Systematic review of Chinese herbal medicine for functional constipation

Chung-Wah Cheng, Zhao-Xiang Bian, Tai-Xiang Wu

INTRODUCTION

Constipation is a common gastrointestinal complaint in clinical practice. It affects an estimated 12%-19% of Americans[1], 14% of Asian[2], and up to 27% of the general population depending on demographic factors, sampling, and definition[3]. A variety of over-the-counter medications are available. It is estimated that in the US alone, more than $800 million is spent annually on laxatives[4], with each constipated patient spending approximately $7900, accounting for 6.5% of the total medical expenditure on lower gastrointestinal diseases[5].

However, many patients are disappointed by current conventional treatments[6,7] and, therefore, seek help from complementary and alternative medicine (CAM)[8].

Many traditional Chinese medicine (TCM) interventions have been used for the treatment of constipation. A recent review listed the current clinical research findings of TCM interventions on treating functional constipation (FC)[9]. However, an analysis on the benefits of individual interventions or individual types of interventions, and the qualities of individual study designs has not been undertaken. To draw valid and comprehensive conclusions and make clinical recommendations, a systematic review of Chinese herbal medicine (CHM) for FC is necessary.

This review aimed to determine the efficacy and safety of CHM for the treatment of FC by summarizing current available randomized controlled trials (RCTs) according to the Cochrane approach, newly revised in 2008.

CRITERIA AND METHODS FOR LITERATURE SEARCH

Criteria for considering studies for this review

The criteria for considering studies for this review are as follows. (1) Types of studies. Only RCTs without
restriction on language and publication types were included; pseudo-RCTs were not considered; (2) Types of participants. Patients of both sexes and of any age or any ethnic group with diagnosed FC according to the Rome criteria (Rome I, II or III) were included while those with secondary constipation due to medication and/or other diseases were excluded; (3) Types of interventions. Any form of CHM in any dose or as add-on combination treatment was considered, including oral and external preparations. Comparisons could include placebo, no intervention, acupuncture, massage, Western conventional medication (WCM) or any other interventions. Studies comparing one kind of CHM to another CHM were also included; (4) Types of outcomes. The responder rate of patients with a mean increase of ≥ 1 complete spontaneous bowel movement (CSBM) per week was considered a primary outcome. This outcome by combining a subjective measure of the completeness of defection with an objective measure of stool frequency was considered to be clinically meaningful[10]. If this outcome measure was not used in the study, the overall effectiveness assessment according to the references of Criteria of Diagnosis and Therapeutic Effect of Diseases and Syndromes in Traditional Chinese Medicine[11], Guidelines for Clinical Research on New Chinese Herbal Medication[2], Guidelines for Clinical Research on New Chinese Herbal Medication (Draft)[18] or criteria made by the authors with details and comparable definitions were also considered. Based on the above criteria, interventions which resulted in improvement in general constipated symptoms and/or objective examination indices, for general improvement ≥ 30% compared to their baselines, were counted as effective. Secondary outcomes including (a) Changes in individual symptoms, such as stool frequency, straining, completeness of defection; (b) Changes in examination indices, such as blood nitric oxide (NO) and substance P (SP) levels, total colon transit test (TCTT) and anorectal pressure; (c) Changes in quality of life assessment as assessed with the Health Related Quality of Life (HRQOL) or other validated scales; (d) Adverse events (AEs), such as functional injury of liver or kidney, nausea, vomiting, diarrhea and allergic reaction.

Search methods for identification of studies
All relevant studies regardless of language or publication status were identified by searching the following databases from 1994, the year of the establishment of Rome criteria, up to the May 18 of 2009. (1) Ovid SP, which included the databases of Cochrane DSR (Cochrane Database of Systematic Reviews), ACP Journal Club, DARE (Database of Abstracts of Reviews of Effects), CCTR (Cochrane Central Register of Controlled Trials), CMR (Cochrane Methodology Register), HTA (Health Technology Assessment), and NHSEED (NHS Economic Evaluation Database), AMED, BIOSIS Previews (2001-2006), Biological Abstracts (1994-2000), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations (1950 to Present), Ovid MEDLINE(R) (1950 to Present), Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations Present, and Ovid MEDLINE(R) Daily Update.

