Clinical Efficacy of Mussel Adhesive Protein Combined with Tongyangxiao Lotion for Grade I-II Mixed Hemorrhoids: A Postprint Study

Authors: Tian Maosheng, Gao Jihua, Xu Jiancheng, Qi Wenyue, Wang Linyue, Gao Ce

Date: 2022-08-12T00:00:00+00:00

Abstract

Background For a long time, the high incidence of hemorrhoidal disease has been a significant concern, severely impacting patients' daily life, work, and study while diminishing their quality of life. The pathogenesis of hemorrhoidal disease is closely associated with the imbalance of anal cushion mucosal barrier function and the disruption of both mucus and mucosal barriers. Consequently, developing simple and efficient treatment modalities has become a priority for clinicians. Objective To comprehensively evaluate the clinical efficacy of mussel adhesive protein (MAP) combined with traditional Chinese medicine Tongyangxiao lotion fumigation and sitz bath in the treatment of grade I and II mixed hemorrhoids. Methods A randomized, controlled, single-blind prospective study design was employed. A total of 298 patients with grade I and II mixed hemorrhoids who met the inclusion criteria were enrolled and randomly allocated to either an experimental group or a control group (n=149 each). Both groups received general interventions including dietary and lifestyle counseling. The experimental group received topical MAP application combined with Tongyangxiao lotion sitz bath, while the control group received only traditional Chinese medicine sitz bath, for a 10-day treatment course. Primary outcome measures included efficacy index and recurrence rate; secondary outcome measures encompassed improvement in clinical symptoms before and after treatment, safety indicators, incidence of adverse events, and quality of life scores. Results The final analysis included 140 patients in the experimental group and 136 in the control group, with comparable baseline characteristics. During the follow-up period, both groups exhibited symptom alleviation; however, the experimental group demonstrated more rapid onset and superior symptom improvement compared to the control group. Post-treatment comparisons revealed significant improvements in VAS scores, clinical symptom scores, anal canal resting pressure values, and HF-QoL scores in both groups, with more pronounced reductions observed

in the experimental group. The experimental group achieved a cure rate of 84.28%, total effective rate of 96.43%, and recurrence rate of 3.23%; corresponding values for the control group were 69.85%, 91.18%, and 5.33%, respectively. No adverse reactions were reported in either group. Conclusion MAP combined with traditional Chinese medicine Tongyangxiao lotion sitz bath can effectively repair anal cushion mucosal injury in hemorrhoid patients. This combination therapy improves clinical symptoms in patients with grade I and II mixed hemorrhoids, reduces internal anal sphincter tone, enhances quality of life, provides rapid onset of action, and demonstrates superior therapeutic efficacy.

Full Text

Clinical Study on the Efficacy of Mussel Adhesive Protein Combined with Tongyangxiao Lotion for Grade I-II Mixed Hemorrhoids

TIAN Maosheng[1,2,3,4], GAO Jihua[2,3]*, XU Jiancheng[2,3], QI Wenyue[1,2,3], WANG Linyue[1,2,3], GAO Ce[2,3], LI Lixia[2,3]

[1]Hebei University of Chinese Medicine, Shijiazhuang 050091, China
[2]The First Affiliated Hospital of Hebei University of Chinese Medicine, Shijiazhuang 050011, China
[3]Key Laboratory of Gastroenterology Research of Integrated Traditional Chinese and Western Medicine of Hebei Province, Shijiazhuang 050011, China
[4]Shanxi Provincial People' s Hospital, Taiyuan 030002, China

Corresponding author: GAO Jihua, Chief Physician, Professor, PhD Supervisor, E-mail: gaojihua2005@163.com

Abstract

Background: The high incidence of hemorrhoidal disease has long been a public health concern, significantly impacting patients' quality of life and daily functioning. The pathogenesis of hemorrhoids is closely associated with disruption of the anal cushion mucosal barrier and impairment of both mucus and mucosal defense systems. Developing simple yet effective therapeutic strategies remains a critical clinical priority.

Objective: To comprehensively evaluate the clinical efficacy of mussel adhesive protein (MAP) combined with traditional Chinese medicine Tongyangxiao lotion in fumigation-sitz bath therapy for grade I–II mixed hemorrhoids.

