

- 2964 One year experience with computer-assisted propofol sedation for colonoscopy
Lin OS, La Selva D, Kozarek RA, Tombs D, Weigel W, Beecher R, Koch J, McCormick S, Chiorean M, Drennan F, Gluck M, Venu N, Larsen M, Ross A
- 2972 Ninety-day readmissions after inpatient cholecystectomy: A 5-year analysis
Manuel-Vázquez A, Latorre-Fragua R, Ramiro-Pérez C, López-Marciano A, Al-Shwely F, De la Plaza-Llamas R, Ramia JM

Clinical Trials Study

- 2978 Early hepatitis B viral DNA clearance predicts treatment response at week 96
Fu XY, Tan DM, Liu CM, Gu B, Hu LH, Peng ZT, Chen B, Xie YL, Gong HY, Hu XX, Yao LH, Xu XP, Fu ZY, He LQ, Li SH, Long YZ, Li DH, Gu JL, Peng SF
- 2987 Effects of Chinese herbal medicine Xiangbin prescription on gastrointestinal motility
Jiang Z, Cao LX, Liu B, Chen QC, Shang WF, Zhou L, Li DY, Guo DA, Chen ZQ

Observational Study

- 2995 Combination of corticosteroids and 5-aminosalicylates or corticosteroids alone for patients with moderate-severe active ulcerative colitis: A global survey of physicians' practice
Ben-Horin S, Andrews JM, Katsanos KH, Rieder F, Steinwurz F, Karmiris K, Cheon JH, Moran GW, Cesarini M, Stone CD, Schwartz D, Protic M, Roblin X, Roda G, Chen MH, Har-Noy O, Bernstein CN

CASE REPORT**3003 Protein-losing pseudomembranous colitis with cap polyposis-like features***Kreisel W, Ruf G, Salm R, Lazaro A, Bengsch B, Globig AM, Fisch P, Lassmann S, Schmitt-Graeff A*

ABOUT COVER

Editorial board member of *World Journal of Gastroenterology*, Dar-In Tai, MD, PhD, Professor, Department of Gastroenterology and Hepatology, Chang Gung Memorial Hospital, Taipei 105, Taiwan

AIMS AND SCOPE

World Journal of Gastroenterology (*World J Gastroenterol*, *WJG*, print ISSN 1007-9327, online ISSN 2219-2840, DOI: 10.3748) is a peer-reviewed open access journal. *WJG* was established on October 1, 1995. It is published weekly on the 7th, 14th, 21st, and 28th each month. The *WJG* Editorial Board consists of 1375 experts in gastroenterology and hepatology from 68 countries.

The primary task of *WJG* is to rapidly publish high-quality original articles, reviews, and commentaries in the fields of gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, hepatobiliary surgery, gastrointestinal oncology, gastrointestinal radiation oncology, gastrointestinal imaging, gastrointestinal interventional therapy, gastrointestinal infectious diseases, gastrointestinal pharmacology, gastrointestinal pathophysiology, gastrointestinal pathology, evidence-based medicine in gastroenterology, pancreatology, gastrointestinal laboratory medicine, gastrointestinal molecular biology, gastrointestinal immunology, gastrointestinal microbiology, gastrointestinal genetics, gastrointestinal translational medicine, gastrointestinal diagnostics, and gastrointestinal therapeutics. *WJG* is dedicated to become an influential and prestigious journal in gastroenterology and hepatology, to promote the development of above disciplines, and to improve the diagnostic and therapeutic skill and expertise of clinicians.

INDEXING/ABSTRACTING

World Journal of Gastroenterology (*WJG*) is now indexed in Current Contents[®]/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch[®]), Journal Citation Reports[®], Index Medicus, MEDLINE, PubMed, PubMed Central, Digital Object Identifier, and Directory of Open Access Journals. The 2015 edition of Journal Citation Reports[®] released by Thomson Reuters (ISI) cites the 2015 impact factor for *WJG* as 2.787 (5-year impact factor: 2.848), ranking *WJG* as 38 among 78 journals in gastroenterology and hepatology (quartile in category Q2).

FLYLEAF

I-IX Editorial Board

EDITORS FOR THIS ISSUE

Responsible Assistant Editor: *Xiang Li*
Responsible Electronic Editor: *Cui-Hong Wang*
Proofing Editor-in-Chief: *Lian-Sheng Ma*

Responsible Science Editor: *Yuan Qi*
Proofing Editorial Office Director: *Jin-Lei Wang*

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Damian Garcia-Olmo, MD, PhD, Doctor, Professor, Surgeon, Department of Surgery, Universidad Autonoma de Madrid; Department of General Surgery, Fundacion Jimenez Diaz University Hospital, Madrid 28040, Spain

Stephen C Strom, PhD, Professor, Department of Laboratory Medicine, Division of Pathology, Karolinska Institutet, Stockholm 141-86, Sweden

Andrzej S Tarnawski, MD, PhD, DSc (Med), Professor of Medicine, Chief Gastroenterology, VA Long Beach Health Care System, University of California, Irvine, CA, 5901 E. Seventh Str., Long Beach,

CA 90822, United States

EDITORIAL BOARD MEMBERS
All editorial board members resources online at <http://www.wjgnet.com/1007-9327/editorialboard.htm>

EDITORIAL OFFICE
Jin-Lei Wang, Director
Yuan Qi, Vice Director
Ze-Mao Gong, Vice Director
World Journal of Gastroenterology
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: editorialoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>

PUBLISHER
Baishideng Publishing Group Inc
7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
Telephone: +1-925-2238242
Fax: +1-925-2238243
E-mail: bpoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>

<http://www.wjgnet.com>

PUBLICATION DATE
April 28, 2017

COPYRIGHT
© 2017 Baishideng Publishing Group Inc. Articles published by this Open-Access journal are distributed under the terms of the Creative Commons Attribution Non-commercial License, which permits use, distribution, and reproduction in any medium, provided the original work is properly cited, the use is non commercial and is otherwise in compliance with the license.

SPECIAL STATEMENT
All articles published in journals owned by the Baishideng Publishing Group (BPG) represent the views and opinions of their authors, and not the views, opinions or policies of the BPG, except where otherwise explicitly indicated.