Data collection and analysis
The title and abstract of the search results were scanned and full articles for all potentially relevant trials were retrieved. A data extraction form was used to extract data on study characteristics including methods, participants, interventions and outcomes. The reasons for the exclusion of studies were recorded accordingly.
The treatment effects of all CHM interventions were analyzed using Review Manager (Version 5.0). Mean difference with 95% confidence interval was used for continuous data while relative risks with 95% confidence interval was used for binary data. The risk of bias on sequence generation, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and other potential threats to validity were assessed as “YES” (low risk of bias), “NO” (high risk of bias) and “UNCLEAR” (uncertain risk of bias) according to the criteria described in the Cochrane Handbook for Systematic Reviews of Interventions 5.0.1[14].

**SUMMARY OF LITERATURE**

**Description of studies**

A total of 62 articles were identified. Of these, four articles were excluded because they were reviews[9,15-17], two articles were excluded because they dealt with secondary constipation[18,19], ten articles were excluded because they did not include CHM[20-29], and two articles were excluded because they evaluated combination treatment of WCM and CHM by comparing with massage or WCM[30,31]. This left 44 studies which claimed to be “randomized controlled” trials for FC.

Of these studies, three were not real RCTs because they used the admission sequence for treatment allocation, and thus were excluded[32-34]. Six studies were suspected of being published more than once by the authors or publishers, and were excluded[35-40]. This further screening left 35 studies for review. The screening process is summarized in a flow diagram (Figure 1).

**Characteristics of included studies**

A total of 3571 participants (ranging in age from 1 mo to 93 years) were included in these 35 studies. With the exception of two[41,42] in 3 parallel groups, all studies used a 2 parallel group design. Thirty six CHM interventions, including add-on with WCM treatment, were investigated by comparing with another CHM and/or WCM. The details of CHM interventions are listed in Table 3.

**Risk of bias:** The methodological quality of each study's randomization sequence, allocation concealment, blinding, incomplete outcome data, selective outcome reporting and potential threats are summarized in Figures 2 and 3.

**Randomization & allocation concealment:** Only two studies clearly stated a random component in the sequence generation process, Liu et al[43] used randomization software while Xie et al[44] used an open random allocation schedule in sequence generated with a random number table. For the others, the words “random allocation” were cited in abstracts and/or main texts but without description.

**Blinding:** None of the participants, personnel or outcome assessors were blinded in any of these studies. Although minority outcome measures were based on the objective examination results, such as blood NO and SP levels, total colon transit time and anorectal pressure, the risk of both performance bias and detection bias with regard to general symptom improvement and safety issues were deemed very high.

**Flow of participants and intention-to-treat:** None of the trials reported the withdrawal, drop-out and/or loss to follow up rates. The method of handling missing data regarding intention-to-treat or per protocol analysis was not addressed.

**Selective outcome reporting:** Five studies had a high risk of bias with regard to selective outcome reporting[45-49] because the data on individual symptoms, overall improvement and colon transit test pre-specified were reported incompletely in the results. Thus further meta-analysis could not be implemented.

---

**Table 3 Details of CHM interventions in the included studies**

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Preparation form</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>LiuWei Auxiliary</td>
<td>Capsule</td>
<td>4</td>
</tr>
<tr>
<td>LiuWeiAnXiao Capsule/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LiuWeiNengXiao Capsule</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MaRen Auxiliary</td>
<td></td>
<td>7</td>
</tr>
<tr>
<td>MaRenPill/MaZiRenPill</td>
<td>Pill</td>
<td>2</td>
</tr>
<tr>
<td>MaRenRunChang Wan</td>
<td>Pill</td>
<td>1</td>
</tr>
<tr>
<td>Modified MaRenRunChang Wan</td>
<td>Pill</td>
<td>1</td>
</tr>
<tr>
<td>MaRen Capsule</td>
<td>Capsule</td>
<td>1</td>
</tr>
<tr>
<td>MaRen Soft Capsule</td>
<td>Capsule</td>
<td>2</td>
</tr>
<tr>
<td>RunChangTongBianNongSuo Pill</td>
<td>Pill</td>
<td>2</td>
</tr>
<tr>
<td>Others (in single investigation)</td>
<td>Decoction</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>(w/o modification)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Decoction</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>(w/modification)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Capsule</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>Pill</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>Solution</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Granule</td>
<td>1</td>
</tr>
</tbody>
</table>

CHM: Chinese herbal medicine.
Other potential threats to validity: MaRen Capsule, which is derived from the ancient formula MaZiRenWan, was used as the control for treating FC in the Syndrome of Qi and Yin Deficiency in the study by Fan et al. As MaZiRenWan is the representative formula for treating heat constipation (excessive constipation), it is therefore, not suitable for patients suffering from FC with Qi and Yin deficiency, and such a study design was a potential source of bias in assessing the efficacy and safety of MaRen Capsule.