Methods: This prospective, randomized, controlled, single-blind study enrolled 298 eligible patients with grade I–II mixed hemorrhoids, randomly assigned to experimental and control groups (n=149 each). Both groups received standard dietary and lifestyle counseling. The experimental group received topical MAP combined with herbal sitz bath, while the control group received herbal sitz

bath alone. Treatment duration was 10 days. Primary outcome measures included efficacy index and recurrence rate. Secondary outcomes encompassed clinical symptom improvement, safety indicators, adverse events, and quality-of-life scores.

Results: A total of 276 patients completed the study (experimental group: 140; control group: 136). Baseline characteristics were comparable between groups. During follow-up, both groups showed symptom relief, with the experimental group demonstrating faster onset and superior improvement. Post-treatment VAS scores, clinical symptom scores, anal canal resting pressure, and HF-QoL scores improved significantly in both groups, with greater reductions in the experimental group. The experimental group achieved an 84.28% cure rate and 96.43% total effective rate, with 3.23% recurrence; the control group showed 69.85% cure rate, 91.18% total effective rate, and 5.33% recurrence. No adverse reactions were observed in either group.

Conclusion: MAP combined with Tongyangxiao lotion sitz bath repairs anal cushion mucosal injury, improves clinical symptoms, reduces internal anal sphincter tension, and enhances quality of life in grade I–II mixed hemorrhoid patients. This combination therapy offers rapid onset and superior efficacy, providing a promising non-surgical approach.

Keywords: Hemorrhoidal disease; Mussel adhesive protein; Tongyangxiao lotion; Anal cushion mucosal barrier; Clinical efficacy

Introduction

A 2015 national epidemiological survey revealed that the overall prevalence of anorectal diseases reached 50.10%, with 98.09% of symptomatic cases attributable to hemorrhoids, yielding a hemorrhoid-specific prevalence of 49.14% [[1]]. Hemorrhoids have become a common clinical condition, characterized by bleeding, prolapse, pain, and pruritus that severely impair work and quality of life. As understanding of hemorrhoid pathogenesis has evolved, the anal cushion prolapse theory has gained widespread acceptance. The biological barrier function of anal cushion mucosa is intimately related to disease development, making mucosal protection a focal point in current research. The therapeutic principle emphasizes treating symptomatic hemorrhoids [[2]-[4]]; while 9.3% of patients require surgery, over 90% can achieve symptom relief through non-surgical approaches including dietary therapy, sitz baths, magnetotherapy, oral laxatives, venoactive drugs, analgesics, syndrome-based Chinese medicine, topical agents, and sclerotherapy [[5]-[10]]. Local rectal administration delivers medication directly to lesions, maintaining therapeutic concentrations and yielding favorable outcomes [11], representing a key research direction in colorectal surgery.

Mussels, treasures from the sea, secrete byssal threads that firmly adhere to underwater surfaces. This property has been harnessed to develop mussel ad-

hesive protein (MAP), a biomaterial with promising biomedical applications due to its excellent adhesiveness, biodegradability, flexibility, and water resistance. MAP contains 20% lysine and abundant catechol amino acids (L-3,4-dihydroxyphenylalanine, DOPA), forming a reticular biological scaffold that promotes cell adhesion and migration [[10],[13]]. As an effective mucosal protective agent for anal cushions, MAP can repair and reconstruct mucosal barrier function, making it an ideal candidate for topical hemorrhoid therapy [[13]].

Herbal fumigation and sitz bath represent traditional Chinese external treatment modalities [14]. Tongyangxiao lotion was developed by Professor Gao Jihua, chief expert of the Colorectal Department at Hebei Provincial Hospital of Chinese Medicine, based on nearly 40 years of clinical experience. Emphasizing non-surgical hemorrhoid treatment to prevent disease progression, Professor Gao posits that hemorrhoids predominantly manifest as damp-heat syndrome. Tongyangxiao lotion, administered via fumigation-sitz bath, exerts heat-clearing, dampness-drying, hemostatic, antipruritic, and detumescent effects, suitable for conservative management and postoperative care [14].

