

World Journal of *Meta-Analysis*

World J Meta-Anal 2019 November 28; 7(9): 406-435



Contents

Irregular Volume 7 Number 9 November 28, 2019

REVIEW

- 406 Treatment of early stage (T1) esophageal adenocarcinoma: Personalizing the best therapy choice
Kumble LD, Silver E, Oh A, Abrams JA, Sonett JR, Hur C

MINIREVIEWS

- 418 Mechanisms of action of aqueous extract from the *Hunteria umbellata* seed and metformin in diabetes
Ejelonu OC
- 423 Fecal microbiota transplantation: Historical review and current perspective
Leung PC, Cheng KF

META-ANALYSIS

- 428 Use of music during colonoscopy: An updated meta-analysis of randomized controlled trials
Heath RD, Parsa N, Matteson-Kome ML, Buescher V, Samiullah S, Nguyen DL, Tahan V, Ghouri YA, Puli SR, Bechtold ML

ABOUT COVER

Editorial Board Member of *World Journal of Meta-Analysis*, Xiangchun Shen, PhD, Director, Postdoc, Professor, Teacher, School of Pharmaceutical Sciences, State Key Laboratory of Functions and Applications of Medicinal Plants, Guizhou Medical University, Guian New District 550025, Guizhou Province, China

AIMS AND SCOPE

The primary aim of *World Journal of Meta-Analysis (WJMA, World J Meta-Anal)* is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality meta-analysis and systematic review articles and communicate their research findings online. *WJMA* mainly publishes articles reporting research results and findings obtained through meta-analysis and systematic review in a wide range of areas, including medicine, pharmacy, preventive medicine, stomatology, nursing, medical imaging, and laboratory medicine.

INDEXING/ABSTRACTING

The *WJMA* is now abstracted and indexed in China National Knowledge Infrastructure (CNKI), China Science and Technology Journal Database (CSTJ), and Superstar Journals Database

RESPONSIBLE EDITORS FOR THIS ISSUE

Responsible Electronic Editor: *Yan-Xia Xing*
 Proofing Production Department Director: *Yun-Xiaojuan Wu*

NAME OF JOURNAL

World Journal of Meta-Analysis

ISSN

ISSN 2308-3840 (online)

LAUNCH DATE

May 26, 2013

FREQUENCY

Irregular

EDITORS-IN-CHIEF

Giuseppe Biondi-Zoccai

EDITORIAL BOARD MEMBERS

<https://www.wjnet.com/2308-3840/editorialboard.htm>

EDITORIAL OFFICE

Jin-Lei Wang, Director

PUBLICATION DATE

November 28, 2019

COPYRIGHT

© 2019 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjnet.com/bpg/gerinfo/240>

PUBLICATION MISCONDUCT

<https://www.wjnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Fecal microbiota transplantation: Historical review and current perspective

Ping-Chung Leung, King-Fai Cheng

ORCID number: Ping-Chung Leung (0000-0002-0195-4688); King-Fai Cheng (0000-0001-5062-1073).

Author contributions: Leung PC conceived and designed the study; Leung PC and Cheng KF wrote the manuscript; Cheng KF collected related references.

Conflict-of-interest statement: The authors declare that they have no conflict of interest.

Open-Access: This article is an open-access article that 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

Received: September 5, 2019

Peer-review started: September 5, 2019

First decision: October 14, 2019

Revised: October 21, 2019

Accepted: October 25, 2019

Article in press: October 25, 2019

Published online: November 28, 2019

P-Reviewer: Amedei A, Bezmin Abadi AT, Parker W

Ping-Chung Leung, King-Fai Cheng, Institute of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, China

Ping-Chung Leung, State Key Laboratory of Research on Bioactivities and Clinical Applications of Medicinal Plants (The Chinese University of Hong Kong), Hong Kong, China

Corresponding author: Ping-Chung Leung, PhD, Professor, Director, Centre for Clinical Trials on Chinese Medicine, Institute of Chinese Medicine, The Chinese University of Hong Kong, Hong Kong, China. pingleung@cuhk.edu.hk

Telephone: +852-2-2528868

Abstract

There is a growing interest in the use of fecal transplantation for chronic intestinal conditions. We aim to review the methodology and safety of fecal microbiota transplantation and the evidence to support its use in treating a variety of diseases. We reviewed the history of fecal transplantation in China and found that there were varieties of fecal material used in ancient China. The first written record on fecal treatment was found in an ancient tomb in Middle China. This paper explores the historical and current perspectives of fecal microbiota transplantation. The ancient fecal transplantations did not have any background support from life science. In those ancient days, short of knowledge about bacteria, clinicians were aiming at a change of intestinal environment. Today, we aim at a change of the intestinal microbiome.