Effects of interventions

None of the trials reported the responder rate on complete spontaneous bowel movement; instead overall effectiveness in which patients with improvement in general constipation symptoms and/or objective examination indices, was commonly used as a primary outcome measure.

CHINESE HERBAL MEDICINE VS PLACEBO/NO TREATMENT

(COMPARISON 01)

None of the included trials used a placebo control, but one used no treatment as a control. General treatment was allowed for all participants in both groups, such as increased fibre and liquid intake, physical exercise and defeacation habit training. The total effectiveness rates of Modified MaRenRunChang Pill and the control were 91.4% and 59.6%, respectively (P < 0.01). Reported AE was included two cases of diarrhea and one case of nausea and loss of appetite.

CHINESE HERBAL MEDICINE VS WESTERN CONVENTIONAL MEDICINE

(COMPARISON 02)

Twenty-six studies, including two with three parallel groups, tested 24 different CHM interventions compared with cisapride, polyethylene glycol 4000 (PEG), mosapride, phenolphthalein, itopride and bifidobacterium.

CHM vs cisapride

Nine studies compared nine different CHM interventions with cisapride or add-on with cisapride and/or lactulose. Eight studies reported total effectiveness rates in the group using CHM which varied from 83.3%-96.7%, while these rates varied from 39.6%-80.5% in the cisapride group (RR 0.24, 95% CI 0.17 to 0.34). The difference suggested that CHM was more effective than cisapride (Figure 4).

The study by Li et al. showed that 92.6% of the CHM group and 68.3% of the cisapride group had normal stool consistency on the fifteenth day of treatment (half of treatment course) (P < 0.01). Sustainable improvement was
noted on the seventh day of the follow-up period when 95.2% and 80.3% of participants reported normal stool consistency, respectively (P < 0.05). The stool interval was shortened significantly from 4.4 ± 1.4 d to 2.2 ± 1.3 d during treatment and 2.1 ± 1.1 d during the post-treatment follow-up period for the CHM treatment group, but not for the cisapride control group. Both groups had shown a significant increase in barium strips excretion in the total colon transit (after treatment) in the treatment group and from 29.86% ± 11.32% (during treatment) and 73.2% ± 12.16% (after treatment) in the cisapride control group. Both groups had shown a statistically significant improvement with regard to abdominal bloating and TCM symptoms (P < 0.05), but not stool frequency, hardness of stool, straining and abdominal pain (P > 0.05).

Six out of nine studies did mention safety measures. All adverse events were reported among patients receiving cisapride in two studies. 43 (43/68) cases in the study by Chen et al. reported diarrhea, gas or abdominal pain and four needed to reduce the dose by half due to adverse reactions. In the study by Cai et al., one (1/60) case reported headache and two (2/60) cases reported lassitude after taking cisapride. No cases were withdrawn due to adverse events.

CHM vs PEG

Eight studies compared seven different CHM interventions with PEG or add-on with PEG treatment. Six studies reported that the total effectiveness rates in the group using CHM or add-on with PEG varied from 92%-100%, while these rates were 18.5%-94% in the PEG group (RR 0.14; 95% CI 0.06-0.34). This finding suggested that CHM or add-on with PEG was more effective than PEG alone (Figure 5).

