

Full Length Research Paper

Traditional Chinese medicine for intestinal adhesion: A meta-analysis of randomized controlled trials

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For many years, traditional Chinese medicine (TCM) has been used to treat patients with intestinal adhesion. However, no meta-analysis has been previously conducted to investigate the benefits of TCM therapy in patients with such disorder. This paper aims to summarize the beneficial effects of applying TCM as an adjuvant in patients with intestinal adhesion through conducting a meta-analysis. Until October 2016, seven databases have been retrieved to conduct randomized controlled trials (RCTs) and investigate the effects of applying TCM as an adjuvant treatment in patients with the mentioned disorder. The risk of bias has been assessed according to Cochrane Handbook guidelines. 24 of the 169 potentially relevant trials met the inclusion criteria. However, their methodological qualities were low. The application of TCM as an adjuvant was associated with a significantly lower incidence of intestinal adhesion, as well as higher total effective rate. Compared with the controls as adjuvant treatment, TCM therapy promoted incision healing and reduced the recovery time of borborygmus, anal exhaust time and first defecation time as well as gastrointestinal decompression duration. However, the pooled data for the studies showed there was no difference in blood plasma fibrinogen (FIB). This meta-analysis suggests that TCM therapy appears to cause additional beneficial effects in patients with intestinal adhesion. However, available studies are not adequate to draw a conclusion on the efficacy of TCM due to the methodological flaws of the included trials. Hopefully this work will provide useful experience for further studies; better designed trials are needed to confirm the findings in this study.

Key words: Traditional Chinese medicine, intestinal adhesion, meta-analysis

INTRODUCTION

Intestinal adhesion is a medical condition characterized by connected loops of intestine with other abdominal organs via fibrous tissue bands. It remains an inevitable event of abdominal operations which can cause a large

amount of complications (Valerio, 2014). Literature has reported that the incidence of post-operative intestinal adhesion accounts for 79 to 90% of the patients who are undergoing or underwent laparotomy, and it is still on rise

(over 90%) (Valerio, 2014). Postsurgical adhesions are a principal factor that contributes to the increase in mortality and morbidities with operated patients, who may experience other related conditions such as life-threatening ileus, chronic abdominal pelvic discomfort, chronic pelvic pain, infertility, dyspareunia, and intestinal obstruction, accounting for approximately 75% of all the cases (Ozogul et al., 1998). The pathological mechanism is associated with tissue ischemia, injury, and local overstimulated inflammatory response which are caused by foreign bodies and reduced fibrinolytic activity. The inflammatory response to surgical injury is thought to be one of the factors that result in the formation of adhesion because it leads to the decrease in gastrointestinal activities including contractile activity and gastrointestinal transit. Tumor necrosis factor alpha (TNF- α), interleukin (IL), transforming growth factor beta 1 (TGF- β 1) and other cytokines play an important role in regulating the formation of adhesion, which follows the sequence of tissue inflammation, fibrin deposition, fibrin organization, collagen formation and maturation with the formation of adhesions (Singer et al., 1996a).

Injury, in any form, results in the depression of fibrinolytic activity by releasing the plasminogen activator inhibitors 1 and 2 (PAI1 and PAI2) from mesothelial, endothelial, and inflammatory cells. So medicines that interfere with fibrinolytic activity can cause adhesion formation at the fibrin organization phase. Whereas anti-inflammatory drugs such as steroids can affect later phases and interfere with collagen formation. The mechanisms involved in this process were demonstrated to be secondary to their anti-inflammatory effects inhibition of fibroblast emigration, or depression of procollagen gene expression through the decreased transforming growth factor-beta (TGF- β) secretion (Murata et al., 2006; Singer et al., 1996b). In brief, researchers have identified the four main aspects of the methods to prevent intestinal adhesions formation:

1. Adoption of minimally invasive surgical procedures like laparoscopic surgery to reduce peritoneal trauma;
2. Prevention of fibrin formation with pharmacological agents, such as corticosteroids, heparin or tissue plasminogen activator, sodium hyaluronate, urokinase, application of anti-adhesive film modified chitosan (Murata et al., 2006; Singer et al., 1996b);
3. Reduction of the contact between organs and intra-abdominal contents by using biodegradable barriers such as sodium hyaluronate (SHA), seprafilm, seprafilm anti-adhesion film (Akyildiz et al., 2008);
4. Use of various biologically active substances such as intraoperative use of biological polysaccharide flushing

liquid. In order to avoid side effects, an ideal barrier should be biocompatible, biodegradable, and surgically easy to handle and should act locally. Unfortunately, only certain materials meet those requirements. Besides there exist no large prospective, randomized, double-blind human studies which can demonstrate their efficacy; 5. Some of them are only effective in the short term. Some have no impact on inflammation activity, while others have severe detrimental impacts (Akyildiz et al., 2008).

Therefore, the development of new available drugs to combat intestinal adhesion is of great clinical significance. For the past decades, physicians in Asia have accumulated a tremendous amount of knowledge and experiences in treating adhesive adhesion for decades. This shows that traditional Chinese medicine (TCM) can reduce the production, inflammatory factors and the effusion of fibrin, as well as increase the activity of plasminogen activators, which demonstrates sound effect in stimulating post operational gastrointestinal peristalsis and preventing the occurrence of post operational intestinal adhesion (Wang and Shao, 2010). Oral TCM, *in vitro* application of TCM, acupuncture or electro-acupuncture point injection, and therapeutic TCM enema are performed as indicated, which have been perceived to be less expensive, safer, and more effective than conventional western therapies (Li et al., 2016). At present, no published meta-analysis has been previously done to the benefits of applying TCM as adjuvant treatment in patients with intestinal adhesion. Therefore, this meta-analysis is conducted to quantitatively summarize the add-on effect of TCM in patients with this condition on the basis of the available randomized controlled trials (RCTs).

MATERIALS AND METHODS

Data sources and searches

To identify relevant randomized clinical trials (RCTs), two reviewers (Lian Liu and Song Wei Su) have systematically searched the Medical Literature Analysis and Retrieval System Online (MEDLINE), Excerpta Medica data BASE (EMBASE), Cochrane Central Register, China National Knowledge Infrastructure Database, Chinese Scientific Journals Full Text Database, Wanfang Data Knowledge Service Platform, and the Chinese Biomedical Literature Service System with search keywords including - 'Traditional Chinese medicine' 'traditional Chinese herb' 'Chinese herb' 'TCM' 'herbal medicine' 'ointment' 'TCM enema' 'acupuncture', 'electro-acupuncture' 'intestinal adhesion,' and 'randomized controlled trial,' 'RCT'. In this study, papers dating from the earliest citation in the databases until August 2016 were included. The references of all the selected publications and reviews were manually searched for further relevant articles. Publication languages and types like conference proceedings,

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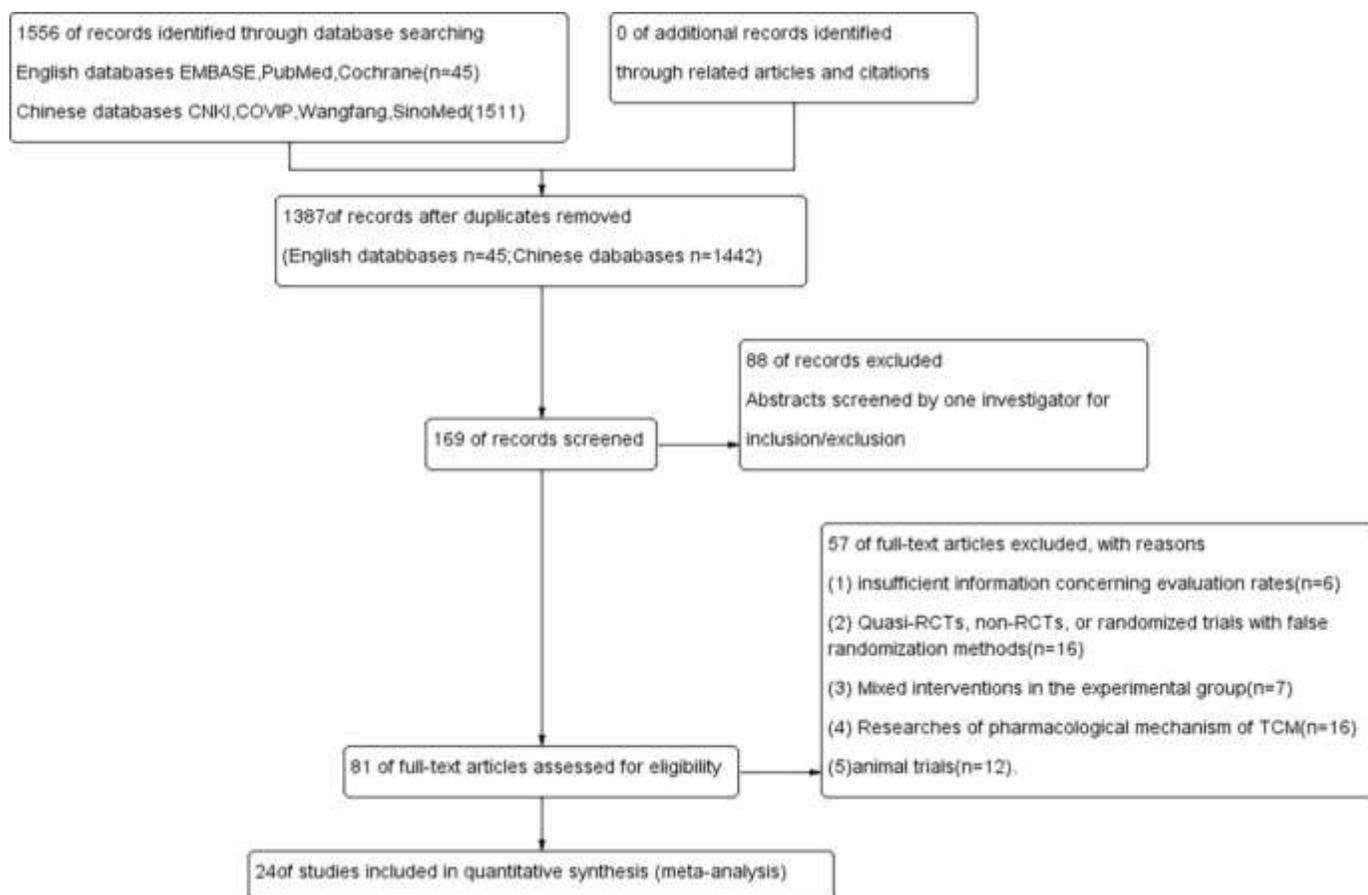