Key words: Fecal transplantation; Microbiota; Intestinal microbiome; Microenvironment

©The Author(s) 2019. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: There is a growing interest in the use of fecal transplantation for chronic intestinal conditions. In the article, we reviewed the history of fecal transplantation in China. The first written record on the oral use of fecal matter was in 770 BC. Although the ancient fecal transplantations did not have any evidence from life science, the ancient healers were fully aware of the acting value of gastrointestinal variety. Today, researchers in the field are working on various ways to change the microbiome at different levels of the gut.

Citation: Leung PC, Cheng KF. Fecal microbiota transplantation: Historical review and current perspective. *World J Meta-Anal* 2019; 7(9): 423-427

S-Editor: Zhang L
L-Editor: Filipodia
E-Editor: Xing YX



URL: <https://www.wjgnet.com/2308-3840/full/v7/i9/423.htm>

DOI: <https://dx.doi.org/10.13105/wjma.v7.i9.423>

INTRODUCTION

The gastrointestinal tract harbors a diversity of microflora, and any alterations may contribute to problems like chronic gastrointestinal infections and inflammatory bowel diseases^[1,2]. Recently, the microflora has also been shown to be potentially responsible for cardiac, metabolic and autoimmune conditions and some neoplasms^[3-5]. In 1958, Eisman *et al*^[6] reported the first four cases of fecal transplantation for the control of pseudomembranous enterocolitis. The successful control of chronic diarrhea was assumed to be due to a change of the intestinal microflora.

In recent years, there is a growing interest in the use of fecal transplantation for chronic intestinal conditions, including ulcerative colitis, celiac disease, irritable bowel syndrome and *Clostridium difficile* infection^[7-10]. Many assumed that fecal transplantation was new technique not realizing that it was an established practice in ancient China. We aim to review the historical methodology and safety of fecal microbiota transplantation and the evidence to support its use in treating a variety of diseases.

HISTORICAL REVIEW OF FECAL TRANSPLANTATION IN CHINA

The first written record on the oral use of fecal matter was contained in one of the oldest Text of Chinese Medicine excavated in an ancient tomb in Middle China, called "Fifty-two Treatment Formulae"^[11]. It was estimated that the document was written in 770 BC. Some details of the preparation of a fecal product called "golden juice" were given, and it was indicated for detoxication^[12]. The authors did not encounter stories about medicinal use of fecal material in other ancient cultures while searching through relevant literature (British Encyclopedia).

The next record appeared in an important classic for medical teaching in the Han Dynasty (206 BC to AD 220), and the indications given were gastrointestinal emergencies^[13]. Fecal material was reported to be used during epidemics.

Ge Hong (AD 284-364), a well-known Taoist healer, compiled a treatment guide "Handbook of Emergency Conditions" in which many medicinal items and formulae containing fecal matter of human, chicken, dog, cattle, horse, *etc.* were described^[12].

Subsequently, classics compiled in the following dynasties, Song (AD 960-1279), Ming (AD 1368-1644) and Qing (AD 1644-1912), all contained supplemented versions of fecal preparations, which had already been described or were new inventions^[14]. Clinical applications ranged from detoxication in emergency events, removal of harmful causes in infections, treatment of severe gastrointestinal problems like uncontrolled diarrhea and vomiting and most recently as an anti-allergic decoction in severe anaphylaxis-like emergencies^[15].

Many different types of "fecal medicine" have been described. A table of eleven frequently described items is given (Table 1). Over 1550 recorded prescriptions containing different fecal substances are available for scrutiny^[16].