INSTRUCTIONS TO AUTHORS
Full instructions are available online at <http://www.wjgnet.com/bpg/gerinfo/204>

ONLINE SUBMISSION
<http://www.f6publishing.com>

Clinical Trials Study

Effects of Chinese herbal medicine Xiangbin prescription on gastrointestinal motility

Zhi Jiang, Li-Xing Cao, Bo Liu, Qi-Cheng Chen, Wen-Fan Shang, Lu Zhou, Dan-Yan Li, De-An Guo, Zhi-Qiang Chen

Zhi Jiang, Li-Xing Cao, Bo Liu, Qi-Cheng Chen, Wen-Fan Shang, Dan-Yan Li, Zhi-Qiang Chen, Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou 510120, Guangdong Province, China

Lu Zhou, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing 100005, China

De-An Guo, Shanghai Research Center for Modernization of Traditional Chinese Medicine, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 201203, China

Author contributions: Jiang Z, Cao LX and Liu B contributed equally to the work and should be regarded as co-first authors; Jiang Z, Cao LX, Chen QC and Shang WF performed the research; Zhou L verified the design; Guo DA and Chen ZQ designed the research and should be regarded as co-corresponding authors; Jiang Z wrote the paper; Shang WF and Li DY collected and analyzed the data.

Supported by Guangdong Provincial Department of Science and Technology, No. [2013]173.

Institutional review board statement: The study was reviewed and approved by the Ethical Committee of the Second Affiliated Hospital, Guangzhou University of Chinese Medicine.

Clinical trial registration statement: This study was registered in the Chinese Clinical Trial Registry, and the registration number is ChiCTR-OCS-13003561.

Informed consent statement: All study participants, or their legal guardian, provided signed informed consent prior to study enrollment.

Conflict-of-interest statement: All authors declare no conflict of interest.

Data sharing statement: We share the statistical results at <http://www.chictr.org.cn/searchproj.aspx>.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Correspondence to: Dr. Zhi-Qiang Chen, Second Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou 510120, Guangdong Province, China. zhi57@163.com
Telephone: +86-20-81887233
Fax: +86-20-81867705

Received: January 11, 2017

Peer-review started: January 12, 2017

First decision: February 23, 2017

Revised: March 11, 2017

Accepted: March 20, 2017

Article in press: March 20, 2017

Published online: April 28, 2017

Abstract

AIM

To investigate the effects of Xiangbin prescription (XBP), a Chinese herbal concoction, on gastrointestinal motility.

METHODS

Forty healthy volunteers were recruited for this randomized controlled trial of XBP. Antroduodenal manometry was used to monitor gastrointestinal

motility in these subjects. After the subjects had fasted for at least 12 h, XBP ($n = 30$) or placebo ($n = 10$) was orally administered and gastrointestinal motility was recorded for 4 h. Plasma motilin and ghrelin were measured by enzyme-linked immunosorbent assay.

RESULTS

Oral administration of XBP significantly increased the amplitude of duodenal contractions [19.5 (13.0-26.7) *vs* 16.9 (12.3-23.9), $P < 0.05$], jejunal contractions [18.3 (15.3-25.0) *vs* 15.4 (11.7-23.9), $P < 0.01$], and the motility index of duodenal contractions [522.0 (146.0-139.0) *vs* 281.0 (76.5-1006.0), $P < 0.01$] in phase II of the migratory motor complex (MMC), which subsequently initiated the MMC cycle [74.0 (30.0-118.0) *vs* 116.5 (24.0-219.0), $P < 0.05$], shortened the duration of phase I of the MMC [42.0 (0.0-90.0) *vs* 111.5 (42.0-171.0), $P < 0.01$], and lengthened the duration of phase II of the MMC [120 (21-240) *vs* 58 (16-170), $P < 0.01$] compared to the duration before XBP administration. There were significant differences in the amplitude of jejunal contractions [19.8 (14.0-30.0) *vs* 18.0 (13.0-28.5), $P < 0.05$], the motility index of duodenal contractions [236.0 (115.0-306.0) *vs* 195.0 (109.0-310.0), $P < 0.05$], and jejunal contractions [214.0 (95.0-403.0) *vs* 178.0 (55.0-304.0), $P < 0.01$] in phase III of the MMC. Oral administration of XBP greatly increased plasma motilin (57.69 ± 9.03 *vs* 49.38 ± 8.63 , $P < 0.01$) and ghrelin (279.20 ± 104.31 *vs* 238.73 ± 115.59 , $P < 0.01$) concentrations compared to concentrations after oral administration of the placebo.

CONCLUSION

XBP can stimulate duodenal and jejunal motility and increase the concentrations of plasma motilin and ghrelin. The clinical applicability of XBP in treating GDIM deserves investigation.

Key words: Antroduodenal manometry; Gastrointestinal motility; Migrating motor complex; Xiangbin concoction; Motilin; Ghrelin

© The Author(s) 2017. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Disorders of gastrointestinal motility are heavy medical burdens to patients and the society, and development of effective and safe drug treatments for these disorders has proven challenging. Xiangbin prescription is an effective prokinetic Chinese herbal concoction. The core of this randomized, double-blind study is to investigate the effects of Xiangbin prescription on gastrointestinal motility in 40 healthy volunteers.

Jiang Z, Cao LX, Liu B, Chen QC, Shang WF, Zhou L, Li DY, Guo DA, Chen ZQ. Effects of Chinese herbal medicine Xiangbin prescription on gastrointestinal motility. *World J Gastroenterol* 2017; 23(16): 2987-2994 Available from: URL: <http://www.wjgnet.com>

INTRODUCTION

Many diseases of the digestive system are associated with disorders of gastrointestinal motility (DGIM), such as gastroesophageal reflux disease, gastroparesis, diarrhea, adhesive bowel obstruction, postoperative ileus, and chronic constipation. DGIM is a worldwide medical burden that affects about 20%-50% of adults in the Western world and 60% of adults in China. Studies on DGIM date back to around a century ago, but the development of effective and safe drug treatments for DGIM has always proven challenging^[1-3], and prokinetic drugs for the treatment of DGIM are still not widely available in China. Migratory motor complexes (MMC) are waves of electrical activity observed in the gastrointestinal system during fasting, which are well characterized by the appearance of gastrointestinal contractions in the interdigestive state, and are believed to be physiologically important for normal digestive functions^[4]; various studies have indicated that DGIM is partly associated with disruptions in MMC rhythm^[5-7]. Antroduodenal manometry is a valuable clinical tool for evaluating MMC^[8,9] and has been used to investigate motility patterns in normal people and patients.