This clinical trial collected a large sample of grade I–II mixed hemorrhoid cases to validate preliminary findings, elucidate mechanisms, and provide clinical data supporting MAP and Tongyangxiao lotion application, offering novel insights for non-surgical hemorrhoid treatment.

Methods

1.1 Case Source This prospective, randomized, controlled, single-blind study enrolled patients with grade I–II mixed hemorrhoids who presented to the Colorectal Department of Hebei Provincial Hospital of Chinese Medicine between January 1, 2021, and December 31, 2021.

1.1.1 Diagnostic Criteria (1) Western Medicine Criteria: Based on the *Chinese Guidelines for Diagnosis and Treatment of Hemorrhoids (2020)* (Colorectal Disease Committee, Chinese Association of Integrative Medicine) [[5]], hemorrhoids are classified as internal, external, or mixed. The Goligher classification system categorizes internal hemorrhoids into four grades based on prolapse severity [[17]].

(2) Traditional Chinese Medicine Criteria: Based on the national standard *Clinical Terminology of Traditional Chinese Medicine Diseases* (GB/T 16751.1-1997) issued by the State Administration of Traditional Chinese Medicine and the 13th Five-Year National Planning Textbook *Surgery of Traditional Chinese Medicine* [[18]]. Mixed hemorrhoids result from damp-heat descending to the anus causing vessel obstruction, or constitutional deficiency with straining during defecation, heavy lifting, or childbirth leading to venous stasis. Symptoms include: intermittent hematochezia (dripping, spurting, or blood on tissue, bright red, not mixed with stool); prolapse (spontaneous

reduction or requiring manual replacement, may occur with prolonged standing or coughing); anal discomfort (pain, foreign body sensation, heaviness, discharge, perianal pruritus). Signs feature a mass spanning the dentate line with indistinct boundaries between internal and external components and disappearance of the intersphincteric groove.

1.1.2 Case Selection **(1) Inclusion Criteria:** Age 18–65 years, any gender; meeting TCM and Western diagnostic criteria for mixed hemorrhoids with grade I–II classification; presenting with bleeding (staining, dripping, or spurting) that stops spontaneously after defecation, prolapse that reduces spontaneously, possibly accompanied by pain, heaviness, or moist pruritus; providing informed consent for conservative treatment.

(2) Exclusion Criteria: Colorectal bleeding, swelling, or pain from organic lesions; severe primary cardiac, hepatic, renal, or hematopoietic diseases, malignancy, severe endocrine/metabolic or neurological disorders; allergy to study medications or components; suspected alcohol or drug abuse; infectious diseases; pregnancy or lactation; investigators' assessment of unsuitability.

(3) Withdrawal/Dropout Criteria: Development of concomitant conditions or complications precluding continuation; severe adverse events; participant-initiated withdrawal (reasons documented); poor compliance or loss to follow-up.

1.2.1 Sample Size Estimation PASS 15.0 software calculated the sample size based on a cure rate of 85% from previous literature, using one-sided testing with α=0.05 and power=0.9, yielding n=129 per group. Accounting for 15% attrition, 298 patients were required (149 per group).

1.2.2 Randomization and Blinding A random number generator created allocation sequences, which were converted into grouping variables using visual binning. An Excel allocation table assigned eligible patients sequentially. The single-blind design assigned Physician A to randomization and medication distribution (unblinded at study completion), while Physician B conducted follow-up visits and data recording.

1.2.3 Treatment Protocol Both groups received dietary and lifestyle counseling. The experimental group received topical MAP combined with herbal sitz bath; the control group received herbal sitz bath alone. Treatment duration was 10 days. For combined therapy, herbal sitz bath preceded MAP application, followed by 10 minutes of bed rest. MAP anal dressing was provided by Jiangyin Berison Biochemical Technology Co., Ltd. Tongyangxiao lotion (herbal granules containing: Phellodendron 15g, Sophora flavescens 30g, Angelica sinensis 15g, Atractylodes 15g, Gentiana macrophylla 15g, Asarum 6g, Mirabilite 30g, Alum 15g, Saposhnikovia 15g, Zanthoxylum 15g, Galla chinensis 15g) was provided by the Pharmacy Department of the First Affiliated Hospital of Hebei

University of Chinese Medicine. Each dose was dissolved in 3000ml hot water at 38–42°C for 15-minute sitz baths, administered twice daily. The protocol was approved by the Hebei University of Chinese Medicine Ethics Committee (Approval No. YXLL-2021010).