The unfavorable stigma attached to the use of fecal matter in the past is unavoidable. Obviously, the majority of the items described have become less popular, although they remain respectable. Herb Books and some senior traditional practitioners still favor these applications^[16]. While it is easy to be skeptical about ancient practices and label them as simple superstition or folk lore, one may objectively analyze the logic behind the historical uses. In return to this objective exercise, lessons can be learned that may serve the current field and help the further development of fecal transplantation.

VARIETIES OF FECAL MATERIAL USED IN ANCIENT CHINA

Looking at the variety of fecal products and their ancient applications, their correlation with the ancient logic of Traditional Chinese Medicine could be identified as follows.

Table 1 Eleven Chinese Medicine fecal compositions

No.	Official name	Classic medical monograph	Fecal origin	Property and flavor	Clinical indications
1	White clove	Yunnan Bencas (Herb Book)	Sparrow	Bitter, warm	Gastrointestinal disorder
2	Silk worm sand	Bencao Gangmu (Herb Dictionary)	Silk worm	Sweat, bitter, warm	Vomit, diarrhea, rheumatism
3	Chicken white	Ancient Bencao (Ancient Herb Book)	Chicken	Bitter, salty, cold	Detoxicate, diuretic
4	Golden juice	Handbook of Emergency Conditions	Human male	Slight-bitter, cold	Detoxicate, severe fever
5	Bipolar pin	Handbook of Distinguished Clinician	Rat	Bitter, salty	Abdominal cramp, fever
6	Perfume of dragon	Ancient Bencao (Herb Book) extension	Whale	Sweet, sour, warm	Analgesia, diuretic, bronchial spasm
7	Human yellow	Special Bencao (Herb Book)	Human	Bitter, salty, cold	Detoxicate, severe infection
8	Moon sand	Original classic	Rabbit	Bitter, cold	External infection
9	Penta crease	Original Bencao (Herb Book)	Small bat	Sweat, bitter, warm	External use
10	Moonlight sand	Special Bencao (Herb Book)	Bat	Bitter, cold	External use, eye infection
11	Flying dragon	Bencao Gangmu (Herb Dictionary)	Pigeon	Bitter, warm	Infection

Principle of detoxication

This principle advocates the use of a toxic agent to counteract an intoxicated state. Ge Hong used “golden juice” in emergency gastrointestinal disorders presenting with high fever^[17].

Principle of homeopathic medicine

This principle advises the use of fecal material in a situation of uncontrolled repeated gastrointestinal upset. It was believed that in an event of uncertain pathological cause, pushing the clinical problem to the extreme would allow a natural defense to better develop^[18].

Principle resembling vaccination

Life substances from the guts, *i.e.* fecal matter, were used for severe gastrointestinal problems resistant to standard treatment^[19].

Principle of anti-allergy or anti-poisonous invasion

Skin allergy and infections caused by insects and small animals were treated with their fecal material^[20].

PROCEDURES OF FECAL FORMULATION IN ANCIENT CHINA

The procedures described in the classic literature describing the preparation of fecal material is illustrated below.

Simple collection and drying of fecal material

This crude method was reserved for the droppings of insects and small animals. The products were to be used externally^[20].

Adding special herbal components to initiate specific effects

Prescriptions of Traditional Chinese Medicine demanded one champion herb to be supported by one or more partners. Glycyrrhiza was the component widely used with human fecal matter in the most ancient description^[12].

Creating an acceptable outlook of the fecal preparation

Detailed instructions for maintaining cleanliness and filtering out unfavorable components were given. As an example, Ge Hong’s well respected “golden juice” followed this procedure: (1) Feces were collected from healthy boys; (2) Clean spring water was used to form a suspension; (3) The suspension was put into a red earth vase to be buried underground for up to 12 mo; and (4) On maturity, the fecal fluid already separated into three layers: the surface yellow layer was the “golden juice,” and the middle brownish layer and the bottom debris were to be discarded.

This way of preparation must have involved fermentation and the fecal matter would have influenced the replication and selection of the microbiome involved. If “golden juice” were providing any bioactive influence, it is to be speculated whether the effect was biotic or antibiotic. Whether the juice could just be providing a special environment for the gastrointestinal microbiome to change, adapt and reorganize

deserves careful speculations^[12,20].