Figure 1. Summary of the literature identification and selection process. CNKI indicates the Chinese National Knowledge Infrastructure Database; CQVIP, the Chinese Scientific Journals Full Text Database; Sino Med, the Chinese Biomedical Literature Service System; TCM, traditional Chinese Medicine; RCTs, Randomized Clinical Trials.

abstract-only articles, and thesis were not limited as long as they met the inclusion criteria.

Study selection

Studies

RCTs were included. Trials were excluded if any of the following factors was identified:

- (1) Inadequate information relevant to evaluation rates;
- (2) Quasi-RCTs, non-RCTs, or randomized trials with false randomization methods;
- (3) Mixed interventions in the experimental group;
- (4) Researches of pharmacological mechanism of TCM;
- (5) Animal trials (Figure 1).

Participants

Patients diagnosed with intestinal adhesion based on any set of explicit criteria were included. Also peritoneal adhesion and intestinal adhesion obstructions were excluded. No limitations were set regarding the participant's age, gender, and surgical types or TCM application. The classification of the degree of intestinal

adhesion was governed by Nair's standard 5-level classification (Nair et al., 1974): (1) Absence of intestinal adhesion (grade 0); (2) Intestinal adhesion of grade I, with an adhesion band observed between the bowels or between the bowel and the abdominal wall; (3) Intestinal adhesion of grade II, where two adhesion bands are observed; (4) Intestinal adhesion of grade III, where more than two adhesion bands are observed but the bowel is not adherent to the abdominal wall; (5) Intestinal adhesion of grade IV in which the bowel is adherent to abdominal wall regardless of the number of adhesion bands.

Interventions

The focused experimental groups received any type of TCM therapy. No limitations had been set on dosages, formulations, routes of administration of TCM, or the types of conventional therapy.

The comparison of TCM with conventional therapy included nothing by mouth (NPO), maintaining the balance of electrolyte and acid-base, continuous gastrointestinal decompression, nutritional support and symptomatic treatment, intra peritoneal pharmacological treatment (medical chitosan and biological polysaccharide flushing liquid etc) and pharmacological treatment (antibiotics dexame thasone, immune potentiator and mosapride etc (Table 1).

Table 1. Basic characteristics of the included studies.

Study	Sample size E/C	Gender: (Male/Female) Age E/C (Mean \pm SD) years	E/C	Duration of experiments	of surgical procedures	Conventional western medicine Of control group	TCM therapy of experimental group	Main outcomes
Wang GC and Shao ML2010	40(24/16)	Gender:E:16/8 C:10/6 Age:E:2-11 C:5-10		2004-2008	Pediatric abdominal surgery	1. Continuous gastrointestinal decompression 2.Supportive therapy	Salvia Magnolia mixture stomach tube injection, 20 ml/time, at 4 h intervals	①③④⑥
Li ZQ al.,2016	96(48/48)	Gender:E:26/22 C:20/28 Age:E:18-70 M=38.46 \pm 2.57 C:15-73M=37.58 \pm 2.64;		2008.6-2013.3	E: Appendectomy 16, cesarean section 10, hysterectomy 4, repair of gastrointestinal perforation 8, repair of abdominal viscera rupture 4, radical operation for carcinoma of colon 2 c:appendectomy16, cesarean section 6, hysterectomy 6, repair of gastrointestinal perforation 10, repair of abdominal viscera rupture 2, radical operation for carcinoma of colon 4	Dexamethasone0.5mg	1. Xingqi Xiaozhi Decotion Oral, 1 dose/day, 200 mL/time, 2 times/days 2. Acupuncture of zhusanli point, at 3 days intervals,15 day/course	②
Zheng YX2013	81(42/39)	Gender:E:25/17 C:26/13 Age:E:17-65M=37.1 C:16-70M=36.3		2008.8-2010.8	Purulent appendicitis	Conventional western treatment	External application of fresh ginger on Shenque point at 0.3 cm thickness, 1 time/day, 7 days/course	①③④
Xie J 2014	48(28/20)	Gender:E:22/6 C:16/4 Age:E:57-79,M=68 C:4-78,M=66		2012.1-2013.1	E:Abdominal anterior resection of rectum (Dixon)24,abdominal perineal combined resection retention anal sphincter surgery (Bacon) 4 C: Abdominal anterior resection of rectum (Dixon)15, abdominal perineal combined resection retention anal sphincter surgery(Bacon)5	1.Application of medical chitosan and Biological polysaccharide flushing liquid 2.NPO,Continuous gastrointestinal decompression, Nutritional support, Symptomatic treatment 3.Maintain the electrolyte and acid-base balance 4: Pharmacological treatment (immunopotentiator,Thymalfasin, mosapride)	1. TCM retention enema, enema, 200 ml/time, 2 times/day 2. External application of same TCM on shenque, zhongwan, shangwan point, 30 min/time, 2 times/day, for 7-10 days	①
Chen M2014	100(50/50)	Gender:E:26/24 C:25/25 Age:E:18-68 (45.10 \pm 21.10) C:20-70 (48.30 \pm 20.3		2011.4-2013.8	Suppurative appendicitis 33, simple appendicitis 25, gangrenous appendicitis 13, perforated appendicitis 16, periappendicural abscess13	Conventional western treatment	1. Simo Decotion oral, 20 mL/time, 3 times/day 2. Acupuncture and moxibustion on zhusanli, shangjuxu, neiguan,gongsun, zhongwan point 20 min/time,1 time/day	①③④

Table 1. Contd.

Yang SM et al. 2007	40(20/20)	Gender:E:13/7 C:11/9 Age:E:48.24-14.6 C:47.94-11.4	2002.5-2005.5	E: Adhesive intestinal obstruction 6, subtotalgastrectomyanastomotic stenosis 2, Pyloric obstruction 1, gastroduodenal perforation 1, ileocecus abscess 3, choledocholithiasisstenosis of common bile duct 7 C:Adhesive intestinal obstruction 8, pyloric obstruction 2, lleocecus abscess 3, choledocholithiasisstenosis of common bile duct 7	External Application of 1%sodium hyaluronate6mL	No.1 Chang zhanlian tablets 8 piece, No. 2 Chang zhanlian 8 piece, for 10 days, orolor Jejunum built-in tube injection	①③④⑤⑧
Liu WP2013	58(31/27)	E:25-65M=42 C:28-56M=40	2010.1-2012.1	Abdominal operation	1.NPO, Continued decompression 2.Maintain water, electrolyte and acid-base balance 3.Total parenteral nutrition support 4.Applicationof H ₂ receptor antagonists and somatostatin 5.Early use ofantibiotics ,adrenalcortexhormones	1. Modified Shaoyao decoction oral, 100 ml/time, 2 times/day 2. High retention enema 300 ml/time, 35-38°C, 1 h/time, 1 time/day, 5 times/1 course, for 2-3 course, at 3 days intervals	②
Lin CY and Zhang LY2012	253(137/116)	NR	2008.1-2009.12	Abdominal operation	Conventional treatment	western External application of self-developed TCM emplastrum on shenque point 1-2 day/time	①
He GZ et al. 2014	58(32/26)	Gender:E:18/14 C:14/12 Age:18-59M=48.5±10.6 C:21-57M=47.8±9.7	2008.7-2011.12	E: Gastric operation 3, appendix operation 7, biliary operation 6, colonic surgery 9, pancreatic operation 2 C: Gynecological operation 3, gastric operation 2, appendix operation 6, biliary operation 5, colonic surgery 7, pancreatic operation 3	Conventional treatment	western 1. Huoxuetongluoliqitongbian decoction oral,1 dose/day, 2 times/day 2. Acupuncture treatment on dachangyu, xiaochuangyu, zhusanli, hegu, neiguan, xiajuxu, zhongfu, xiafu points 3.External application of Liqizhitongtongfu ointment on shenque, zhusanli, dachangyu, xiaochuangyu point, 1 time/day	②

Table 1. Contd.