1.2.4 Efficacy Evaluation Criteria **(1) Primary Efficacy Indicators:** Comprehensive efficacy comprising efficacy index at treatment completion and recurrence rate during follow-up. Recurrence was defined as persistent or recurrent major symptoms requiring additional treatment. Efficacy index was calculated using the Nimodipine method: [(pretreatment total score –post-treatment total score) ÷ pretreatment total score] × 100%, categorized as cured, markedly effective, effective, or ineffective.

(2) Secondary Efficacy Indicators: Clinical symptom improvement, safety indicators, adverse events, and quality-of-life scores.

1.3.1 General Data Collection Baseline data included name, gender, age, occupation, contact information, medical history, allergy history, hemorrhoid duration, specialized examination findings, comorbidities, and concomitant medications.

1.3.2 Follow-up Time Points Patients were evaluated on days 4, 7, and 10 of treatment, with assessments of hematochezia, prolapse, heaviness, mucosal erosion, and hemorrhoid size scores. One month after treatment completion, follow-up was conducted via telephone, WeChat, or clinic visit.

1.3.3 Anorectal Pressure Measurement Anal canal resting pressure was measured before and after treatment.

1.3.4 Pain Assessment The Visual Analogue Scale (VAS) was used to evaluate anal pain before and after treatment, recording maximum pain during defecation and at rest based on patient-reported experience.

1.3.5 Clinical Symptom Improvement Scoring Based on the April 2020 *Clinical Guidelines for Anorectal Diseases in Traditional Chinese Medicine*, symptom scores were evaluated for hematochezia, prolapse, heaviness, mucosal erosion, and hemorrhoid size. Scoring system: Hematochezia (0=none, 2=staining, 4=dripping, 6=spurting); Prolapse (0=none, 2=self-reducing); Heaviness (0=none, 2=mild sensation, 4=mild pain, 6=severe pain); Mucosal status (0=normal, 2=congestion/edema, 4=erosion, 6=bleeding points); Hemorrhoid size (0=normal, 2=one hemorrhoid >1 clock hour, 4=two hemorrhoids >1 clock hour or one >2 clock hours, 6=three hemorrhoids >1 clock hour).

1.3.6 Safety Indicators Vital signs, general condition, and potential adverse reactions were monitored, with documentation of any MAP or Tongyangxiao lotion-related adverse events, including timing, symptoms, and management.

1.3.7 Quality of Life Assessment The HEMO-FISS-QoL (HF-QoL) scale, comprising 23 items across four domains (physical, psychological, defecation, and sexual dysfunction), was administered before and after treatment. Responses of never, rarely, sometimes, often, and always were scored 1–5 respectively [[19],[20]].

1.4 Statistical Methods SPSS 25.0 and GraphPad Prism 8.0 were used for data analysis. Normally distributed continuous data were expressed as mean ± standard deviation; skewed data as median and interquartile range. Paired t-tests were used for within-group comparisons, and independent t-tests for between-group comparisons when variance homogeneity was met; otherwise, corrected t-tests or non-parametric tests were applied. α=0.05; P<0.05 indicated statistical significance.

Results

2.1 Study Completion Status Patient screening is illustrated in [Figure 1: see original paper]. During the study, some cases withdrew or were lost to follow-up. Ultimately, 276 patients completed the trial (experimental group: 140; control group: 136).

2.2 Baseline Characteristics As shown in , no statistically significant differences existed between groups in baseline data distribution (P>0.05), indicating comparable gender, age, disease duration, disease stage, pre-treatment symptoms, anal canal resting pressure, quality of life, and surgical history.

2.3 VAS and Symptom Scores During Follow-up and [Figure 2: see original paper] demonstrate that VAS scores and symptom scores (hematochezia, prolapse, heaviness, mucosal status, hemorrhoid size) decreased progressively in both groups, with significant symptom relief. On day 4, VAS and symptom scores differed significantly between groups (P<0.05), indicating the combined therapy' s superior efficacy emerged early. The experimental group showed marked reductions in VAS and hematochezia scores, demonstrating rapid pain and bleeding relief with shortened onset time. By day 10, the experimental group exhibited superior improvement in pain, hematochezia, prolapse, and mucosal symptoms compared to the control group, with statistically significant differences in mean VAS and symptom scores (P<0.05), confirming the combined regimen' s rapid onset and enhanced efficacy.