The study by Liang et al. comparing CHM with PEG showed a statistically significant improvement with regard to abdominal bloating and TCM symptoms (P < 0.05), but not stool frequency, hardness of stool, straining and abdominal pain (P > 0.05). With the exception of time to defecation, the study by Wu et al. showed that CHM, when compared with PEG significantly improved all symptoms, including stool frequency, sensation of urge to defecate, straining, dry stool, use of rescue drug and total symptom score (P < 0.01). The study by Yang comparing CHM with PEG control, reported that CHM resulted in significant benefit with regard to stool frequency, stool type, difficulty and time of defecation during treatment (P < 0.05). Liu et al. showed that the effectiveness of the CHM intervention was equivalent to PEG with regard to stool frequency, stool type, straining, abdominal bloating, abdominal pain and loss of appetite and excretion rate of the total colon transit.
test. The LiuWeiAnXiao Capsule Collaboration Group\textsuperscript{[41]} reported that those who took CHM showed statistically significant improvement in QoL for components on general feeling, vitality, and daily activities ($P < 0.05$) and difficulty of defecation during follow-up ($P = 0.026$), but not on stool frequency, stool type, and excretion rate of the total colon transit test ($P > 0.05$). Since the outcome measures among these five studies were on different scales, further meta-analysis was not implemented.

Three studies mentioned the issue of safety\textsuperscript{[43,60,61]}. Only one AE (i.e. abnormal facial muscle tone) was reported by a patient receiving PEG from the study of LiuWeiAnXiao Capsule.

**CHM vs mosapride**

Four studies compared four different CHM interventions with mosapride\textsuperscript{[41,42,44,64]}. Two of them in three parallel groups included a CHM arm, a mosapride arm and a CHM plus mosapride treatment arm\textsuperscript{[41,64]}. All studies reported total effectiveness rates in the group using CHM or add-on with mosapride which varied from 65.2\%-100\%, while the effectiveness rate was 54.4\%-82.6\% in the mosapride group (RR 0.33; 95\% CI 0.23 to 0.46). This suggested that CHM or add-on with mosapride was more effective than mosapride alone ($P < 0.01$).

The study by Xie et al\textsuperscript{[44]} comparing CHM with mosapride showed a statistically significant improvement in the bothersome of constipation, straining and TCM Qi deficient symptoms ($P < 0.01$). The combined treatment group in Liu's study\textsuperscript{[41]} showed symptom relief with regard to abdominal pain, abdominal bloating and loss of appetite which was significantly better than both CHM and mosapride alone ($P < 0.01$).

Two studies evaluated the safety of CHM interventions. Two patients (2/38) with abdominal pain from the CHM arm, two (2/40) with diarrhea from the mosapride arm and one (1/42) with diarrhea from the combined treatment arm were reported in the study by Qu et al\textsuperscript{[42]}, Liu\textsuperscript{[41]} reported 17 AEs, nine patients with abdominal pain (two from the CHM arm, two from the mosapride arm and three from the combined treatment arm), five with diarrhea (two from the CHM arm and three from the combined treatment arm), two with active bowel sounds and one with dry mouth (both of the latter from the mosapride arm).

**CHM vs phenolphthalein**

Three studies compared three different CHM interventions with phenolphthalein\textsuperscript{[83,67]}. The total effectiveness rates in the group treated with CHM were 90.8\%-95.8\%, while the comparable rates for phenolphthalein were 72.7\%-73.9\% (RR 0.24; 95\% CI 0.13-0.46). Thus the results suggested that CHM was more effective than phenolphthalein (Figure 7). Only Kang et al\textsuperscript{[41]} mentioned that no AEs were observed.

**Other**

The study by Li et al\textsuperscript{[68]} showed that the total effectiveness of the combined treatment (a TCM intervention add-on with itopride) and itopride alone were 92\% and 76\%, respectively ($P < 0.05$). In total three cases of mild abdominal pain and two cases of loose stool were reported in the combined treatment arm while two cases of mild abdominal pain were reported in the itopride arm.
The study by Meng[69] showed that the total effectiveness of the combined treatment (a TCM intervention add-on with live bifidobacterium) and live bifidobacterium alone were 94% and 64%, respectively (P < 0.01). No studies reported safety issues.

**CHINESE HERBAL MEDICINE vs CHINESE HERBAL MEDICINE (COMPARISON 03)**

Ten different CHM interventions were tested in seven trials[48,50,70-74]. Six of them used MaZiRenWan/MaRenWan or its modifications as control (MaRen auxiliary) while one used LuiWeiNengXiao capsules as control (LuiWei auxiliary).