Traditional Chinese medicine (TCM), which is fully integrated into the modern healthcare system of China, is characterized by the use of a blend of several herbal ingredients to treat illnesses based on patients' symptoms. Xiangbin Prescription (XBP) is a TCM concoction created on the basis of TCM theory and clinical experience^[10]. Clinical studies on using Chinese herbal medicine for the treatment of DGIM have shown some efficacy, but many of them lack standard protocols and objective indicators. Moreover, the molecular mechanisms underlying the drug action of Chinese herbal medicine are currently hot topics of research in TCM.

Motilin and ghrelin are gastrointestinal hormones that play major roles in regulation of gastrointestinal motility^[11,12], but the possible effects of XBP on these hormones have not been reported.

In this study, we conducted a randomized, placebo-controlled, double-blind study to assess the effects of XBP on a variety of gastrointestinal motility variables monitored using antroduodenal manometry and plasma motilin and ghrelin levels. This provided a comprehensive, objective evaluation of the effects of XBP on gastrointestinal motility.

MATERIALS AND METHODS

Ethical approval

All study procedures were approved by the Ethical

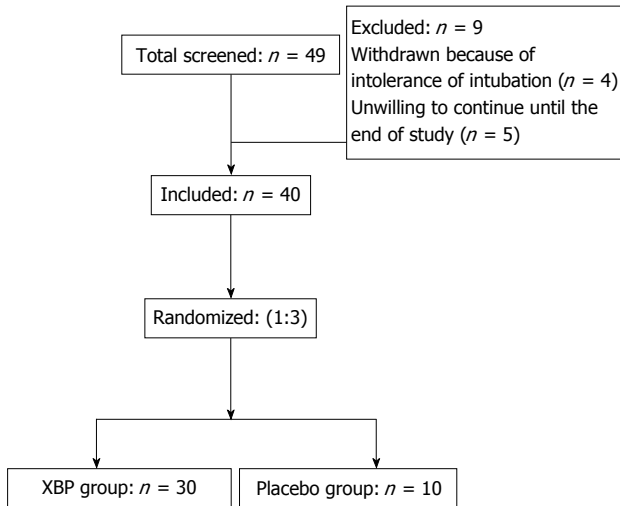


Figure 1 Flow diagram of patient selection. XBP: Xiangbin prescription.

Committee of the Second Affiliated Hospital, Guangzhou University of Chinese Medicine. Written informed consent was obtained from all volunteers, and the study conformed to the ethical principles set forth by the Declaration of Helsinki.

Participants

This study was conducted from October 2013 to December 2014 at the Second Affiliated Hospital of Guangzhou University of Chinese Medicine. Forty healthy volunteers were recruited by the first author and randomly assigned to a control (placebo) group ($n = 10$) or an XBP group ($n = 30$) by the second author, which can be seen in the flow diagram illustrated in Figure 1. A third party was responsible for double blind implementation. The randomization number was put in an envelope, and the same number was affixed to the envelope. The investigator did not know which group the subject would be in, and the color, appearance and drug packets were identical. The subjects of this study had no medical history of gastrointestinal or chronic diseases, psychological disorders, regular use of medications, or the use of a gastrointestinal prokinetic agent for more than one week before study. Participants were asked to stop drinking tea, coffee, and alcohol for at least 12 h and to stop smoking cigarettes for at least 1 h before testing. All volunteers underwent electrocardiographic examination as well as hepatic and renal function tests before and after the experiment.

Preparation of XBP and placebo

XBP is a mixture of five crude herbs: 6 g of amomum villosum lour, 10 g of lindera aggregate (Sims) kosterm, 10 g of prunus persica, 9 g of panax ginseng, and 10 g of aeca catechu to produce a 200-mL concoction, prepared by use of a TCM protocol. Briefly, the weighed herbs and 500 mL of tap water were placed in a heat-resistant glass pot with a lid and

boiled on a heater for 60 min before being passed through a paper filter. The herbs were provided by Kangmei Pharmaceutical Co., Ltd. Two hundred milliliters of filtrated Xiangbin concoction were sterilely packed. The placebo consisted of licorice powder (2 g), caramel powder (0.2 g), bitterant (0.1 g) and starch (3 g)^[7]. Two hundred milliliters of placebo concoction were prepared by the same method as XBP and had the same color and smell. The above ingredients were used for placebo because: (1) literature search showed no reports of licorice and bitterant having a measurable effect on gastroduodenal movements; and (2) preliminary experiments using these placebo ingredients in healthy volunteers showed no significant effect on gastrointestinal motility compared with 0.9% saline.

Antroduodenojejunal manometry

Antroduodenojejunal manometry was performed with a Solar GI HRM-High Resolution manometer with a 21-channel silicone water-perfused catheter (Enschede, the Netherlands) after subjects had fasted overnight for at least 12 h. The 21-channel catheter was connected to capillaries, then each channel was perfused with water at a rate of 0.3 mL/min. The pressure curve was converted into digital data. The participants laid in a lateral position, and the catheter was inserted into the duodenum under fluoroscopic guidance. After the catheter was fixed, antroduodenojejunal manometry was performed in all participants for 4 h under fasting conditions, followed by the administration of 200 mL XBP or placebo at phase I when the pressure curve was steady with no strong contractions. Antroduodenojejunal manometry was recorded for 4 h after administration of XBP or placebo.