2.4 Pre-Post Treatment Comparison and [Figure 3: see original paper] compare pre- and post-treatment VAS scores, symptom scores, anal canal resting pressure, and HF-QoL scores, all of which decreased significantly. Post-treatment differences between groups were statistically significant ($P<0.05$), indicating that the experimental regimen more effectively improved pain, symptoms, sphincter tension, and quality-of-life impairment.

2.5 Safety Evaluation and Follow-up No drug-related complications or adverse reactions occurred in either group, confirming the excellent safety profile of MAP and Tongyangxiao lotion. One-month follow-up of patients achieving "cured" status showed 3 recurrences in 93 patients (3.23%) in the experimental group versus 4 recurrences in 75 patients (5.33%) in the control group, with no statistically significant difference in recurrence rates ($P>0.05$).

2.6 Comprehensive Efficacy Comparison Among 276 enrolled grade I–II mixed hemorrhoid patients, the experimental group achieved 118 cures (84.28%), 12 markedly effective, 5 effective, and 5 ineffective cases, yielding a 96.43% total effective rate. The control group showed 95 cures (69.85%), 19 markedly effective, 10 effective, and 12 ineffective cases, with a 91.18% total effective rate (). Both therapies effectively relieved symptoms with good safety and low recurrence rates, but the experimental group demonstrated statistically superior overall efficacy ($P<0.05$), confirming the combined therapy' s rapid onset and enhanced effectiveness.

Discussion

The pathogenesis of hemorrhoids remains incompletely understood. While external hemorrhoid etiology is relatively clear, internal hemorrhoid physiology and pathology are debated. Proposed mechanisms include venous varicosis, vascular hyperplasia, venous pump dysfunction, arterial distribution patterns, herniation, infection, and pressure gradient theories, with the anal cushion prolapse theory being most widely accepted [[21]-[25]]. The anal cushion represents a specialized anorectal structure present from infancy, not inherently pathological. Only pathological changes with symptoms constitute hemorrhoidal disease; treatment aims to relieve symptoms rather than eliminate tissue [[24],[25]]. The progression from thin infantile structures to enlarged hemorrhoidal tissue explains advanced disease, while early-stage (grade I–II) hemorrhoids present primarily with bleeding, suggesting the anal cushion prolapse theory alone cannot fully explain hemorrhoid pathogenesis [[24]-[26]].

Hemorrhoids predominantly affect the anal cushion, whose mucosa originates from specialized embryonic tissue containing diverse epithelial cells, abundant nerve endings, complex neuroendocrine regulatory mechanisms, and active immune participation [[27],[28]]. This multifunctional biological membrane possesses intrinsic defense capabilities against harmful factors. Goblet and colum-

nar cells secrete mucins, glycoproteins, and polysaccharides forming a mucus protective layer—the first defensive barrier. The stratified epithelium with tight and adherens junctions constitutes a second barrier, blocking toxin invasion [[27],[28]]. When barrier function weakens or mucosa is damaged, local neurohormonal dysregulation, increased vascular permeability, vasodilation, congestion, edema, and muscle hypertonia occur, triggering inflammatory lesions and symptomatic hemorrhoids.

Treatment must address not only symptoms but also protect anal cushion barrier function, mitigating damage from systemic and local pathogenic factors to maintain mucosal integrity, microenvironmental stability, and coordinated vascular-neurohormonal regulation—prerequisites for anorectal health.

MAP was developed specifically for mucosal protection and repair. Mussels secrete MAP through byssal glands to adhere to surfaces in marine environments, forming high-strength, water-resistant protein fibers [[29]-[32]]. MAP' s positive charge enables rapid electrostatic interaction with negatively charged human cells, while hydrophobic effects and physiological conditions (temperature, pH) promote cross-linking into stable polymers that resist fluid 冲刷. Cells are attracted to the positively charged scaffold, facilitating migration and mucosal healing [[30]-[32]]. MAP maintains stable attachment to rectal and anal cushion mucosa in fluid-rich environments, providing durable protection [[13]].