Tai PJ et al.2005	660(330/330)	Gender:E:210/120 C:185/145 13mouths-68 Age:1-76	1991.8-2004.9	E:Appendicectomy102, gastroduodenal ulcer perforation repair 65, subtotal gastrectomy 50, cholecystectomy 42, partial intestinal resection 30, repair of liver rupture 12, open reduction of intussusception in infants 11, rectal carcinoma mile's operation 14, severe acute pancreatitis by membrane incision with peripancreatic catheter drainage 3 c: Appendicectomy 100, gastroduodenal ulcer perforation repair 65, subtotal gastrectomy 50, cholecystectomy 42, partial intestinal resection 30, repair of liver rupture 15, open reduction of intussusception in infants 11, rectal carcinomamile's operation16, pancreatic pseudocystinternal drainage1	1. Conventional gastrointestinal decompression 2. Correcting acid-base imbalance	Modified dachengqi decoction enema, 200 ml/dose, 50-100 ml/time, at 4 h intervals	②
Shi WR et al.2001	60(30/30)	2000.1-2000.12	Gender:E:16/14 C:17/13 Age:16 -60	E:appendicectomy 15, subtotal gastrectomy 2, splenectomy 2, gastric perforation repair 4, repair of jejunum perforation 1, surgical repair of liver rupture 2, cholecystectomy 4 C: Appendicectomy 14, subtotal gastrectomy 3, splenectomy 3, gastric perforation repair 3, repair of liver rupture 4, cholecystectomy 3	Conventional western treatment	Compound rhubarb sausage water enema, 250 ml/time, 30 min/time, 2 times/day	④
Zhang 2015	JQ 74(37/37)	Gender:E:25/12 27/10 M=43.28±2.18 M=44.68±2.48	2012.7-2013.4	Resection of colorectal carcinoma	1.external application of medical chitosan on surgical incision and intestinal wall 2.Enteral nutrition supportment, gastrointestinal decompression 3.Correcting acid-base imbalance 4.Pharmacological treatment(Antibiotics,immunopot entiator,mosapride)	1. TCM retention enema Enema 400 ml/dose, 200 ml/time, 2 times/days 2. External application of the same TCM on shenque, zhongwan, shangwan point) 30 min/time, 2 times/days, for 2 weeks	①
Lu WH 2013	304(202/102)	Gender:E:119/83 C:58/44 E:13-78M=35±2 C:16-80M=36±3	2009.6-2012.6	E:Chronic appendicitis 18, Simple appendicitis 38, suppurative appendicitis 106 , necrotizing appendicitis 40, intestinal adhesion 13 C:chronic appendicitis 12, Simple appendicitis 15, suppurative appendicitis 57, necrotizing appendicitis 18 , Intestinal adhesion 11	External application of medical chitosan on surgical incision and intestinal wall	External application of mirabilite on surgical site, 6 h/time	①

Table 1. Contd.

Zhang YH et al.1999	396(188/208)	1991.12-1997.5	Gender:E:102/86 C:119/89 Age:E:18-65M=42.2 C:14-69M=44.7	E:Appendicitis 87, intestinal obstruction 34, gastric perforation 14, gastroduodenal ulcer 9, acute pancreatitis 8, cholelithiasis 31, intestinal perforation, intestinal necrosis 5 C: Appendicitis 91, intestinal obstruction 33, gastric perforation16, gastroduodenal ulcer 14, acute pancreatitis 7, cholelithiasis 38, intestinal perforation, intestinal necrosis 9	Conventional treatment	western	TaozhiZhipu mixture oral or by nasogastric tube, 30 ml/time, at 8 h intervals	②③④⑤ ⑦ ⑧
Su FC et al. 2000	178(87/91)	1991.12- 1997.5	Gender:E:52/35 C:56/35 Age:E:18-62M=43.6 C:14-63 M=45.7	E:Appendicitis 46, intestinal obstruction 11, gastric perforation 4, acute necrotizing pancreatitis 1, cholelithiasis 21, intestinal perforation, intestinal necrosis 4 C: Appendicitis 55, intestinal obstruction 10, gastric perforation 3, gastroduodenal ulcer 2, cholelithiasis 19, intestinal perforation, intestinal necrosis 2	Conventional treatment	western	TaozhiZhipu mixture oral or by nasogastric tube, 30 ml/time, at 8 h intervals	③④⑤⑦
Wu Q 2014	150(75/75)	2013.1-2013.12	Gender:E:45/30 53/22 Age:E:26-68M=39.0±8.3 C:26-68M=35.0±14.7	E:Appendix operation 21, subtotal gastrectomy 56, cholecystectomy 39, gynecologic surgery 34, C: Appendix operation 21, subtotal gastrectomy 56, Cholecystectomy 39, Gynecologic surgery 34	Conventional treatment	western	Xuefuzhuyu decoction add modified dachengqi decoction oral, 1 dose/day, 3 times/day	②
Zhang JJ2006	349(182/167)	2000-2004	Gender:E:98/84 C:93/74 Age:E:7-73M=46.3 C:2-80M=45.8	Appendectomy 73, Upper gastrointestinal perforation repair with abdominal cavity drainage 27, subtotal gastrectomy 13, simple splenectomy7, exploratory laparotomy 12, intestinal obstruction reduction 14, cholecystectomy 23, Splenectomy 6, other operation 7. C: Appendectomy 28, subtotal gastrectomy 15, Upper gastrointestinal perforation repair 13, Left hemicolectomy 15, cholecystectomy10, Intestinal obstruction reduction17, enterectomy18, Removal of metallic foreign body 13, splenectomy 13, other operation 25	Conventional treatment	western	Simodecotion oral or by gastric tube 100 Ml/time, 2 times/day, for 1-2 weeks	①
Lin ZG and Zhou WJ 2008	145(78/67)	2005.1-2007.11	Gender:E:48/30 C:37/30 Age:E:9-82 C:11-78	E: Appendicectomy 30, cholecystectomy 19, subtotal gastrectomy 4, reduction of intestinal obstruction 10, splenectomy 3, exploratory laparotomy 12 C: Appendicectomy 24, cholecystectomy 20, subtotal gastrectomy 2, intestinal obstruction reduction 9, splenectomy 2, exploratory laparotomy 10	1. gastrointestinal decompression 2. Fluid replacement 3. Antibiotic application and energy boost	NPO,	Simodecotion oral or by gastric tube 100 ml/time, 2 times/day, for 1-2 weeks	②

Table 1. Contd.

Lin XM et al. 2000	60(30/30)	1999.3-1999.10	Gender:E:18/12 C:20/10 Age:E3d-15 C:2d-17	Abdominal operation	Conventional western treatment	Simodecotion oral, at 6 h intervals, for 5-7 days	①③④⑤
Yu SW 2015	90(45/45)	2014.2-2015.2	Gender:E:29/16 C:30/15 Age:E:1-14 M=5.2±1.1 C:1.2-14 M=5.9±1.3	E: Appendicitis 8, intestinal necrosis 9, choledochocyst 11, volvulus 17, C: Appendicitis 7, intestinal necrosis 10, choledochus cyst 10, volvulus 18	1. Reasonable diet 2. Oral belladonna Tablets 10 mg, 3 times/d, 14 days/course	1. Xuefuzhuyu decoction combined with modified dachengqi decoction 2. Oral, 1 dose/day, retention enema, 150-200 ml/time, 14 days/course	②
Zhang H2009	228(114/114)	2005.1-2008.1	NR	Abdominal operation	1.Application of antibiotics 2.Nutritional support	ZhiPu hollow type suppositories retention enema 200 ml/time, 30 min/time, 1 time/days	②
Li PF2014	60(30/30)	2012.6-2013.6	Gender:E:14/16 C:15/15 Age:16-54 E:M=36.37±15.02 C:M=38.23±14.40	Acute supportive appendicitis	1. Semi-recumbent position, encourage early ambulation 2. Anti-inflammatory rehydration 3. Symptomatic and supportive treatment	Electro-acupuncture on Zhongwan, Tianshu, Shangjuxu, Zusanli points voltage 6-9V, 30 min/time, 1 time/days, for 2 days	①③④⑤
Ye BZ 2015	80(40/40)	Gender:E:23/17 C:22/18 Age:E:19-68M (43.26±10.82) C:21-69 (44.89±11.03)	= 2012.3-2013.3	Postoperative suppurative appendicitis	1. Anti-infective therapy 2. Fluid replacement 3. Nutritional support	Self-made traditional Chinese medicine (TCM) enema oral, 250 ml/time	①③⑥
Zhang X2015	150(75/75)	Gender:E:40/35 C:42/33 Age:E:18-66 M=45.5±3.4 C:19-66M=44.9±2.7	2011.1-2013.1	E: Appendicitis perforated appendicitis 55, purulent appendicitis 45 C: Perforated appendicitis 52, purulent appendicitis 48	1.Anti-infective therapy 2. Fluid replacement 3. Nutritional support 4. Analgesic therapy,	Severe abdominal pain: Huang qi jian zhong decoction oral, 1 dose/days, 2 times/days for 1 mouths	②③④⑥

Control group treatments

Control groups were defined as patients who received any type of conventional western therapy for intestinal adhesion, instead of TCM treatments.