DISCUSSION

What do we learn from the ancient history of fecal transplantation?

The ancient fecal transplantations did not have any evidence related to modern life science. However, healers of those days were fully aware that fecal matter may be toxic or harmful. However, under special circumstances the fecal matter could provide unexpected and favorable outcomes. This plausible explanation matches quite well with today's practice of fecal transplantation. Today, we aim at a change of the intestinal microbiome. In those ancient days, clinicians were aiming at a change of the intestinal environment (without the knowledge about bacteria)^[21,22]. The concept and benefits from the old practice were not linked with today's microbiome. Ancient fecal treatment could only be the provision of a specific gastrointestinal environment through the return of unwanted metabolized food and various forms of artificial treatment have been completed (like to "golden juice") before its application as a drug.

Today, we are working on various ways to changes the microbiome at different levels of the gut for a variety of gastrointestinal disorders, which are likely to be related to odd bacterial flora or infection^[23,24]. Because the microbiome in the gut represents a healthy symbiosis between the human body and the organisms, a microenvironment suitable for a stable healthy symbiotic situation is of vital importance to maintain the stability. While we may still need fecal transplant in situations when immediate results are needed, the research direction should include studies on the provision of a favorable microenvironment for the usual symbiotic microbiome. Provision of the vital microenvironment could be preventive against the loss of the normal microbiome in inflammatory conditions. A suitable microenvironment for a healthy microbiome should also be the result after fecal transplantation. In the future, creating suitable oral prescriptions acceptable to all users with the aim of maintaining a favorable microenvironment could be the research direction. Obviously, more details about the symbiotic microbiomes at different levels of the gastrointestinal tract will need to be defined first^[25].

Transplantation of a living microbiome has the intention of providing active, beneficial organisms to the gut, which for various reasons has failed to maintain their satisfactory survival. An unsatisfactory microenvironment necessary for microbial replication could be the cause. After all, it has been reported that as much as 20% to 60% of the human associated microbiome is uncultivable^[26]. Instead of reintroduction of the microbiome, which is difficult to control and lacks standards, a satisfactory restoration of the microenvironments in the gut might be an alternative. With a suitable microenvironment, the spontaneous replication of the original microbiome that should have remained in suitable quantities would become possible^[27].

CONCLUSION

Ancient fecal transplantations were not supported by life science evidences. However, healers of those days were fully aware that even though fecal matter may be toxic or harmful, under special circumstances it could provide unexpected and beneficial outcomes. Today, we aim to change the intestinal microbiome. In those ancient days without knowledge of bacteria, clinicians aimed to change the intestinal environment. Current research on intestinal microbiomes could include study of the intestinal environment that normally sustain their healthy growth.

REFERENCES

- 1 **Smits LP**, Bouter KE, de Vos WM, Borody TJ, Nieuwdorp M. Therapeutic potential of fecal microbiota transplantation. *Gastroenterology* 2013; **145**: 946-953 [PMID: [24018052](#) DOI: [10.1053/j.gastro.2013.08.058](#)]
- 2 **Dethlefsen L**, McFall-Ngai M, Relman DA. An ecological and evolutionary perspective on human-microbe mutualism and disease. *Nature* 2007; **449**: 811-818 [PMID: [17943117](#) DOI: [10.1038/nature06245](#)]
- 3 **Tremaroli V**, Bäckhed F. Functional interactions between the gut microbiota and host metabolism. *Nature* 2012; **489**: 242-249 [PMID: [22972297](#) DOI: [10.1038/nature11552](#)]
- 4 **Mills KH**. TLR-dependent T cell activation in autoimmunity. *Nat Rev Immunol* 2011; **11**: 807-822 [PMID: [22094985](#) DOI: [10.1038/nri3095](#)]
- 5 **Wiedermann CJ**, Kiechl S, Dunzendorfer S, Schratzberger P, Egger G, Oberhollenzer F, Willeit J.