Gastrointestinal motility variables

MMC, which is well characterized by the periodic appearance of gastrointestinal contractions in the interdigestive state^[13,14], consists of four phases. Phase I is a quiescent period with no or few contractions. Phase II consists of intermittent and irregular low amplitude contractions. Phase III consists of short bursts of regular high amplitude contractions (3-5 contractions per minute in the stomach; 10-12 contractions per minute in the duodenum). Phase IV is a short transition period back to the quiescence of phase I. Only a pressure fluctuation more than 10 mmHg is designated a contraction^[9,15]. The full cycle of the MMC was measured from the end of the first MMC phase IV to the end of the second MMC phase IV. The duration of the MMC was measured from the beginning of the MMC phase III to the end of the same MMC III phase. Motility index (MI; mmHg/min) was quantified according to the contraction amplitude (mmHg) \times the number of contractions per minute. The baseline gastrointestinal motility variables were

Table 1 Demographic characteristics of the XBP and placebo groups

	XBP (<i>n</i> = 30)	Placebo (<i>n</i> = 10)	<i>t</i>	<i>P</i> value
Gender (<i>n</i>)				
Male	21	5		0.677
Female	9	5		
Age (mean ± SD)	24.1 ± 2.20	24.0 ± 2.00	0.073	0.536
BMI (mean ± SD)	20.6 ± 2.11	20.7 ± 1.65	-0.039	0.969

XBP: Xiangbin prescription; BMI: Body mass index.

defined according to internationally recognized, unified conceptual descriptions in the gastrointestinal motility field^[16].

The pressure curve was recorded by Solar GI HRM-High Resolution Manometry (Medical Measurement System software, MMS). This software can automatically save all original data regarding pressure curves and gastrointestinal motility indicators and general information about the volunteers; calculations can be completed with this software. The total MMC cycles, the mean MMC cycle duration, the duration of phase I and phase II, and the duration of the MMC of the distal stomach, duodenum and jejunum, mean contraction frequency, amplitude, and MI of phase II and phase III were recorded.

Measurement of plasma motilin and ghrelin

Venous blood was collected 15 min before and after oral administration of XBP or placebo and immediately centrifuged at 3000 rpm at 4 °C. Plasma aliquots were frozen at -80 °C until analysis. Plasma motilin concentrations were measured by the use of human Motilin (MTL) ELISA Kit (Wuhan Huamei Biotech Co., Ltd, China), and human total plasma ghrelin was measured by the use of human Ghrelin ELISA Kit (EMD Millipore Corporation, Billerica, MA 01821 United States). ELISA was performed according to the manufacturer's instructions.

Statistical analysis

Sample size was determined based on the expense of data collection and the need to have sufficient statistical power. Data are presented as mean ± SE, median, or range depending on their distribution and analyzed with PASW Statistics 18.0 (IBM SPSS Inc, Armonk, New York, United States). These means were used for pairwise comparisons between groups using the Wilcoxon signed-rank test. *P*-values < 0.05 were considered statistically significant.

RESULTS

Demographic characteristics and baseline motility variables

The demographic characteristics of the study subjects are given in Table 1. Ten participants received placebo

and 30 participants received XBP. No participants were lost from the study, and data were collected from all participants and analyzed. There were no statistical differences in gender, age, or BMI between subjects who received XBP and those who received placebo.

All catheters were successfully positioned, and a full MMC cycle was recorded in each subject. There were no differences in baseline motility variables between the two groups. The average duration of one complete MMC cycle for all subjects combined was 96 min; the average duration of phase I was 43 min, phase II 38 min, phase III 4 min, and phase IV 11 minutes. Distal stomach contractions of phase III were regular and strong at 2-3 contractions per minute, with an amplitude of more than 40 mmHg. Phase III contractions in the duodenum and jejunum had a frequency of 10-12 contractions per minute.

Effects of XBP or placebo on gastrointestinal motility

The effects of XBP or placebo on the gastrointestinal motility variables are illustrated in Table 2 and Figure 2. Before the administration of either placebo or XBP, the motility variables in the two groups of subjects were similar (*P* > 0.05). Also, the administration of placebo had no significant effect on these measurements.

After the administration of XBP, the MMC cycle became 36% shorter [116.5 (24.0-219.0 min) to 74 (30.0-118.0 min)], the duration of phase I became 49% shorter [82.5 (25.0-180 min) to 42.0 (0.0-90.0 min)], and phase II became 140% longer [50.0 (15.0-134.0) to 120.0 (21.0-240.0 min)] (*P* < 0.05). In the distal stomach, the duration, frequency, and amplitude of phase III increased slightly after the administration of XBP but did not reach statistical significance (*P* > 0.05), and the MI decreased slightly. In the duodenum, the duration, contraction frequency, and MI of phase III increased by 12.5%, 2%, and 7%, respectively (*P* < 0.05). After the administration of XBP, in the jejunum, the duration, amplitude, and MI of phase III increased by 7%, 10%, and 20%, respectively (*P* < 0.05); the amplitude of phase II in the duodenum and jejunum increased by 15% and 19%, respectively (*P* < 0.05); and the MI of phase II in the duodenum and jejunum increased 86% and 114%, respectively (*P* < 0.05). Oral administration of XBP significantly increased the amplitude (15%) and MI (mmHg/30 min) (176%) (*P* < 0.05), subsequently shortened the MMC cycle (32%, *P* < 0.05) and the duration of phase I (165%), and lengthened the duration of phase II (52%) compared to placebo values (*P* < 0.01). Differences in the amplitude of phase III in the distal stomach (increased by 65%, *P* < 0.05), in the MI of phase III in the duodenum (increased by 22%, *P* < 0.05), and in the amplitude (increased by 8%, *P* < 0.05) of phase II and MI (mmHg/30 min) (increased by 158%, *P* < 0.01) in the jejunum were observed between the XBP and placebo groups.