Fumigation-sitz bath is a characteristic technique in Chinese colorectal medicine, first documented in *Fifty-Two Prescriptions* [[33]] and later elaborated in *Standards of Treatment* as effective for dredging meridians, harmonizing blood, dissipating heat-toxin, reducing swelling, and promoting tissue regeneration [[35],[36]]. This method uses heated herbal steam and liquid to enhance local drug absorption, improving circulation, metabolism, and oxygen exchange while alleviating symptoms [[34]].

Tongyangxiao lotion acts locally through percutaneous and mucosal absorption, maintaining barrier cleanliness, reducing pathogenic risk, and enhancing disease resistance. Hemorrhoids predominantly manifest as damp-heat descending and blood stasis. Sophora flavescens (containing alkaloids and flavonoids) inhibits *Staphylococcus aureus* and *E. coli*, exerting heat-clearing and dampness-drying effects [[37],[38]]. Phellodendron (containing berberine) demonstrates anti-inflammatory, antioxidant, and antimicrobial properties [[39]]. Angelica sinensis reduces capillary permeability and inflammation while promoting hematopoiesis [[40]]. Asarum alleviates edema and pain through anti-inflammatory and free radical-scavenging actions [[41]]. Gentiana macrophylla contains flavonoids and triterpenoids with anti-inflammatory and analgesic effects [[42]]. Galla chinensis (containing gallic acid and tannins) promotes protein coagulation for hemostasis and exhibits antimicrobial activity [[43]]. Mirabilite reduces local vascular permeability and inflammation [[44],[45]]. Alum provides astringent, antiparasitic, and dampness-drying effects. Zanthoxylum contains volatile oils and alkaloids with anti-inflammatory, antioxidant, and anticoagulant properties [[46]]. This combination achieves heat-clearing, dampness-drying, hemostatic,

analgesic, antipruritic, and tissue-regenerative effects.

This study selected grade I–II mixed hemorrhoid patients exhibiting anal cushion barrier dysfunction and local neuroendocrine dysregulation with inflammatory, congestive, and ulcerative changes. Clinical trials demonstrated that MAP combined with Tongyangxiao lotion effectively repaired mucosal injury, relieved bleeding, pain, prolapse, and heaviness, improved quality of life, reduced internal anal sphincter tension, and outperformed herbal therapy alone, achieving an 84.26% cure rate with rapid onset and enhanced efficacy, offering a valuable non-surgical approach warranting clinical promotion.

Author Contributions: TIAN Maosheng and GAO Jihua conceived and designed the study, analyzed results, and drafted the manuscript. TIAN Maosheng, XU Jiancheng, QI Wenyue, and WANG Linyue collected literature/data and performed statistical analysis. TIAN Maosheng, QI Wenyue, WANG Linyue, GAO Ce, and LI Lixia revised the manuscript. GAO Jihua supervised quality control and final approval.

Conflict of Interest: None declared.

References: [1] TIAN ZG, CHEN P. Epidemiological survey of common anorectal diseases in Chinese adults [M]. Wuhan: Wuhan University Press; 2015
[2] Gallo G, Martellucci J, Sturiale A, et al. Consensus statement of the Italian society of colorectal surgery (SICCR): management and treatment of hemorrhoidal disease [J]. Tech Coloproctol, 2020, 24(2): 145-164.
[3] Tetsuo Y. Japanese Practice Guidelines for Anal Disorders I. Hemorrhoids [J]. J Anus Rectum Colon, 2017, 1(3): 89-99.
[4] Davis BR, Lee-Kong SA, Migaly J, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids [J]. Dis Colon Rectum, 2018, 61(3): 284-292.
[5] Guidelines for Diagnosis and Treatment of Hemorrhoids in China(2020)[J]. Journal of Colorectal&Anal Surgery, 2020, 26(05): 519-533.
[6] Guidelines for Clinical Diagnosis and Treatment of Hemorrhoids (2006 Edition)[J]. Chin J Gastrointest Surg, 2006, 9(5): 461-463.
[7] ZHANG Y S, HAN B, TIAN ZG. Guidelines for Diagnosis and Treatment of Common Diseases in Anorectal Department of Traditional Chinese Medicine[M]. Beijing: China Traditional Chinese Medicine Press, 2012.
[8] TIAN M S, QI W Y, LIU Z Y, et al. Experimental study on quantitative evaluation model of similar symptoms of hemorrhoids[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2020, 35(10): 5237-5240.
[9] SUN S P, LONG J H, ZHANG S X. Prevalence and influencing factors of hemorrhoidal hemorrhage observed with fluorescence microscopy in hemorrhoidal disease patients[J]. Chinese General Practice, 2020, 23(33): 4190-4195.
[10] ZHOU S Y, AI F, LIU D W, et al. Clinical Observation of TST Combined with Polyoxymethylene Point Injection for Treatment of Mixed Rectal Prolapse and Intramucosal Prolapse[J]. Chinese General Practice, 2021, 24(S2): 76-79.
[11] LI F, TIAN J Z, WANG J Z, et al. Research progress of rectal drug delivery