Outcome measures

The primary outcomes that were taken into in this study were the incidence of intestinal adhesion, the total effective rates after intervention for the duration of treatment and the recovery of gastrointestinal function which was defined as the recovery time of borborygmus, anal exhaust time and anal defecation time by clinical evaluation. Two reviewers also evaluated the average time of incision healing, the termination time of gastrointestinal decompression and blood plasma fibrinogen (FIB) as secondary outcomes.

Data extraction

Two reviewers extracted data independently in a predefined data extraction form. Disagreements were resolved by discussion and consensus with a third reviewer. The extracted data included the first author; study characteristics; participant characteristics (that is, mean age, gender, sample size, surgical procedures, and systemic therapy); the therapy of the experimental and control group treatments; measured outcomes. For studies with insufficient information, the reviewers contacted the primary authors, when possible, to acquire and verify the data.

Risk of bias assessment

Two independent authors assessed the risk of bias in each study via the tool named cochrane risk of bias (Higgins et al., 2011) (Figure 2).

Data synthesis and analyses

In case of meta-analysis, the total effective rates of dichotomous data were pooled by using risk ratios (RRs). All statistical analyses were performed via Review Manager 5.3.1 software (Cochrane Community, London, United Kingdom). The results were compared to tell the differences between experimental and control groups. Cochrane's χ^2 and I^2 tests were used to assess the degree of heterogeneity between studies. In the χ^2 and I^2 tests, there was considerable heterogeneity for P values less than 0.10 or I^2 value above 50% respectively (Higgins et al., 2011). In this case, a random-effects model was used to compute the global RR, MD or SMD. Otherwise, with P values greater than 0.10 and I^2 less than 50%. The between-study heterogeneity was not substantial, and the fixed-effect models were suitable. Clinical heterogeneity was assessed by reviewing the differences in the distribution of participants' characteristics among trials (that is, age, gender, and duration of disorder and surgical procedures, TCM formulas).

RESULTS

Study selection

From a total of 169 titles, the full text of 24 potentially relevant studies was reviewed to confirm their eligibility.

Among these 169 studies, 88 were excluded, including insufficient information relevant to evaluation rates ($n=6$), quasi-RCTs, non-RCTs, or randomized trials with false randomization methods ($n=16$), mixed interventions in the experimental group ($n=7$), and researches of pharmacological mechanism of TCM ($n=16$), animal trials ($n=12$).

Study characteristics

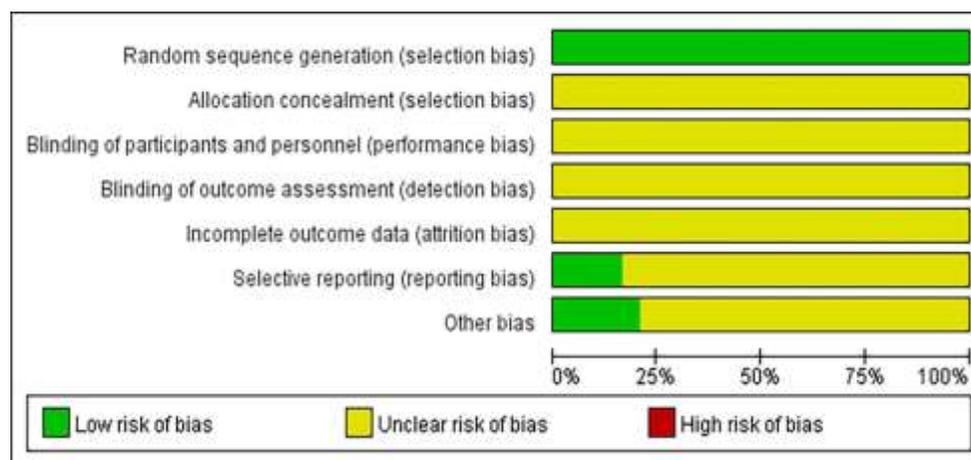
All the 24 trials included in this study were published in Chinese. A total of 3758 participants were included in these trials, with 1955 and 1803 in the experimental and control groups respectively. The sample sizes of these trials ranged from 40 (Wang and Shao, 2010) to 660 (Tai et al., 2005). No trial was reported on adverse events (Table 1). The components and suppliers of the TCM referred in each trial varied from each other. The most common form of internal TCM, applied in 18 trials, was decoction, including Salvia Magnolia mixture (Wang and Shao, 2010), Xingqi Xiaozhi Decotion (Li, 2016), Huangqi, Jianzhong Decotion (Zhang, 2015), Dahuang Mudanpi Decotion (Zhang, 2015), Dachengqi Decotion (Wu and Li, 2014; Yu, 2015), Simo Decotion (Chen, 2014; Zhang, 2006; Lin and Zhou, 2008; Lin et al., 2000), Shaoyao decoction (Liu, 2013), Huoxuetongluoliqitongbian decoction (He et al., 2014), TaozhiZhipu mixture (Zhang, 1999) (Su et al., 2000), Xuefuzhuyu decoction (Wu and Li, 2014; Yu, 2015), ZhiPu hollow type suppositories (Zhang, 2009), other forms of TCM used in clinical trials were acupuncture (Li et al., 2016) and electro-acupuncture (Li, 2014), Chinese-herb Enema in 8 trials (He et al., 2014; Liu, 2013; Xie et al., 2014; Shi et al., 2011; Tai et al., 2005; Ye, 2015; Zhang, 2015; Zhang, 2015), external application of TCM on Shenque or other points in 6 trial (He, 2014; Lu, 2013; Lin and Zhang, 2012; Xie et al., 2014; Zhang, 2015; Zheng et al., 2013), and oral TCM tablets in one trial (Yang et al., 2007) (Table 1). The most common and representative components used were Rhubarb, Rhizoma Coptidis, Rhizoma Chuanxiong, Cortex Moutan, Salvia miltiorrhiza, mirabilite, Radix curcumae, Fructus Aurantiilmaturus, Rhizomacyperi, Astragalusmembranaceus etc (Table 1).

Risks of bias assessment

The methodological qualities of all the included trials were poor (Figure 2). Although all these trials had reported randomization, only three trials adequately depicted the randomization method: one through throwing dice (Li et al., 2016), one with a random number table (Zheng et al., 2013), and another one with operation time sequence number (Yang et al., 2007). Moreover, none of the studies reported information such as the allocation concealment or blinding of participants as well

Table 2. Meta-analysis of incidence of intestinal adhesion of TCM versus conventional therapy.

Study or Subgroup	Experimental		Control		Weight	Risk Ratio M-H,Random,95%CI
	Event	Total	Event	Total		
Chen M2014	9	50	43	50	16.8%	0.21 [0.11, 0.38]
Li PF2014	2	30	8	30	2.8%	0.25 [0.06, 1.08]
Lin CY and Zhang LY2012	6	137	11	116	6.6%	0.46 [0.18, 1.21]
Lin XM et al.2000	0	30	3	30	0.7%	0.14 [0.01, 2.65]
Lu WH 2013	13	202	11	102	10.4%	0.60 [0.28, 1.28]
Wang GC and Shao ML2010	1	24	3	16	1.3%	0.22 [0.03, 1.95]
Xie J 2014	0	28	2	20	0.7%	0.14 [0.01, 2.86]
Yang SM et al.2007	4	20	16	20	7.5%	0.25 [0.10, 0.62]
Ye BZ 2015	3	40	11	40	4.2%	0.27 [0.08, 0.90]
Zhang JJ2006	29	182	75	167	43.7%	0.35 [0.24, 0.52]
Zhang JQ 2015	0	37	4	37	0.7%	0.11 [0.01, 1.99]
Zheng YX2013	4	42	7	39	4.6%	0.53 [0.17, 1.67]
Total (95% CI)		822		667	100.0%	0.33 [0.26, 0.42]
Total events	71		194			
Heterogeneity: Tau ² = 0.00; Chi ² = 7.66, df = 11 (P = 0.74); I ² = 0%						
Test for overall effect: Z = 8.81 (P < 0.00001)						

**Figure 2.** Risk of bias graph.

as study personnel; none reported the details of the blinding of outcome assessment. All the relevant trials did not address incomplete outcome data and selective reporting. No other biases were found and high risk bias was not present in these trials; however, considering their poor methodological quality, it was determined that an unclear risk of bias should be given to all the included trials.

Primary outcomes

Incidence of intestinal adhesion

12 studies contained 1489 subjects (882 in experimental

groups and 667 in the control groups). All subjects from the two groups adopted basic intervention strategies. The pool of the results from these trials showed there existed a great difference in the incidence of intestinal adhesion between the TCM and conventional therapy groups (RR = 0.33, 95% confidence interval [CI]=0.26, 0.42, and $P < 0.00001$) using the fixed-effects model (Heterogeneity: $P = 0.74$, $I^2 = 0\%$) (Table 2).