**CHM vs MaRen auxiliary**

The total effectiveness rates in the group treated with CHM varied from 90.7%-98%, and was 70%-94.1% in the MaRen auxiliary (RR 0.24, 95% CI 0.15 to 0.37) (Figure 8). RunChangTongBian NongSuo Pill was the only intervention compared with the same control in two studies[70,71] (RR 0.32, 95% CI 0.17 to 0.59) (Figure 9). These results suggested that the CHM interventions developed by the study authors were more effective than the MaRen auxiliary.

Li et al[63] found that CHM resulted in a statistically significant improvement in time of defection, abdominal bloating and pain, incompleteness of defection, and total symptoms score by comparing QiLang Mixture with MaRenRuan Capsule (P < 0.05), but not on stool frequency, straining and stool type (P > 0.05). From the studies by Guo et al[50,70] published in 2003 and 2006, RunChangTongBian NongSuoWan resulted in significant improvement in the main constipation related symptoms, such as incompleteness and difficulty of defection, when compared with MaRen Pill/MaZiRen Pill (P < 0.05), but it did not improve the minor symptoms of dry mouth, dizziness and palpitation, and blood NO and SP levels (P > 0.05).

Only two studies reported adverse effects[80,81]. Three cases treated with YiQiRunChang Capsule reported diarrhea or abdominal pain while no AEs were observed in Guo’s study.

**CHM vs LiuWei auxiliary**

The study by Gan et al[69] compared TiaoChang Decoction with LuiWeiNengXiao capsules. The total effectiveness rates were 90% and 83.3%, respectively. Patients taking TiaoChang Decoction showed a significant improvement in constipation-related symptoms compared with LuiWeiNengXiao Capsule, and both were safe for consumption without any prominent AEs reported.

**CHINESE HERBAL MEDICINE vs NON-PHARMACEUTICAL INTERVENTIONS (COMPARISON 04)**

The study by Huang[73] compared massage with FuFangLuLui capsules. The total effectiveness rates were 97.8% and 53.3%, respectively (P < 0.05). Massage was more effective in improving stool frequency, straining, lumpy or hard stool, time to defection, sensation of anorectal blockage, manual maneuvers to facilitate the process, sensation of incomplete evacuation and stool weight for each defection. No AEs were reported.
SUMMARY

This review analyzed 35 randomized trials that were conducted in China and published in Chinese medical journals. The results favored the tested CHM interventions in comparison with controls, WCM and some CHM interventions, but not when compared with massage; however, there was not enough replicable evidence to conclude that any specific CHM intervention is effective for FC.

Furthermore, the results of these trials should be interpreted with caution due to the generally low methodological quality of the included studies. First, all studies provided insufficient information on how the random allocation was generated and/or concealed, which is necessary to avoid selection bias. It has been shown that trials with inadequate concealment of allocation or unclear reporting of the technique used were on average 18% more “beneficial” than effect estimates from trials with adequate concealment (95% CI 5% to 29%) [14]. Second, none of the studies used any blinding method. Lack of blinding to participants, healthcare providers and assessors can introduce performance bias and detection bias. Lack of blinding can also be associated with exaggerated estimated intervention effects-by 9% on average, measured as odds ratio [14]. Third, none of the included studies addressed incomplete outcome data, such as missing data due to attrition or exclusions. Inadequate handling of missing data can compromise statistical analysis. Fourth, none of studies had been registered, despite a statement issued in 2004 by the International Committee of Medical Journal Editors (ICMJE) requiring that all clinical trials must be registered in order to be considered for publication [78]. Therefore, protocols were not available to confirm free of selective reporting, especially for those trials which tended to address statistical conclusions instead of listing the details of individual outcomes [46-48]. Fifth, the majority of experimental CHM interventions were prepared by the investigators without detailed information describing underlying rationales on formulation, dosage, manufacturing process, etc. The quality control processes of their tested interventions are unknown. For all these reasons, independent validation of the findings of these trials is necessary.

With regard to selection of an active control in the trials, it is necessary to consider whether there is evidence to support the efficacy of an active control. If no evidence supports the selection of a control, it may bias the trial results. Among all the active controls selected, only PEG had good supporting evidence for the treatment of constipation [79]. Cisapride, mosapride and itopride have been used as gastroprokinetic agents for the symptomatic treatment of functional dyspepsia [2]. However, the evidence and reliability of these interventions might not have been fully captured because only 48.6% studies (17/35) mentioned the safety of these interventions or investigated AEs as one of the secondary outcome measures. It is recommended that more attention should be given to both recording and reporting the harmful effects of these interventions.