system[J]. Chinese Traditional Patent Medicine, 2019, 41(5): 1115-1118.
[12] AN W Z, LIU Q, FU W L, et al. Research progress in mussel adhesion proteins[J]. Mil Med Sci, 2021, 45(10): 798-801.
[13] GAO J H, TIAN M S, QI W Y, et al. Expert consensus on the treatment of anorectal skin and mucous membrane injury with Mussel Adhesive Protein Dressing[J]. Chinese Journal of Coloproctology, 2021, 41(8): 77-80.
[14] CHENG Y, ZHOU J, HOU Y M, et al. Evaluation of the clinical effect of sophora flavescens decoction fumigation combined with box moxibustion at Baliao acupoint on treating postoperative complications in patients with high complicated anal fistula on the basis of propensity score matching[J]. Chinese General Practice, 2017, 20(3): 342-346.
[15] WANG N, ZHU Z N, WANG F, et al. Experimental Study on Acute Toxicity and Irritation of Tongyangxiao Lotion[J]. Journal of Hebei Medical University, 2007(1): 38-39.
[16] GAO J H, CHEN X Q, QI L Q, et al. Clinical study on application of Tongyangxiao lotion after anorectal surgery[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2005(8): 508-509.
[17] Madigan M R. Surgery of the anus, rectum and colon: 5th edn[J]. J R Soc Med, 1984, 77(9): 808.
[18] CHEN H F. Traditional Chinese Medicine Surgery (New Century 4th Edition)[M]. Beijing: China Traditional Chinese Medicine Press, 2016.
[19] Abramowitz L, Bouchard D, Siproudhis L, et al. Psychometric properties of a questionnaire (HEMO-FISS-QoL) to evaluate the burden associated with hemorrhoidal disease and anal fissures[J]. Colorectal Disease, 2019, 21(1) 48-58.
[20] Giua C, Minerba L, Piras A, et al. The effect of sucralfate-containing ointment on quality of life in people with symptoms associated with haemorrhoidal disease and its complications: the results of the EMOCARE survey[J]. Acta Biomed, 2021, 4, 92(1): e2021029.
[21] Pata F, Sgró A, Ferrara F, et al. Anatomy, Physiology and Pathophysiology of Haemorrhoids[J]. Rev Recent Clin Trials, 2021, 16(1): 75-80.
[22] Sandler RS, Peery AF. Rethinking What We Know About Hemorrhoids[J]. Clin Gastroenterol Hepatol. 2019, 1, 17(1): 8-9.
[23] Ng KS, Holzgang M, Young C. Still a Case of "No Pain, No Gain" ? An Updated and Critical Review of the Pathogenesis, Diagnosis, and Management Options for Hemorrhoids in 2020[J]. Ann Coloproctol. 2020, 1, 36(3): 133-147.
[24] AN S X, HUANG B. The pathogenesis and basic research of hemorrhoids[J]. Chinese Clinicians, 2014, 42(5): 20-22.
[25] WANG J, LI D. Research progress on pathophysiology of hemorrhoids[J]. Chinese Journal of Pathophysiology, 2010, 26(1): 193-196.
[26] Margetis N. Pathophysiology of internal hemorrhoids[J]. Ann Gastroenterol, 2019, 3, 32(3): 264-272.
[27] ZHANG D M. Biological characteristics and clinical significance of anal cushion mucosa[C] Proceedings of the 11th National Conference on Colorectal and Anal Diseases of Integrated Traditional Chinese and Western Medicine, 2006: 40-44.
[28] ZHANG D M. Sensory function of anal cushion and its clinical signifi-