- Association of endotoxemia with carotid atherosclerosis and cardiovascular disease: prospective results from the Bruneck Study. *J Am Coll Cardiol* 1999; **34**: 1975-1981 [PMID: 10588212 DOI: 10.1016/s0735-1097(99)00448-9]
- 6 **Eiseman B**, Silen W, Bascom GS, Kauvar AJ. Fecal enema as an adjunct in the treatment of pseudomembranous enterocolitis. *Surgery* 1958; **44**: 854-859 [PMID: 13592638]
- 7 **Gough E**, Shaikh H, Manges AR. Systematic review of intestinal microbiota transplantation (fecal bacteriotherapy) for recurrent *Clostridium difficile* infection. *Clin Infect Dis* 2011; **53**: 994-1002 [PMID: 22002980 DOI: 10.1093/cid/cir632]
- 8 **Brandt LJ**. American Journal of Gastroenterology Lecture: Intestinal microbiota and the role of fecal microbiota transplant (FMT) in treatment of *C. difficile* infection. *Am J Gastroenterol* 2013; **108**: 177-185 [PMID: 23318479 DOI: 10.1038/ajg.2012.450]
- 9 **Vermeire S**, Joossens M, Verbeke K, Hildebrand F, Kathleen M, Broeck KV. Sa1922 Pilot study on the safety and efficacy of faecal microbiota transplantation in refractory Crohn's disease. *Gastroenterology* 2013; **142**: S-360 [DOI: 10.1016/S0016-5085(12)61356-0]
- 10 **Borody TJ**, Khoruts A. Fecal microbiota transplantation and emerging applications. *Nat Rev Gastroenterol Hepatol* 2011; **9**: 88-96 [PMID: 22183182 DOI: 10.1038/nrgastro.2011.244]
- 11 **Shi XH**. Fecal therapy and Fecal Microecology. *Zhongguo Weishengtaixue Zazhi* 2017; **11**: 128-131
- 12 **Ge Hong**. Handbook of Emergency Conditions. 1st edition. Beijing: China Chinese Medicine Publisher, 2016.
- 13 **Zhang ZJ**. Interpretation of Jin-Kui. 1st edition. Beijing: Peoples Health Publisher, 2005.
- 14 **Qiu LX**. Intelligent use of child feces. *Guangming Zhongyi Zazhi* 2012; **27**: 2069-2070
- 15 **Yang YS**, Wang ZK. Advance in study on fecal microbiota transplantation. *Weichangbingxue Zazhi* 2014; **19**: 1-5 [DOI: 10.3969/j.issn.1008-7125.2014.01.001]
- 16 **Su ZQ**, Zhang WJ, Zhang YS, Wang DC, Meng XM, Wang WX, Wu JR, Li J, Ding X. Literature Study on Fecal Class Chinese Medicines and their application in the ancient prescriptions. *Beijing Zhongyiyao Daxue Xuebao Zazhi* 2016; **39**: 376-382 [DOI: 10.3969/j.issn.1006-2157.2016.05.006]
- 17 **Yin H**. Fundamentals of Traditional Chinese Medicine. 1st edition. Beijing: Foreign Language Press Beijing, 1992.
- 18 **Wheeler CE**. An Introduction to the Principles and Practice of Homeopathy. An Introduction to the Principles and Practice of Homeopathy. London: London Publisher, 1983.
- 19 **O'Brien KA**, Xue CC. A Comprehensive Guide to Chinese Medicine. In: The Theoretical Framework of Chinese Medicine. Singapore: World Scientific Publisher 2003; 47-84 [DOI: 10.1142/9789812794987_0003]
- 20 **Shi XH**. Feces Therapy and Fecal Microecology. *Zhongguo Weishengtaixue Zazhi* 2017; **29**: 128-131
- 21 **Zhang F**, Luo W, Shi Y, Fan Z, Ji G. Should we standardize the 1,700-year-old fecal microbiota transplantation? *Am J Gastroenterol* 2012; **107**: 1755; author reply p.1755-1755; author reply p.1756 [PMID: 23160295 DOI: 10.1038/ajg.2012.251]