Total effectiveness rates

Eleven studies contained 2015 subjects (1009 in experimental groups and 841 in the control groups). Results of meta-analysis which adopted the random-effects model

Table 3. Meta-analysis of incidence of intestinal adhesion of TCM versus conventional therapy.

Study or Subgroup	Experimental		Control		Weight	Risk Ratio
	Event	Total	Event	Total		M-H,Random,95%CI
Chen M2014	9	50	43	50	16.8%	0.21 [0.11, 0.38]
Li PF2014	2	30	8	30	2.8%	0.25 [0.06, 1.08]
Lin CY and Zhang LY2012	6	137	11	116	6.6%	0.46 [0.18, 1.21]
Lin XM et al.2000	0	30	3	30	0.7%	0.14 [0.01, 2.65]
Lu WH 2013	13	202	11	102	10.4%	0.60 [0.28, 1.28]
Wang GC and Shao ML2010	1	24	3	16	1.3%	0.22 [0.03, 1.95]
Xie J 2014	0	28	2	20	0.7%	0.14 [0.01, 2.86]
Yang SM et al.2007	4	20	16	20	7.5%	0.25 [0.10, 0.62]
Ye BZ 2015	3	40	11	40	4.2%	0.27 [0.08, 0.90]
Zhang JJ2006	29	182	75	167	43.7%	0.35 [0.24, 0.52]
Zhang JQ 2015	0	37	4	37	0.7%	0.11 [0.01, 1.99]
Zheng YX2013	4	42	7	39	4.6%	0.53 [0.17, 1.67]
Total (95% CI)		822		667	100.0%	0.33 [0.26, 0.42]
Total events	71		194			
Heterogeneity: Tau ² = 0.00; Chi ² = 7.66, df = 11 (P = 0.74); I ² = 0%						
Test for overall effect: Z = 8.81 (P < 0.00001)						

Table 4. Forest plot of comparison: Total effective rates.

Study or Subgroup	Experimental			Control			Weight	Mean Difference
	Mean	SD	Total	Mean	SD	Total		IV,Random, 95%CI
Chen M2014	23.1	9.8	50	35.1	15.3	50	8.6%	-12.00[17.04,-6.96]
Li PF2014	25.77	6.68	30	29.7	7.1	30	10.2%	-3.93[-7.42,-0.44]
Lin XM et al.2000	16.0	6.0	30	34.0	10.0	30	9.5%	-18.00[-22.17,-13.83]
Su FC et al. 2000	16.2	7.24	87	21.76	11.25	91	10.8%	-5.56 [-8.33, -2.79]
Wang GC and Shao ML2010	24.1	4.6	24	38.7	5.5	16	10.4%	-14.60[-17.86,-11.34]
Yang SM et al.2007	26.2	7.7	20	43.9	11.2	20	7.7%	-17.70[-23.66, -11.74]
Ye BZ 2015	23.29	5.83	40	37.08	9.27	40	10.3%	-13.79[-17.18, -10.40]
Zhang X2015	24.01	10.26	75	36.05	14.15	75	9.7%	-12.04[-16.00, -8.08]
Zhang YH et al.1999	17.02	8.36	188	23.34	14.05	208	11.2%	-6.32 [-8.57, -4.07]
Zheng YX2013	26.62	4.77	42	35.67	2.95	39	11.6%	-9.05 [-10.76, -7.34]
Total (95% CI)			586			599	100.0%	-10.97 [-13.71, -8.23]
Heterogeneity: Tau ² = 16.04; Chi ² = 66.75, df = 9 (P < 0.00001); I ² = 87%								
Test for overall effect: Z = 7.85 (P < 0.00001)								

(Heterogeneity: P < 0.00001, I² = 93%) indicated a greatly higher total effectiveness rate for TCM therapy as compared with that of the control groups (RR = 1.32, 95% CI = 1.17, 1.48, and P < 0.00001) (Table 3).

Recovery time of borborygmus

Ten studies contained 1185 subjects (586 in experimental groups and 599 in the control groups). Results of meta-analysis by using the random-effects model (Heterogeneity: P < 0.00001, I² = 87%) indicated significant effect in the

experimental groups compared to the control groups (MD = -10.97, 95% CI = -13.71, -8.23, and p < 0.00001) (Table 4).

Anal exhaust time

Eleven studies contained 1245 subjects (616 in experimental groups and 629 in the control groups). Results of meta-analysis which applied the random-effects model (Heterogeneity: P < 0.00001, I² = 93%) indicated significant effect in the experimental groups as compared

Table 5. Forest plot of comparison: Recovery time of Borborygmus.

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Chen M2014	31.2	9.8	50	45.3	10.1	50	9.3%	-14.10[-18.00,-10.20]
Li PF2014	31.7	7.85	30	37.23	7.86	30	9.3%	-5.53 [-9.51, -1.55]
Lin XM et al.2000	26.0	5.0	30	57.0	15.0	30	8.5%	-31.00[-36.66, -25.34]
Shi WR et al.2001	38.3	4.025	30	50.1	3.957	30	10.0%	-11.80 [-13.82, -9.78]
Su FC et al. 2000	31.45	12.07	87	43.25	20.54	91	8.9%	-11.80 [-16.72, -6.88]
Wang GC and Shao ML2010	32.0	5.0	24	69.0	10.0	16	8.7%	-37.00 [-42.29,-31.71]
Yang SM et al.2007	42.0	16.3	20	66.5	8.5	20	7.2%	-24.50 [-32.56,-16.44]
Ye BZ 2015	31.59	7.9	40	48.26	12.07	40	9.1%	-16.67 [-21.14,-12.20]
Zhang X2015	32.1	10.16	75	46.34	11.2	75	9.5%	-14.24 [-17.66,-10.82]
Zhang YH et al.1999	32.73	12.07	188	44.25	20.14	208	9.6%	-11.52 [-14.76, -8.28]
Zheng YX2013	35.41	5.02	42	47.03	3.11	39	10.0%	-11.62 [-13.42, -9.82]
Total (95% CI)			616			629	100.0%	-16.80 [-20.83,-12.77]
Heterogeneity: Tau ² = 41.36; Chi ² = 146.07, df = 10 (P < 0.00001); I ² = 93%								
Test for overall effect: Z = 8.18 (P < 0.00001)								

Table 6. Forest plot of comparison: Anal exhaust time.

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Li PF2014	39.03	7.02	30	44.23	7.04	30	23.3%	-5.20 [-8.76,-1.64]
Lin XM et al.2000	49.0	9.0	30	68.0	15.0	30	19.5%	-19.00 [-25.26,-12.74]
Su FC et al. 2000	39.08	19.06	87	49.17	15.69	91	21.1%	-10.09 [-15.23,-4.95]
Yang SM et al.2007	53.6	19.2	20	77.9	15.2	20	13.3%	-24.30 [-35.03,-13.57]
Zhang YH et al.1999	38.08	19.06	188	51.17	20.36	208	22.9%	-13.09 [-16.97,-9.21]
Total (95% CI)			355			379	100.0%	-13.26 [-18.89,-7.63]
Heterogeneity: Tau ² = 32.19; Chi ² = 23.60, df = 4 (P < 0.0001); I ² = 83%								
Test for overall effect: Z = 4.62 (P < 0.00001)								

to the control groups (MD = -16.80, 95% CI = -20.83, -12.77, and $P < 0.00001$) (Table 5).

Anal defecation time

Five studies contained 734 subjects (335 in experimental groups and 379 in the control groups). Results of meta-analysis by which applied the random-effects model (Heterogeneity: $P < 0.0001$, $I^2 = 83\%$) indicated significant effect in the experimental groups compared to the control groups (MD = -13.26, 95% CI = -18.89, -7.63, and $P < 0.00001$) (Table 6).

Secondary outcomes

Average time of incision healing

Only three studies which involved 270 participants

reported average time of incision healing (139 in experimental groups and 131 in the control groups). With random-effects modeling (Heterogeneity: $P = 0.009$, $I^2 = 79\%$), the pooled data for the 3 studies showed there existed a difference between the experimental (139) and the control groups (131) in terms of the average time of incision healing (MD = -1.90, 95% CI = -2.69, -1.10, and $p < 0.00001$) (Table 7).

Termination time of gastrointestinal decompression

Only 2 studies which involved 574 participants reported the termination time of gastrointestinal decompression. With random-effects modeling (Heterogeneity: $P = 0.08$, $I^2 = 66\%$), the pooled data for the two studies showed there existed a difference between the experimental (275) and control groups (299) in terms of the average time of incision healing (MD = -26.11, 95% CI = -31.65, -20.56,

Table 7. Forest plot of comparison: Anal defecation time.