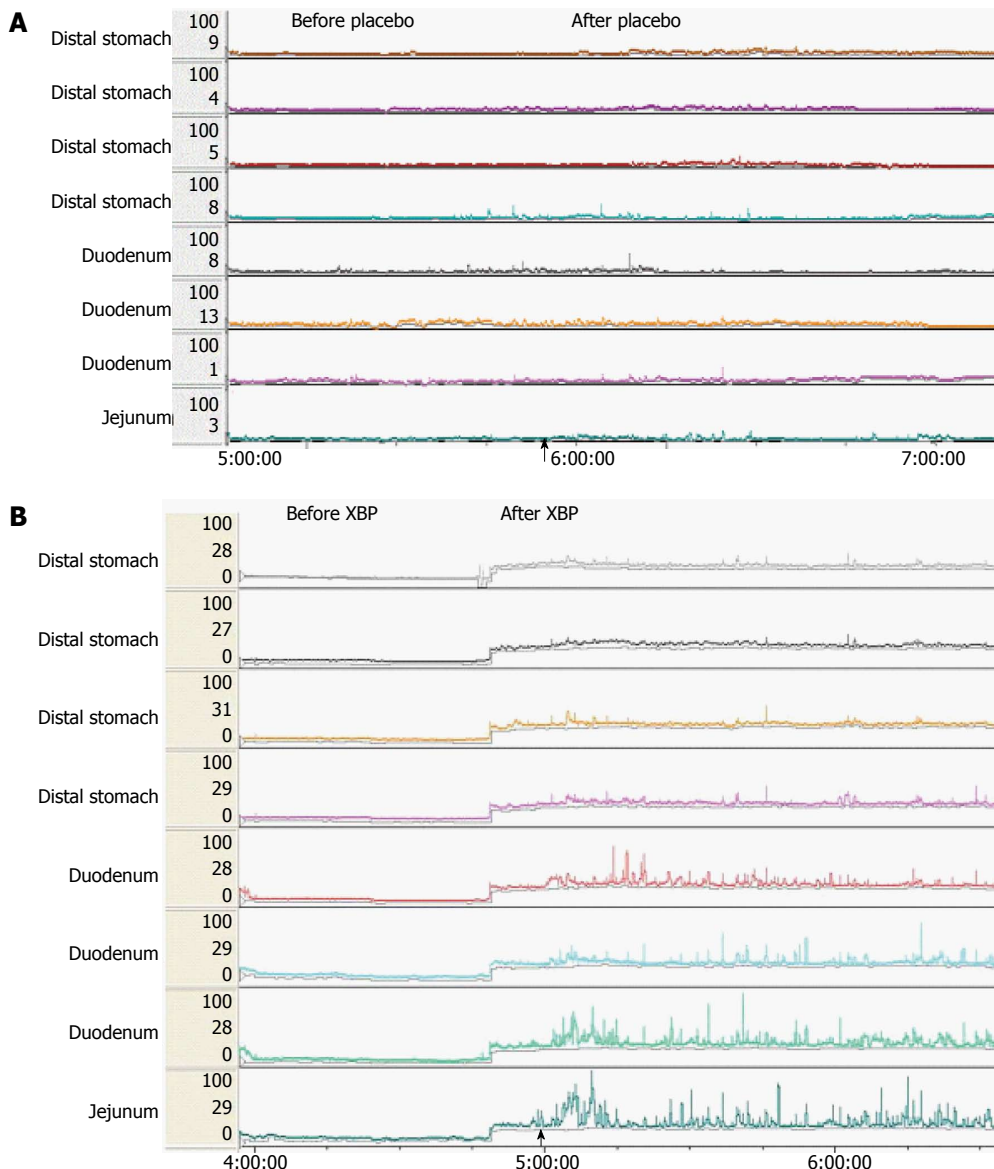


Figure 2 Gastrointestinal motility tracings before and after placebo or XBP treatment. A: Representative pressure curves after administration of placebo; B: Representative pressure curves after administration of XBP. XBP: Xiangbin prescription.

Effect of XBP or placebo on plasma motilin and ghrelin

Table 3 presents the effect of XBP and placebo on plasma motilin and ghrelin levels. Whereas placebo had no effect on these hormones ($P = 0.179$), concentrations of both had increased compared to the baseline values after the administration of XBP ($P < 0.01$).

Adverse events

The subjects' electrocardiographic recordings and tests of hepatic and renal function were normal before and after the experiments, and no recognizable adverse events occurred during the study.

DISCUSSION

In the present study, XBP was found to significantly increase the contractions of the duodenum and

jejunum with minimal effects on the distal stomach. The main findings were: (1) XBP significantly shortened the duration of a complete MMC cycle, shortened the duration of phase I of the MMC cycle, and increased the duration of phase II of the MMC cycle; (2) XBP significantly increased the motility of the duodenum and jejunum at phase III of the MMC cycle, such as increasing the duration, contraction frequency, and MI of phase III; and (3) XBP significantly increased the plasma concentrations of motilin and ghrelin. This study provided a comprehensive evaluation of the effects of XBP on gastrointestinal motility and documented that XBP, a TCM concoction, can significantly affect motility of the normal human gastrointestinal tract, a finding which raises the possibility of XBP having therapeutic value in the treatment of diseases or conditions associated with gastrointestinal dysmotility. Our study is also the first to report the effects of XBP on plasma

Table 2 Gastrointestinal motility variables before and after placebo or Xiangbin prescription administration