cance[J]. Journal of Colorectal Surgery, 2003(3): 204-208.
[29] Waite J H, Tanzer M L. Polyphenolic Substance of Mytilus edulis: Novel Adhesive Containing L-Dopa and Hydroxyproline[J]. Science, 1981, 212(4498): 1038-1040.
[30] Fan Z, Pan J, Claesson P M. Electrochemical and AFM studies of mussel adhesive protein (Mefp-1) as corrosion inhibitor for carbon steel[J]. Electrochimica Acta, 2011, 56(3): 1636-1645.
[31] Lee B P, Messersmith P B, Israelachvili J N, et al. Mussel-Inspired Adhesives and Coatings[J]. Annu Rev Mater Res, 2011, 8, 1(41): 99-132.
[32] GAO M, ZHANG C H, ZHOU J, et al. Review of Mussel Adhesive Protein[J]. Anhui Agricultural Sciences, 2011, 39(32): 19860-19862.
[33] MA J X. A Textual Research on Mawangdui Ancient Medical Books[M]. Hunan Science and Technology Press, 1992.
[34] BA L S, ZHANG Y M. Anorectology of Ba[M]. Shangha: Shanghai Science and Technology Press, 2016.
[35] QIAO H Y. An example of a case study of traditional Chinese medicine fumigation and washing in the treatment of anorectal disease[J]. Chinese Folk Therapy, 2015, 23(2): 39-40.
[36] ZHANG L, LIANG X M, FAN X H, et al. Meta-analysis of traditional Chinese medicine fumigation and sitz bath in the treatment of postoperative pain with mixed hemorrhoids[J]. China Medicine Herald, 2018, 15(21): 129-133.
[37] WANG S Y, WANG L L, ZHANG J. Research progress on chemical constituents, pharmacological effects and processing methods of Sophora flavescens[J]. Chinese Journal of Veterinary Medicine, 2019, 53(10): 71-79.
[38] LIU J R, ZHANG Y, YANG L Y, et al. Authenticity of Sophora flavescens and modern research[J]. Chinese Medicine Herald, 2021, 27(7): 78-81.
[39] DA Q, HU Y, LEI L, et al. Research progress on the research, chemical composition and pharmacological action of processed products of Phellodendron phellodendri[J]. Asia Pacific Traditional Medicine, 2020, 16(10): 205-208.
[40] MA Y C, WU W X, HU J H, et al. Research progress on chemical constituents and pharmacological effects of Angelica sinensis[J]. Chinese Medicine Journal, 2022, 50(01): 111-114.
[41] SHI J J, SHI B, MIAO M S. Study on Anti-inflammatory and Analgesic Effects of Asarum External Application[J]. Chinese Medicine Journal, 2011, 26(10): 1191-1193.
[42] PEN M C, AI X H. Research progress on chemical constituents, pharmacological effects and clinical application of Chinnia chinensis[J]. Central South Pharmacy, 2021, 19(06): 1243-1249.
[43] GUO J H, CHEN L L, ZHANG X M, et al. Pharmacological effects and research progress of gall[J]. Scientific and technological innovation, 2019(2): 49-50.
[44] BAO M J. Study on the Pharmacological Action of Glauber' s Salt[J]. Electronic Journal of Clinical Medicine Literature, 2019, 6(30): 166+179.
[45] LIU S Y, BAI M, YANG Y L, et al. Study on Anti-inflammatory Effect of Glauber' s Salt[J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2012, 27(2): 312-315.

[46] YANG J Y, LI Y, FAN Z W, et al. Research status of the authentic medicinal material Sichuan pepper[J]. Guangming Journal of Chinese Medicine, 2020, 35(1): 146-148.

Note: Figure translations are in progress. See original paper for figures.