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Wang GC and Shao ML2010	6.3	0.5	24	8.1	0.4	16	42.0%	-1.80 [-2.08, -1.52]
Ye BZ 2015	8.24	2.06	40	11.37	2.85	40	24.2%	-3.13 [-4.22, -2.04]
Zhang X2015	8.44	1.62	75	9.58	2.45	75	33.8%	-1.14 [-1.80, -0.48]
Total (95% CI)			139			131	100.0%	-1.90 [-2.69, -1.10]
Heterogeneity: $\tau^2 = 0.37$; $\chi^2 = 9.47$, $df = 2$ ($P = 0.009$); $I^2 = 79\%$								
Test for overall effect: $Z = 4.68$ ($P < 0.00001$)								

Table 8. Forest plot of comparison: Average time of incision healing.

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Su FC et al. 2000	69.45	11.25	87	92.54	21.3	91	46.8%	-23.09[-28.06,-18.12]
Zhang YH et al.1999	70.04	15.25	188	98.8	25.62	208	53.2%	-28.76[-32.87,-24.65]
Total (95% CI)			275			299	100.0%	-26.11[-31.65,-20.56]
Heterogeneity: $\tau^2 = 10.66$; $\chi^2 = 2.97$, $df = 1$ ($P = 0.08$); $I^2 = 66\%$								
Test for overall effect: $Z = 9.23$ ($P < 0.00001$)								

Table 9. Forest plot of comparison: Blood plasma fibrinogen (FIB).

Study or Subgroup	Experimental			Control			Weight	Mean Difference IV, Random, 95%CI
	Mean	SD	Total	Mean	SD	Total		
Yang SM et al.2007	4.58	0.96	20	5.61	1.31	20	41.2%	-0.88[-1.53,-0.23]
Zhang YH et al.1999	0.45	0.03	188	0.5	0.55	208	58.8%	-0.13 [-0.32, 0.07]
Total (95% CI)			208			228	100.0%	-0.44 [-1.16, 0.29]
Heterogeneity: $\tau^2 = 0.22$; $\chi^2 = 4.70$, $df = 1$ ($P = 0.03$); $I^2 = 79\%$								
Test for overall effect: $Z = 1.17$ ($P = 0.24$)								

and $P < 0.00001$) (Table 8).

Blood plasma fibrinogen (FIB)

Only 2 studies contained 436 participants which reported the Blood plasma fibrinogen (FIB). With random-effects modeling (Heterogeneity: $P = 0.08$, $I^2 = 66\%$), the pooled data for the two studies showed no difference between the experimental (208) and control groups (228) in the blood plasma fibrinogen (SMD = -0.44, 95% CI = -1.16, 0.29, and $P = 0.24$) (Table 9).

Adverse events

No studies reported adverse events in the experimental groups or the control groups. It seemed to be safe to use

TCM in clinical practice. However, this point needed further investigation.

Assessment of Publication Bias

In this review, funnel plots of incidence, total effective rate, the recovery time of borborygmus and anal exhaust time were evaluated in Figure 3. Visual inspection of funnel plots was not substantially symmetrical, suggesting some evidences of publication bias.

DISCUSSION

Summary of evidence

Even though most of the trials were small in terms of size

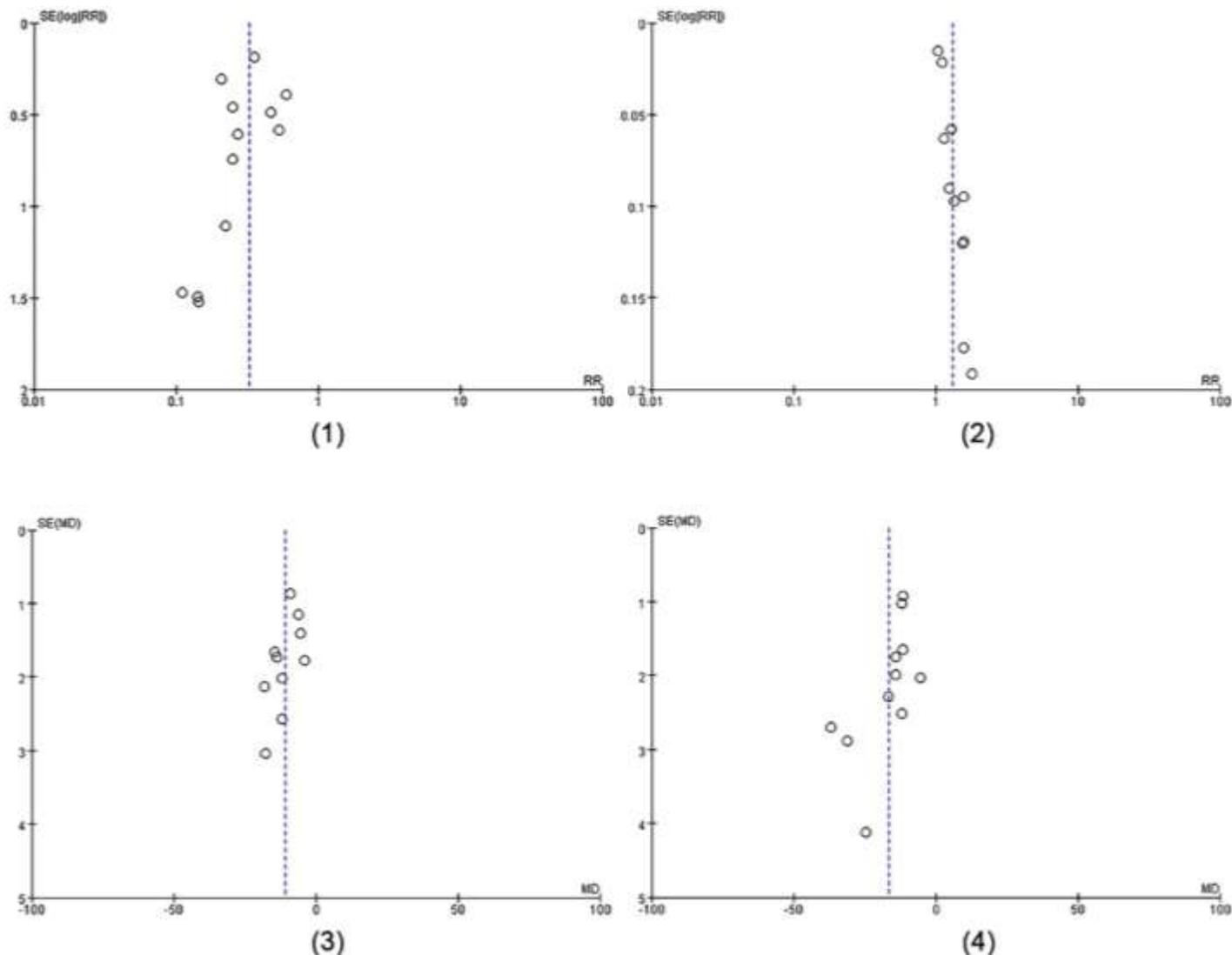


Figure 3. (1) Funnel plot of incidence; (2) total effective rate; (3) the recovery time of borborygmus; (4) Anal exhaust time.

with poor methodological quality, the analysis of the pooled data showed a consistently superior effect of TCM in terms of incidence, total effective rate, and the recovery of gastrointestinal function and incision healing as compared with to the control groups. However, the pooled data for the two studies showed no difference in the blood plasma fibrinogen (FIB), which was not in accordance with the included research. In addition, only one study reported the prothrombin time (PT) and the activated partial thromboplast in time (APTT) of TCM group was longer than that of control group after TCM therapy (Yang et al., 2007). Additionally another study reported that the whole blood viscosity, plasma viscosity were significantly lower in the TCM group than that in the control group (Zhang et al., 1999), which demonstrated that TCM could prevent postoperative intestinal adhesion through anticoagulation, fibrinolysis and the reduction of

abdominal fibrinogen concentration (Yang et al., 2007; Zhang et al., 1999). Furthermore, only one study reported that the serum IL-2 of the TCM enema group was significantly higher than that of the control group, which meant that TCM enema could promote the immune response after abdominal surgery and improve anti-infection ability. Also results showed that the blood gastrin and motilin levels in the enema group were significantly higher than those in the control group, both of which can enhance gastrointestinal motility (Shi et al., 2011). However, these evaluation indexes were not analyze due to the unavailability of more available studies, more sensitive and effective physiological and biochemical indexes. And seroimmunological indicators needed further evaluation in the future. There were few adverse effects, and no patients dropped out of their trials due to adverse effects.

Possible rationales for EA-TCM for treatment of intestinal adhesion

TCM holistic medical system has developed through accumulating intelligence from ancient theories (such as the seminal text of TCM titled the 'Yellow Emperor's Inner Canon') and daily life experiences as well as continuous refining and experimenting by generations of practitioners. The comprehensive approach of TCM emphasizes focuses more on disease prevention through the restoration of syndromes (Zheng) or "pathophysiologic" status. From the TCM perspective of TCM, body constitution is transient in nature and a disease may ensue when the inner harmony of a human body is disrupted in response to the external environment (Low et al., 2016). According to principle of determination of treatment based on the TCM of differentiation syndrome, intestinal adhesion of the patients were divided into stagnation of qi and blood stasis type, syndrome of intestinal heat and fu-organ excessiveness type and accumulation of cold evil in the intestines type, the scholars added or subtracted some kinds of TCM herbs according to various clinic manifestation in clinical practice, which were based on the TCM principles. Although the components and methods of TCM used in each trial in our meta-analysis varied, the treatment principles were consistent: purging the bowels and activating blood circulation, reduce the production or inflammatory factors and the effusion of fibrin, increase the activity of plasminogen activators and so on and so forth (Xie et al., 2014).