MMC	Before placebo (n = 10)	After placebo (n = 10)	Before XBP (n = 30)	After XBP (n = 30)
Number	2.0 (1-3)	1.5 (1-3)	2.0 (1-3)	2.0 (1-4)
Cycle (min)	125.0 (30.0-178.0)	70.0 (51.0-104.0)	116.5 (24.0-219.0)	74.0 (30.0-118.0) ^{a,c}
Duration of phase I (min)	81.0 (40.0-168.0)	111.5 (42.0-171.0)	82.5 (25.0-180.0)	42.0 (0.0-90.0) ^{b,d}
Duration of phase II (min)	56.5 (21.0-154.0)	58.0 (16.0-170.0)	50.0 (15.0-134.0)	120.0 (21.0-240.0) ^{b,d}
Duration of phase III (min)				
Distal stomach	3.2 (2.0-4.0)	2.7 (1.3-3.7)	3.0 (2.1-7.1)	3.7 (1.9-15.6)
Duodenum	2.8 (2.2-3.9)	2.5 (1.3-4.9)	3.2 (1.5-8.2)	3.6 (1.5-5.5) ^a
Jejunum	2.9 (1.5-3.9)	2.8 (1.3-3.9)	2.4 (1.4-6.2)	2.5 (1.3-5.2)
Frequency of phase III				
Distal stomach	2.8 (2.3-3.4)	2.7 (2.3-2.9)	2.7 (2.4-3.1)	2.9 (1.2-4.7)
Duodenum	10.1 (8.8-11.1)	9.9 (8.9-10.9)	10.0 (6.9-11.4)	10.2 (8.4-11.5) ^a
Jejunum	10.0 (8.1-12)	9.9 (8.9-10.9)	10.1 (4.2-11.1)	10.5 (7.8-19.0) ^a
Amplitude of phase III (mmHg)				
Distal stomach	31.5 (24.0-50.3)	29.1 (21.0-41.5)	46.4 (30.0-60.7)	49.5 (33.7-72.7) ^c
Duodenum	21.5 (14.0-25.7)	19.0 (13.7-27.0)	21.0 (14.5-28.8)	21.3 (13.5-28.0)
Jejunum	17.8 (16.0-22.7)	17.3 (14.3-27.0)	18.0 (13.0-28.5)	19.8 (14.0-30.7) ^a
MI				
MI of phase III (mmHg/min)				
Distal stomach	140.0 (74.0-220.0)	96.5 (55.0-117.0)	134.5 (51.0-224.0)	132.0 (48.0-218.0)
Duodenum	197.0 (125.0-324.0)	120.0 (74.0-312.0)	195.0 (109.0-310.0)	236.0 (115.0-306.0) ^{a,d}
Jejunum	202.0 (129.0-325.0)	151.0 (101.0-295.0)	178.0 (55.0-304.0)	214.0 (95.0-403.0) ^b
Amplitude of phase II (mmHg)				
Distal stomach	20.0 (14.0-24.0)	16.3 (13.0-18.0)	18.7 (14.0-22.0)	19.0 (12.5-56.7)
Duodenum	18.2 (14.0-20.0)	19.5 (14.3-22.0)	16.9 (12.3-23.9)	19.5 (13.0-26.7) ^{a,d}
Jejunum	15.3 (13.7-20.8)	16.9 (15.1-18.0)	15.4 (11.7-23.9)	18.3 (15.3-25.0) ^{b,d}
MI of phase II (mmHg/30 min)				
Distal stomach	170.0 (13.0-480.0)	128.0 (90.0-204.0)	157.5 (24.0-444.0)	169.0 (20.0-1080.0)
Duodenum	264.5 (154.0-432.0)	189.0 (57.0-403.0)	281.0 (76.5-1006.0)	522.0 (146.0-1392.0) ^{b,d}
Jejunum	378.0 (126.0-456.0)	187.0 (39.0-447.0)	226.0 (51.0-1099.0)	483.0 (100.0-2076.0) ^{b,d}

^a*P* < 0.05, ^b*P* < 0.001 *vs* before XBP; ^c*P* < 0.05, ^d*P* < 0.01 *vs* after placebo. XBP: Xiangbin prescription; MMC: Migratory motor complex; MI: Motility index.

Table 3 Plasma concentrations of motilin and ghrelin before and after xiangbin prescription or placebo administration (pg/mL)

	XBP			Placebo		
	Before	After	<i>P</i> value	Before	After	<i>P</i> value
Motilin	51.37 ± 6.60	57.69 ± 9.03	< 0.001	50.11 ± 9.9	49.38 ± 8.63	0.179
Ghrelin	229.1 ± 83.27	279.20 ± 104.31	< 0.001	232.45 ± 97.38	238.73 ± 111.59	0.293

ghrelin concentrations. It was reassuring that the study subjects experienced no untoward side effects of XBP.

The pharmacology of XBP is incompletely understood; although various beneficial effects have been ascribed to its herbal components^[17], its therapeutic efficacy has not been validated in rigorous studies. Some of the reputed effects are: amomum villosum lour and lindera aggregate (Sims) kosterm recuperate gastrointestinal function; panax ginseng enhances disease resistance and promotes the recovery of gastrointestinal function motility; prunus persica accelerates blood flow and repairs surgical injuries in the gastrointestinal tract; and areca catechu stimulates gastrointestinal motility^[17]. A previous study demonstrated that XBP may be a promising prokinetic agent for DIGM and can improve postoperative bowel motility^[18].

Various herbs in XBP may have various activities. For example, arecoline is an effective component of areca, and areca can stimulate the motility of isolated colonic smooth muscle strips^[18,19]; several studies have

described areca as a prokinetic herb^[20,21]. Ginsenoside, one of the active ingredients of panax ginseng, exerts a physiological and pharmacological effect on gastrointestinal motility^[22]. Ginsenoside Rf regulates intestinal motility by modulating the pacemaker potential of interstitial cells of Cajal, an effect that is mediated by activating non-selective calcium channels and chloride channels, through a mechanism involving intracellular Ca²⁺ mobilization^[23]. Slow waves and spike potential are generated by sets of interstitial cells of Cajal, which intermingle with gastric smooth muscle cells^[22]. The possibility that XBP exerts a prokinetic effect through the action on the intestinal cells of Cajal should be considered. Amomifrutus has been widely used to treat gastrointestinal dysmotility and gastroparesis^[19,20]. Semen persicae has a positive role in regulating blood flow and relaxing the bowels^[21].

Our finding that XBP can increase plasma motilin and ghrelin concentrations may have important implications. A previous study suggested that gastrointestinal hormones and neural factors mediate the initiation

of the MMC^[24]. Motilin, a 22-amino-acid peptide, is a gastrointestinal hormone released by the endocrine Mo cells of the duodenal and proximal jejunum mucosa during fasting. Motilin is closely associated with the appearance of the MMC and intestine phase III contractions^[25]. It is conceivable that XBP promotes plasma motilin release and enhances motilin secretion through Mo cell receptors. Ghrelin, the closest family member of motilin, is an endogenous ligand of the growth hormone secretagogue receptor, discovered in the rat stomach. Ghrelin has emerged as a functional hormone with important effects on gastrointestinal motility and accelerating gastric emptying^[24,26]. In our study, the increase of ghrelin concentrations induced by XBP correlated with increased frequency, amplitude, and MI of phase II contractions of the duodenum and jejunum. It has been reported that ghrelin is important for phase II contraction and that coordination of motilin and ghrelin is necessary for initiating phase III contraction of the MMC^[27]. The mechanisms of XBP's actions on gastrointestinal motility require further investigation, but the possibility that XBP helps coordinate the actions or secretion of motilin and ghrelin to create a prokinetic effect is intriguing.