This systematic review has several methodological limitations. First, all the data were collected from the reports without directly contacting the trial authors. Therefore, many items of the “Risk of bias” assessment tool could only be classified as “unclear”. Second, most of the included studies were small and without formal sample size calculation. The results were likely to be underpowered. Third, in some cases, different CHM interventions were grouped together for analysis. The results might have been compromised by the heterogeneity within each CHM intervention and by study design. Fourth, in general, the concept of TCM syndrome was not considered when analyzing the data, as some studies only targeted a WCM disease in a particular type of TCM symptom. Therefore, the actual therapeutic effect might not have been fully captured.

CONCLUSION

CHM interventions or CHM combined treatments showed benefit in the treatment of FC when compared with cisapride, PEG, mosapride, phenolphthalein, itopride and bifidobacterium alone, but not when compared with massage. However, the evidence and reliability of these conclusions are compromised by methodological flaws and lack of replicable validation. Further well-designed, randomized, double-blind, placebo-controlled trials need to be carried out and reported in detail according to the Consolidated Standards of Reporting Trials (CONSORT) and/or CONSORT for TCM Statements.

REFERENCES

cases. *Xinglin Zhongyiya* *Zhongyiya* 2008; 28: 26-27


50 Fan DB, Qin XB, Xu JZ, BAI HH, Zeng YH, Zeng GQ, Yin HY. YiQiRunChang capsules for the treatment of QiYin deficiency constipation in 100 cases. *Yunnan Zhongyi Zhongyao Zazhi* 2009; 30: 33

51 Li FZ, Shen JL, Yi QL. Modified MaRen RunChang pills for treating functional constipation in 58 cases. *Henan Zhongyi Xuequn Zazhi* 2004; 19: 62-63


53 Cai HQ. TongBian granules for the treatment of chronic functional constipation in 60 cases. *Zhongguo Minjian Liaoza* 2004; 12: 45-46

54 Chen ZH, Zeng EM, BuZhongYiQi pills combined with cisapride for the treatment of senile functional constipation in 68 cases. *Zhongguo Zhongxi Jiehe Xiaohua Zazhi* 2004; 12: 243-244


59 Xiong GH. ZengYi TongBian formulation for the treatment of functional constipation in 86 cases. *Zhongwai Yiliao* 2008; 35: 67


61 Yan X, Guo MY. Low dose of LiuWeiAnXiao capsules combined with polyethylene glycol 4000 for the treatment of senile functional constipation in 25 cases. *Zhongguo Zhongxi Jiehe Xiaohua Zazhi* 2006; 14: 56-57

62 Wang WW, Li X. Two stages Integrated therapy for chronic functional constipation in 35 cases. *Jiangsu Zhongyiya* 2006; 27: 33

63 Liang C, Wu XB. A clinical study of method promoting the function of Spleen and Stomach, circulation of Qi and removing the stasis blood for the treatment of senile functional constipation. *Sichuan Zhongyi* 2008; 26: 82-84

64 Wang XP, Zhu RH. An efficacy observation of YiQIjian-PiRunChang decoction for the treatment of slow transit constipation in 50 cases. *Yunnan Zhongyi Zhongyao Zazhi* 2007; 28: 8-9


66 Wang QC. ErBai decoction for the treatment of senile functional constipation in 46 cases. *Shandong Zhongyi Zazhi* 2004; 23: 696


71 Guo SY, Xu JY, Gao LY. A clinical observation of RunChangTongBian NongSuo pills for the treatment of chronic functional constipation in 30 cases and its effect on blood SP and NO levels. *Zhongyi Yanjiu* 2006; 19: 26-28

72 Jiang XD, Zhang Q, Liu D. Clinical study on the purge decoction for 70 patients with the senile functional constipation. *Zhongguo Minkaing Yixue* 2007; 19: 1071, 1145


74 Chen Y. Clinical observation of “ChangBi Decoction” in treating slow transit constipation. *Shanghai Zhongyiya Zazhi* 2009; 43: 36-37


S-Editor Tian L · L-Editor Webster JR · E-Editor Lin YP