The most common compositions in these TCM formulas were Berberine Hydrochloride (Berberine), a natural plant alkaloid derived from *Rhizoma Coptidis*, since research results showed it could significantly lower expression of inflammatory cytokines interleukin-1 β (IL-1 β), Interleukin 6 (IL-6), transforming growth factor- β (TGF- β), tumor necrosis factor- α (TNF- α), and clinical TCM practitioners used it as a promising strategy to prevent adhesion by down regulating intercellular adhesion molecule-1 (ICAM-1) and reduce inflammation by inhibiting the transforming growth factor-activated kinase 1 (TAK1)/c-Jun N-terminal kinase (JNK) and TAK1/nuclear factor- κ B (NF- κ B) signaling (TAK1/JNK and TAK1/NF- κ B signaling) after abdominal surgery, which brought out a good therapeutic approach for the management of postoperative abdominal adhesion and inflammation (Zhang et al., 2014).

Rhein-arginine (RhA), which is derived from rhubarb, could prevent the formation of postoperative intestinal adhesion in two ways: (1) Reducing vascular permeability, reducing seepage, inhibiting connective tissue proliferation and suppressing excessive expression of inflammatory cytokines; (2) Reducing the hydroxyproline (Hyp) contents of cecal, reducing the expression of transforming growth factor beta 1 (TGF- β 1), inhibiting increased activity of plasminogen activator inhibitor (PAI)

and increasing tissue-type-plasminogen activator (t-PA) activity. As a result, the activity of plasminogen was enhancing the fibrinogen effusion to dissolved (Yin, 2009).

Ligustrazine was extracted from *Rhizoma Chuanxiong*. It was a piece of herbal medicine which could promote blood circulation, increase the amount of opened tiny blood vessel, speed up the blood circulation, resist blood platelet congregation, and restrain the smooth muscle constriction showing prominent anti-inflammatory property. Furthermore, reduce the percentage of the blood WBC as well as the concentration of the plasma fibrinogen (FIB), and the serum levels of IL-1 α , IL-6, TNF- α , inhibit the proliferation of hypertrophic scar fibroblasts and decrease the degree of peritoneal adhesions (Shi, 2007).

Paeonol was the main effective constituent in *Cortex Moutan*, which could significantly reduce the blast of fibrocyte proliferation which was affected by the inflammatory factor lipopolysaccharide (LPS) and tumor necrosis factor (TNF). It also has the up-regulation effects in mesothelial cell proliferation, while mesothelial cell and blast of fibrocyte are very important cells in the process of peritoneal adhesion. This Chinese herb can also modulate the excreting of tissue-type plasminogen activator (t-PA) /plasminogen activator inhibitor (PAI) by changing the interaction of macrophages and mesothelial cells. Furthermore, this Chinese herb could also promote fibrin dissolving. Thus, it can prevent peritoneal adhesion from occurring (Yang, 2007).

Salvianolate, which was derived from *Salvia Miltiorrhiza*, significantly reduces the extent of postoperative intestinal adhesion—by obviously decreasing the levels of IL-1 β , TNF- α and TGF- β 1 expression levels, and inhibiting fibrous connective tissue hyperplasia. And *Salvia Miltiorrhiza*, had been shown to prevent intestinal adhesion in rat models due to its pharmacological effects to minimize postoperative depression of local fibrinolytic activity, reduce the severity of postoperative adhesions, and alleviate the pathological injuries at the site of adhesion (Sui et al., 2007)

In addition to the aforementioned single compositions of herbs, the compound TCM formula, which based on the functional classification principle of *junchenzuoshi* rules, and the traditional principle of syndrome differentiation, lay emphasis on holistic health care, demonstrated more remarkable curative effect. The pharmacodynamics molecules in TCM ingredient molecules could be divided into *jun*-component, *chen*-component, *zuo*-component, and *shi*-component in each decoction (Long et al., 2008). For example, *Salvia Magnolia* mixture, had enterokinetic and decreasing peristalsis affection, and significantly lower blood viscosity and reduce plasma fibrinogen levels to effectively prevent the occurrence of adhesion (Wang and Shao, 2010). *Dahuangmudanpi* decoction could suppress growth and proliferation of peritoneal adhesion

fibroblasts and promote apoptosis (Zhang, 2015). TaozhiZhipu mixture has good effect on stimulating post operational gastrointestinal peristalsis and preventing the occurrence of post operational intestinal adhesion (Su et al., 2000; Zhang et al., 1999). Modified Da Cheng Qi decoction could obviously decrease the concentration of the fibrinogen in abdominal exudates and accelerate the decomposition of the fibrinogen, and could evidently reduce the severity of adhesion (Wu and Li, 2014; Yu, 2015). Zhi Pu hollow type suppositories has good anti-inflammatory effect, affect blood WBC, TNF- α content, FIB level and can adjust moiling, gastrin, glucagon levels to promote peristalsis, maintain and protect the integrity of intestinal serosa to protect the outer layer of mesothelial cells, forming a layer of barrier, but also may control the proliferation of fibroblasts (Zhang, 2009); Xue Fu Zhu Yu prescription, the promoting blood flow principle representative prescription, could treat abdominal accretion effectively through anti-oxidation, improving hemorrhheology situation (Wu and Li, 2014; Yu et al., 2015). Huoxuetong luoliqitongbian decoction could decrease fibrinogen(FIB) in plasma and celiac liquid, increase fibrin degradation products(FDP) density, suppress transforming growth factor (TGF- β) mRNA expression in the adhesion tissue, improve exudation and fibrosis, and decrease the degree of peritoneal adhesion significantly etc (He et al., 2014).

Apart from TCM decoction, to some extent, enema with TCM could decrease the expression of the IgG antigen and serum TNF- α levels (Liu, 2013; Xie et al., 2014). The result suggested the TCM enema could lower fibrinogen and cut down fibrin and lessen inflammatory effect in tissue (He et al., 2014). On the other hand, it increased blood glutathione peroxidase (GSH-Px) content which was against the destroying of strong oxidative free radical to tissues and strengthened the second line of defense against free radical. All these effects contributed to the prevention of inflammatory and preventive of postoperative intestinal adhesions (Shi et al., 2011; Tai et al., 2005; Zhang, 2015).

TCM form acupuncture was known to inhibit pain and promote gastrointestinal motility. Those acupoints (e.g. zhusanli, shangjuxu, neiguan, gongsun, zhongwan) were selected because they were well-known meridians for treating gastrointestinal disorders. Acupuncture could relieve the edema of the obstructive intestinal tissues, improve the ultrastructure injury of the obstructive intestinal tissues, and promote the recovery of the function and morphology of the mitochondria as well as rough surface endoplasmic reticulum (RSER). Acupuncture could also elevate the synthesis and secretion of SIgA, increase CD₄⁺ lymphocytes and ratio of CD₈⁺/CD₈⁺, enhance the intestinal local immunity and reduce the intestinal bacteria translocation (Chen et al., 2014; Li et al., 2016). Early postoperative electro-acupuncture could significantly lower the elevated levels of inflammatory mediators such as tumor necrosis factor- α (TNF- α), nitric oxide (NO), nitric oxide synthase (NOS),

and the expression of vascular endothelial growth factor (VEGF) to decrease angiogenesis. The activation of cholinergic anti-inflammatory pathway might be another mechanism through which electro-acupuncture exerts the anti-inflammatory and inhibitive effects on abdominal adhesion (Li et al., 2014).

Conclusion

Our study highlights that searching on complementary and alternative therapies may have potential benefits for common diseases. Unfortunately, there exist considerable knowledge deficits about TCM especially in western world. Therefore, in the modern clinical practice, in order to make TCM serve people all over the world better and to accelerate the promising TCM-based new drug development, future studies should be based on the classical medical prescriptions, which refers to those recorded in the books before Han dynasty and 'Treatise on Febrile and Miscellaneous Diseases' written by Zhang Zhongjing. Furthermore, it is necessary to bring the ancient practice of TCM into line with modern western medicine standards governed by the principle of 'unification, simplification, coordination, and optimization' (Liu et al., 2016). While the fact that TCM may be effective in treating intestinal adhesion is encouraging, it is not conclusive due to the low methodological quality of the RCTs. However, this study hope to provide useful experience for further studies on TCM and more high-quality RCTs, with low risk of bias and adequate sample sizes, in order to demonstrate its true effects.

CONFLICT OF INTERESTS

The authors have not declared any conflict of interests.