This study has limitations. It is a short-term study, so the long-term effects of XBP on gastrointestinal motility and its possible side effects are unknown. Also, the studies were conducted only in the fasting state, so the postprandial effects of XBP are also unknown. Finally, although effects of XBP on gastrointestinal motility could be demonstrated by high resolution manometry, whether these effects reflect clinically useful prokinetic activity remains to be determined. The safety profile of XBP must be evaluated in longer term studies.

Nonetheless, since disorders of gastrointestinal motility, including postoperative gastrointestinal dysfunction (ileus), are common, and treatments are often inadequate, investigation of novel agents such as TCM is worthy of pursuit.

In conclusion, this short-term study of fasting, healthy human subjects documented that the Chinese traditional herbal concoction XBP safely stimulated duodenal and jejunal motility. XBP also increased plasma concentrations of motilin and ghrelin, which suggests that XBP helps coordinate the actions or secretion of motilin and ghrelin to promote MMC activity and a prokinetic effect. Although this study implicates that XBP may have a potential value in the treatment of DGIM and other diseases or conditions associated with gastrointestinal dysmotility, the clinical applicability of these observations and thorough pharmacological characterizations of the components of XBP responsible for its effect on gastrointestinal motility deserve further investigation.

COMMENTS

Background

The burden of disorders of gastrointestinal motility (DGIM) is heavy for both

the patient's family and the society. However, the development of effective and safe drug treatments for DGIM has always proven challenging. Administration of Xiangbin Prescription (XBP) has been revealed to exhibit some effects on DGIM, but the mechanisms of action are still unknown and objective evaluation of the effects of XBP has not been performed.

Research frontiers

Chinese herbal medicine has been proven to be effective in many diseases or disorders, but the mechanisms remain to be elucidated. Currently, the molecular mechanisms underlying the drug action of Chinese herbal medicine are a hot topic of research in Traditional Chinese medicine.

Innovations and breakthroughs

XBP has been shown to have some efficacy in treating DIGM, but it has not been evaluated under standard protocols or objective measurements. This study for the first time provided a comprehensive evaluation of the effects of XBP on gastrointestinal motility and highlighted the possible therapeutic use of XBP in the treatment of DGIM. This study first explored the preliminary mechanism underlying the drug action of XBP in gastrointestinal motility.

Applications

This study demonstrated that XBP can be used for the therapy of DGIM and other diseases or disorders involved in gastrointestinal dysmotility, but a future study on the thorough pharmacological characterizations of the components of XBP responsible for its effects on gastrointestinal motility is still needed.

Terminology

Migratory motor complexes are waves of electrical activity well characterized by the appearance of gastrointestinal contractions in the interdigestive state. XBP is a concoction created by five crude herbs: amomum villosum, linden, aggregate kosterm, prunus persica, panax ginseng, and aeca catechu on the basis of traditional Chinese medicine. Antroduodenal manometry was used to evaluate gastrointestinal motility and performed with a Solar GI HRM-High Resolution manometer.

Peer-review

This study investigated the effects of Chinese medicine XBP on gastrointestinal motility as well as the plasma ghrelin and motilin concentrations in healthy volunteers. It is a randomized controlled double-blind trial. The manuscript has detailed information on experimental design. This is a well conducted study and gives a clear conclusion with a limited number of volunteers. The study's design and results are meaningful to future studies on Chinese medicine.

REFERENCES

- 1 **Katz PO**, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2013; **108**: 308-28; quiz 329 [PMID: 23419381 DOI: 10.1038/ajg.2012.444]
- 2 **Sandler RS**, Everhart JE, Donowitz M, Adams E, Cronin K, Goodman C, Gemmen E, Shah S, Aydic A, Rubin R. The burden of selected digestive diseases in the United States. *Gastroenterology* 2002; **122**: 1500-1511 [PMID: 11984534]
- 3 **Kidane B**, Manji F, Lam J, Taylor BM. Use of Serotonergic Drugs in Canada for Gastrointestinal Motility Disorders: Results of a Retrospective Cohort Study. *Scientifica* (Cairo) 2016; **2016**: 5797804 [PMID: 27313955 DOI: 10.1155/2016/5797804]
- 4 **Miyano Y**, Sakata I, Kuroda K, Aizawa S, Tanaka T, Jogahara T, Kurotani R, Sakai T. The role of the vagus nerve in the migrating motor complex and ghrelin- and motilin-induced gastric contraction in suncus. *PLoS One* 2013; **8**: e64777 [PMID: 23724093 DOI: 10.1371/journal.pone.0064777]
- 5 **Bouin M**, Sassi A, Savoye G, Denis P, Ducrotté P. Effects of enteral feeding on antroduodenal motility in healthy volunteers with 2 different fiber-supplemented diets: a 24-hour manometric study. *JPEN J Parenter Enteral Nutr* 2004; **28**: 169-175 [PMID: 15141410 DOI: 10.1177/0148607104028003169]
- 6 **Ciriza-de-los-Ríos C**, Canga-Rodríguez-Valcárcel F, Castel-de-