- 22 **El-Matary W**, Simpson R, Ricketts-Burns N. Fecal microbiota transplantation: are we opening a can of worms? *Gastroenterology* 2012; **143**: e19; author reply e19-e19; author reply e20 [PMID: 22732575 DOI: 10.1053/j.gastro.2012.04.055]
- 23 **Bakken JS**, Borody T, Brandt LJ, Brill JV, Demarco DC, Franzos MA, Kelly C, Khoruts A, Louie T, Martinelli LP, Moore TA, Russell G, Surawicz C; Fecal Microbiota Transplantation Workgroup. Treating *Clostridium difficile* infection with fecal microbiota transplantation. *Clin Gastroenterol Hepatol* 2011; **9**: 1044-1049 [PMID: 21871249 DOI: 10.1016/j.cgh.2011.08.014]
- 24 **Frank DN**, Robertson CE, Hamm CM, Kpadeh Z, Zhang T, Chen H, Zhu W, Sartor RB, Boedeker EC, Harpaz N, Pace NR, Li E. Disease phenotype and genotype are associated with shifts in intestinal-associated microbiota in inflammatory bowel diseases. *Inflamm Bowel Dis* 2011; **17**: 179-184 [PMID: 20839241 DOI: 10.1002/ibd.21339]
- 25 **Arumugam M**, Raes J, Pelletier E, Le Paslier D, Yamada T, Mende DR, Fernandes GR, Tap J, Bruls T, Batto JM, Bertalan M, Borruel N, Casellas F, Fernandez L, Gautier L, Hansen T, Hattori M, Hayashi T, Kleerebezem M, Kurokawa K, Leclerc M, Levenez F, Manichanh C, Nielsen HB, Nielsen T, Pons N, Poulain J, Qin J, Sicheritz-Ponten T, Tims S, Torrents D, Ugarte E, Zoetendal EG, Wang J, Guarner F, Pedersen O, de Vos WM, Brunak S, Doré J; MetaHIT Consortium, Antolin M, Artiguenave F, Blottiere HM, Almeida M, Brechot C, Cara C, Chervaux C, Cultrone A, Delorme C, Denariac G, Dervyn R, Foerster KU, Friss C, van de Guchte M, Guedon E, Haimet F, Huber W, van Hylckama-Vlieg J, Jamet A, Juste C, Kaci G, Knol J, Lakhdari O, Layec S, Le Roux K, Maguin E, Mérieux A, Melo Minardi R, M'rini C, Muller J, Oozeer R, Parkhill J, Renault P, Rescigno M, Sanchez N, Sunagawa S, Torrejon A, Turner K, Vandemeulebrouck G, Varela E, Winogradsky Y, Zeller G, Weissenbach J, Ehrlich SD, Bork P. Enterotypes of the human gut microbiome. *Nature* 2011; **473**: 174-180 [PMID: 21508958 DOI: 10.1038/nature09944]
- 26 **NIH HMP Working Group**; Peterson J, Garges S, Giovanni M, McInnes P, Wang L, Schloss JA, Bonazzi V, McEwen JE, Wetterstrand KA, Deal C, Baker CC, Di Francesco V, Howcroft TK, Karp RW, Lunsford RD, Wellington CR, Belachew T, Wright M, Giblin C, David H, Mills M, Salomon R, Mullins C, Akolkar B, Begg L, Davis C, Grandison L, Humble M, Khalsa J, Little AR, Peavy H, Pontzer C, Portnoy M, Sayre MH, Starke-Reed P, Zakhari S, Read J, Watson B, Guyer M. The NIH Human Microbiome Project. *Genome Res* 2009; **19**: 2317-2323 [PMID: 19819907 DOI: 10.1101/gr.096651.109]
- 27 **Johnsen PH**, Hilpüsch F, Cavanagh JP, Leikanger IS, Kolstad C, Valle PC, Goll R. Faecal microbiota transplantation versus placebo for moderate-to-severe irritable bowel syndrome: a double-blind, randomised, placebo-controlled, parallel-group, single-centre trial. *Lancet Gastroenterol Hepatol* 2018; **3**: 17-24 [PMID: 29100842 DOI: 10.1016/S2468-1253(17)30338-2]



Published By Baishideng Publishing Group Inc
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-2238242
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