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REFERENCES

- Akyildiz H, Akcan A, Sozuer E, Kucuk C, Yilmaz N, Deniz K (2008). The preventive effect of Met-RANTES on postoperative intraperitoneal adhesion formation in the rat model. *Surgery* 144(3):404-409.
- Chen M (2014). Clinical observation of Simo decoction combined with acupuncture and moxibustion therapy in the Prevention of appendectomy postoperative intestinal adhesion. *J. Emerg. Tradit.*

- Chin. Med. 23(12):2329-2331.
- He GZ, Dai ZD, Wu MS (2014). Curative effect observation of comprehensive therapy in the treatment of postoperative intestinal adhesion of 32 cases. Hunan J. Tradit. Chin. Med. 30(10):45-47.
- Higgins JP, Altman DG, Gotzsche PC, Juni P, Moher D, Oxman AD, Savovic J, Schulz KF, Weeks L, Sterne JA (2011) The Cochrane Collaboration's tool for assessing risk of bias in randomized trials. *Br. Med. J.* 343:d5928.
- Li PF (2014). The Clinical Research of Electric-acupuncture Prevent Acute Suppurative Appendicitis Postoperative Intestinal Adhesion. Shanxi University of Chinese Medicine. Master Dissertation.
- Li ZQ, Feng CL, Wang Wei (2016). Clinical observation of Xing Qi Xiaozhi Decoction in the treatment of abdominal postoperative intestinal adhesion of 48 cases. Hebei J. Tradit. Chin. Med. 38(4):528-530.
- Lin CY, Zhang LY (2012). Curative effect observation of external application of Chinese medicine plaster on Shenjue point in preventing of appendicitis postoperative intestinal adhesions. *Guide of China Medicine* 10(17):284-285.
- Lin XM, Zhang GL, Zheng JD, Deng MX (2000). Clinical observation of Si Mo Decoction in preventing intestinal adhesion of pediatric patients. *Straight Pharm. J.* 12(3):100-101.
- Lin ZG, Zhou WJ (2008). Clinical Observation on Prevention of Postoperative Intestinal Adhesion by Si Mo Decoction. *Modern J. Integr. Tradit. Chin. Western Med.* 17(16):2517-2518.
- Liu WP (2013) Clinical observation of retention enema with traditional Chinese medicine in the treatment of postoperative intestinal adhesion, *Guangming. J. Chin. Med.* 28(3):518-519.
- Liu Z, Guo F, Wang Y, Li C, Zhang X, Li H, Diao L, Gu J, Wang W, Li D, He F (2016). BATMAN-TCM: a Bioinformatics Analysis Tool for Molecular mechanism of Traditional Chinese Medicine. *Sci. Rep.* 6:21-46.
- Long W, Liu PX, Gao J (2008). Computer Virtual Screening Technology Applying to the Study of Functional Classification in Pharmacodynamic Molecules of TCM Prescription Huanglian Detoxifying Decoction. *Herald Med.* 27(1):23-25.
- Low CT, Lai PC, Li HD, Ho WK, Wong P, Chen S, Wong WC (2016). Neighbourhood effects on body constitution-A case study of Hong Kong. *Soc. Sci. Med.* 158:61-74.
- Lu WH (2013). The prevention of Appendectomy postoperative intestinal adhesion. *China Pract. Med.* 8(32):94-96.
- Murata P, Kase Y, Tokita Y, Takeda S, Sasaki H (2006). Intestinal ischemia/reperfusion injury aggravates talc-induced adhesions in rats. *J. Surg. Res.* 135(1):45-51.
- Nair SK, Bhat IK, Aurora AL (1974). Role of proteolytic enzyme in the prevention of postoperative intraperitoneal adhesions. *Arch. Surg.* 108(6):849-853.
- Ozogul Y, Baykal A, Onat D, Renda N, Sayek I (1998). An experimental study of the effect of aprotinin on intestinal adhesion formation. *Am. J. Surg.* 175(2):137-141.
- Shi WR, Huang XY, Zhou QS, Lin ZL (2011). The clinical curative effect of Compound Rhubarb enema liquid for prevention of abdominal postoperative intestinal adhesion. *Bull. Med. Res.* 30(12):44-46.
- Shi Yi (2007). The preventive effect of ligustrazing hydrochloride micro emulsion on the abdominal adhesion. Nanjing University of Traditional Chinese Medicine. Doctor's Thesis.
- Singer ER, Livesey MA, Barker IK, Hurtig MB, Conlon PD (1996a). Development of a laboratory animal model of postoperative small intestinal adhesion formation in the rabbit. *Can. J. Vet. Res.* 60(4):296-304.
- Singer ER, Livesey MA, Barker IK, Hurtig MB, Conlon PD (1996b). Utilization of the serosal scarification model of postoperative intestinal adhesion formation to investigate potential adhesion-preventing substances in the rabbit. *Can. J. Vet. Res.* 60(4):305-311.
- Su FC, Ma BJ, Pan MY, Yuan QL, Ye XH (2000). Clinical observation on TaozhiZhipu mixture on the prevention of postoperative intestinal adhesion. *Chin. J. Integr. Tradit. Western Med.* 6(6):404-406.
- Sui XB, Zhang Q, Qiu HS, Zhou JC, Gu XD, Lu ZX, Li C, Jin LJ, Wang G (2007). Mechanism of salvianolate in preventing postoperative intestinal adhesion in rats. *J. Chin. Integr. Med.* 5(5):521-525.
- Tai PJ, Yang XL, Li HX, Tai XC, Ju WD, Li MJ (2005). Clinic experience of Compound Dachengqi Decoction on postoperative intestinal adhesion. *Med. J. Liaoning* 19(3):164-166.
- Valerio M (2014). Peritoneal adhesions after laparoscopic gastrointestinal surgery. *World J. Gastroenterol.* 17:4917-4925.
- Wang GC, Shao ML (2010). Clinical observation of Salvia Magnolia mixture in the treatment of intestinal adhesion in children. *China Pract. Med.* 5(14):42-43.
- Wu Q, Li M (2014). Clinical observation of XuefuZhuayu Decoction combined with Dachengqi Decoction Jiajian in the treatment of postoperative intestinal adhesion of abdominal pain or 75 patients Zhejiang J. Tradit. Chin. Med. 49(12):900-902.
- Xie J, Liu L, Zhang W (2014). Clinical effect evaluation of biological polysaccharide flushing liquid combined with postoperative retention enema with traditional Chinese Medicine on the prevention of postoperative intestinal adhesion. *Chin. J. Coal Ind. Med.* 17(10):1677-1679.
- Yang H (2007). The study and research of Chinese herds-Paeonol to preventing and curing the harmful peritoneal adhesion Master Dissertation of Tianjin Medical university.
- Yang SM, Zhou ZL, Yin M, Li W (2007). The Treatment of Abdominal Adhesions by Integration of TCM and Modern Medicine. *Liaoning J. Tradit. Chin. Med.* 34(12):1772-1774.
- Ye BZ (2015). Nursing observation of retention enema with traditional Chinese medicine in the treatment of Suppurative appendicitis postoperative intestinal adhesion. *Modern Pract. Med.* 27(11):1256-1257.
- Yin JL (2009). Study on the therapeutic effect and mechanism of Rhein-arginine on postoperative intestinal adhesion. Master Dissertation of Yangzhou University.
- Yu SW (2015). Clinical observation of Xuefuzhuayu Decoction combined with Dachengqi Decoction Jiajian in the treatment of postoperative intestinal adhesion of abdominal pain or 75 patients. *Asia-Pacific Tradit. Med.* 11(16):119-121.
- Zhang H (2009). Study on ZhiPu hollow type suppositories of prevention and treatment of Postoperative Intestina1 adhesion, Guangzhou University of Chinese Medicine, Doctoral Dissertation.
- Zhang JJ (2006). Curative effect observation of Si Mo Decoction in promoting adnominal postoperative intestinal peristalsis and in preventing intestinal adhesion. *Modern J. Integr. Tradit. Chin. Western Med.* 15(15):2090-2092.
- Zhang JQ (2015). Clinical observation of intraperitoneal biopolysaccharide washing combined with traditional Chinese medicine enema in prevention of colorectal postoperative intestinal adhesion. *J. SiChuan Tradit. Chin. Med.* 33(11):105-107.
- Zhang X (2015). Clinical observation and treatment on the appendicitis complicated with postoperative intestinal adhesion of 150 cases. *Northern Pharm. J.* 12(3):27-29.
- Zhang Y, Li X, Zhang Q, Li J, Ju J, Du N, Liu X, Chen X, Cheng F, Yang L, Xu C, Bilal M U, Wei Y, Lu Y, Yang B (2014). Berberine hydrochloride prevents postsurgery intestinal adhesion and inflammation in rats. *J. Pharmacol. Exp. Ther.* 349(3):417-426.
- Zhang Y, Liang B, Jiang Z (1999). Clinical study on preventive effect of taozhizhipu mixture on postoperative intestinal adhesion. *Chinese Journal of Integrated Traditional and Western Medicine* 19(5):273-275.
- Zheng YX, Zheng YF, Su W, Zhang YM (2013). Clinical Observation of Shenque warming Moxibustion on the prevention of suppurative appendicitis postoperative intestinal adhesion. *Chin. J. Information Tradit. Chin. Med.* 20(2):83-85.