- Lucas I, Lora-Pablos D, de-la-Cruz-Bértolo J, Castellano-Tortajada G. How useful is esophageal high resolution manometry in diagnosing gastroesophageal junction disruption: causes affecting this disruption and its relationship with manometric alterations and gastroesophageal reflux. *Rev Esp Enferm Dig* 2014; **106**: 22-29 [PMID: 24689712]
- 7 **Xu X**, Li Q, Zhou L, Ru L. Neurochemical mechanism of the gastrointestinal interdigestive migrating motor complex in rats with acute inflammatory stomach ache. *Neural Regen Res* 2012; **7**: 2136-2143 [PMID: 25558227 DOI: 10.3969/j.issn.1673-5374.2012.27.008]
- 8 **Ghoshal UC**, Paliwal M, Das K, Yachha SK, Sachdeva S, Misra A. Antroduodenal manometry: experience from a tertiary care center. *Indian J Gastroenterol* 2008; **27**: 53-57 [PMID: 18695303]
- 9 **Patcharatrakul T**, Gonlachanvit S. Technique of functional and motility test: how to perform antroduodenal manometry. *J Neurogastroenterol Motil* 2013; **19**: 395-404 [PMID: 23875108 DOI: 10.5056/jnm.2013.19.3.395]
- 10 **Zhi-Qiang C**. [Syndrome typing based strategies for postoperative gastrointestinal dysfunction in the perioperative phase]. *Zhongguo Zhong Xi Yi Jie He Za Zhi* 2013; **33**: 149-154 [PMID: 23646464]
- 11 **Kuroda K**, Hequing H, Mondal A, Yoshimura M, Ito K, Mikami T, Takemi S, Jogahara T, Sakata I, Sakai T. Ghrelin Is an Essential Factor for Motilin-Induced Gastric Contraction in *Suncus murinus*. *Endocrinology* 2015; **156**: 4437-4447 [PMID: 26441238 DOI: 10.1210/en.2015-1561]
- 12 **Kitazawa T**, Shimazaki M, Kikuta A, Yaosaka N, Teraoka H, Kaiya H. Effects of ghrelin and motilin on smooth muscle contractility of the isolated gastrointestinal tract from the bullfrog and Japanese fire belly newt. *Gen Comp Endocrinol* 2016; **232**: 51-59 [PMID: 26704852 DOI: 10.1016/j.ygcen.2015.12.013]
- 13 **Moon SB**, Park KJ, Moon JS, Choe EK, So IS, Jung SE. Migrating motor complex changes after side-to-side ileal bypass in mouse ileum ex-vivo: mechanism underlying the blind loop syndrome? *J Korean Surg Soc* 2011; **80**: 251-259 [PMID: 22066044 DOI: 10.4174/jkss.2011.80.4.251]
- 14 **Code CF**, Marlett JA. The interdigestive myo-electric complex of the stomach and small bowel of dogs. *J Physiol* 1975; **246**: 289-309 [PMID: 1142245]
- 15 **Takahashi T**. Mechanism of interdigestive migrating motor complex. *J Neurogastroenterol Motil* 2012; **18**: 246-257 [PMID: 22837872 DOI: 10.5056/jnm.2012.18.3.246]
- 16 **Takahashi T**. Interdigestive migrating motor complex -its mechanism and clinical importance. *J Smooth Muscle Res* 2013; **49**: 99-111 [PMID: 24662475]
- 17 **Xie DP**, Li W, Qu SY, Zheng TZ, Yang YL, Ding YH, Wei YL, Chen LB. Effect of areca on contraction of colonic muscle strips in rats. *World J Gastroenterol* 2002; **8**: 350-352 [PMID: 11925623 DOI: 10.3748/WJG.v8.i2.350]
- 18 **Chen ZQ**, Cao LX, Shang WF, Yang RX, Ye F, Chen QC, Pang FX, Jiang J, Liu P, Zhou L. Effect of Xiangbin Prescript on gastrointestinal motility in dogs after abdominal surgery. *Zhongyi Zazhi* 2015; **56**: 1953-1957
- 19 **Gilani AH**, Ghayur MN, Saify ZS, Ahmed SP, Choudhary MI, Khalid A. Presence of cholinomimetic and acetylcholinesterase inhibitory constituents in betel nut. *Life Sci* 2004; **75**: 2377-2389 [PMID: 15350815 DOI: 10.1016/j.lfs.2004.03.035]
- 20 **Xie DP**, Chen LB, Liu CY, Zhang CL, Liu KJ, Wang PS. Arecoline excites the colonic smooth muscle motility via M3 receptor in rabbits. *Chin J Physiol* 2004; **47**: 89-94 [PMID: 15481791]
- 21 **Jeng JH**, Chang MC, Hahn LJ. Role of areca nut in betel quid-associated chemical carcinogenesis: current awareness and future perspectives. *Oral Oncol* 2001; **37**: 477-492 [PMID: 11435174]
- 22 **Lee HC**, Yin PH, Yu TN, Chang YD, Hsu WC, Kao SY, Chi CW, Liu TY, Wei YH. Accumulation of mitochondrial DNA deletions in human oral tissues -- effects of betel quid chewing and oral cancer. *Mutat Res* 2001; **493**: 67-74 [PMID: 11516716]
- 23 **Chen D**, Xiong Y, Jiang C, Lv B, Liu F, Wang L, Lin Y. Effects of ginsenosides on rat jejunal contractility. *Pharm Biol* 2014; **52**: 162-168 [PMID: 24073926 DOI: 10.3109/13880209.2013.821137]
- 24 **Zhang L**. Curative Effect of Supplemented Tao-Ren-Cheng-Qi Concoction in Treatment of Thoracolumbar Vertebral Compression Fractures Complicated with Abdominal Distension and Constipation. *Chengdu Dazue Yixueyuan Xuebao* 2014; **37**: 82-83
- 25 **Kim BJ**, Nam JH, Kim KH, Joo M, Ha TS, Weon KY, Choi S, Jun JY, Park EJ, Wie J. Characteristics of gintonin-mediated membrane depolarization of pacemaker activity in cultured interstitial cells of Cajal. *Cell Physiol Biochem* 2014; **34**: 873-890
- 26 **Mager U**, Degenhardt T, Pulkkinen L, Kolehmainen M, Tolppanen AM, Lindström J, Eriksson JG, Carlberg C, Tuomilehto J, Uusitupa M; Finnish Diabetes Prevention Study Group. Variations in the ghrelin receptor gene associate with obesity and glucose metabolism in individuals with impaired glucose tolerance. *PLoS One* 2008; **3**: e2941 [PMID: 18698404 DOI: 10.1371/journal.pone.0002941]
- 27 **Sanger GJ**. Motilin receptor neuropharmacology: revised understanding. *Curr Opin Pharmacol* 2012; **12**: 641-646 [PMID: 22858405 DOI: 10.1016/j.coph.2012.07.012]

P- Reviewer: Thompson JR **S- Editor:** Ma YJ **L- Editor:** Wang TQ
E- Editor: Wang CH





Published by **Baishideng Publishing Group Inc**
7901 Stoneridge Drive, Suite 501, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: <http://www.f6publishing.com/helpdesk>
<http://www.wjgnet.com>



ISSN 1007-9327

