# Research Progress in the Treatment of Radiation Enteritis with Traditional Chinese Medicine

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Abstract: Radiation enteritis (RE) is an inflammatory response induced by radiation exposure and represents an intestinal complication arising from radiotherapy for malignant tumors in the pelvic and abdominal cavity as well as the retroperitoneum. It can affect the rectum, colon, and small intestine, severely impacting patients' quality of life. According to Traditional Chinese Medicine (TCM), the fundamental pathogenesis of RE lies in the accumulation of heat-toxicity and damage to the spleen and stomach. Treatment should focus on the disease characteristics of deficiency in origin and excess in manifestation, as well as individualized therapy aimed at nourishing and protecting the spleen and stomach. The therapeutic principles follow the clearing of heat-toxicity, resolving dampness, strengthening the spleen, astringing the intestines, and stopping diarrhea. This article reviews the understanding of the etiology and pathogenesis of RE in modern medicine and TCM, as well as relevant research on TCM treatments, including internal treatment, external treatment, comprehensive internal and external treatment, integrated traditional Chinese and Western medicine treatment, and prevention. The following summarizes the progress of related research in recent years.

Keywords: Radiation Enteritis, Traditional Chinese Medicine, Chinese Herbal Medicine, Research Progress.

## 1. Introduction

Radiation enteritis (RE) is an inflammatory response induced by radiation exposure and represents a gastrointestinal complication arising from radiotherapy for malignant tumors in the pelvic and abdominal cavities as well as the retroperitoneum, which can affect the rectum, colon, and small intestine [1]. Based on the time of onset and disease course, it can be classified into acute radiation enteritis (ARE) and chronic radiation enteritis (CRE). Approximately 60% to 70% of patients experience acute RE symptoms such as abdominal pain, diarrhea, and hematochezia, while around 5% to 15% of patients develop chronic RE symptoms including intestinal ulcers, bleeding, perforation, and intestinal stenosis. Between 2% and 17% of patients require surgical intervention, and the mortality rate is 15% to 25% [2-3]. In recent years, the incidence of RE has shown an upward trend. The treatment of RE limits the use of radiation doses, thereby affecting the quality of life and prognosis of tumor patients, posing a challenging issue in clinical oncologic radiotherapy. Currently, Western medicine still lacks a standardized strategy for the pharmacological prevention and treatment of RE. Traditional Chinese Medicine (TCM) has conducted in-depth research and exploration into the pathogenesis and clinical treatment of RE based on its holistic approach, syndrome differentiation and treatment, and the integration of disease and syndrome. This article reviews the research progress in the treatment of RE with TCM as follows.

## 2. Etiology and Pathogenesis

Based on the clinical manifestations of this disease, traditional Chinese medicine (TCM) categorizes it under the diagnostic and treatment frameworks of "dysentery," "diarrhea," "intestinal heat with bleeding," and "abdominal pain," with the disease located primarily in the large intestine and related to the spleen, stomach, and kidney [4]. Cancer patients often have internal deficiency of vital qi, dysfunction of zang-fu organs, abnormal circulation of qi, blood, and body fluids, with accumulation of carcinogenic toxins internally. When combined with the invasion of fiery and toxic heat (radiation), the interaction of "fire, blood stasis, and toxins" obstructs the intestines, resulting in a condition characterized by deficiency in the root and excess in the branch, as well as a mixture of deficiency and excess [5-6]. In the early stage (acute phase) of the disease, there is a tendency towards excess, with qi stagnation and blood stasis, as well as damp-heat accumulation being common; in the later stage (chronic phase), there is a tendency towards deficiency, with spleen-stomach qi deficiency and spleen-kidney yang deficiency being predominant [7].

#### 3. Syndrome Differentiation and Treatment

Syndrome differentiation and treatment are the basic principles and core of disease diagnosis and treatment in traditional Chinese medicine (TCM). Due to the complex pathogenesis of radiation enteritis, accurate syndrome differentiation is the premise and basis for the treatment of this disease with Chinese herbal medicine. Sun Shumei et al. [8] identified five syndromes through TCM syndrome differentiation and found that ARE typically first appears 10 to 20 days after the start of radiotherapy, with damp-heat accumulation in the intestine being the most common syndrome, followed by spleen deficiency with dampness excess and qi-blood deficiency. In the middle to late stages, the proportions of spleen deficiency with dampness excess and qi-blood deficiency syndromes increased significantly compared to the initial stage, while severe excess and deficiency syndromes such as internal blockage of blood stasis and toxins, and spleen-kidney deficiency, were relatively rare. Timely and accurate syndrome differentiation, followed by flexible modification of treatment according to the syndrome, is essential for achieving optimal therapeutic effects. Chen Yuchao [9] believes that the acute phase is mostly characterized by damp-heat accumulation, which should be treated primarily with heat-clearing and dampness-draining methods, while the chronic phase mostly manifests as three syndromes: qi-yin deficiency, spleen deficiency with dampness excess, and spleen-stomach yang

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deficiency, which should be treated primarily with tonifying deficiency and strengthening the body's resistance. By addressing the different priorities of the root and branch in the acute and chronic phases and applying treatments flexibly, significant therapeutic effects can be achieved. Professor Liu Jianhua et al. [10] believe that treatment should be based on clearing heat and detoxifying, strengthening the spleen, and replenishing qi. Lu Jingen et al. [11] suggest that the basic principle should be to strengthen the body's resistance and eliminate pathogens, with priority given to treating the symptoms in urgent cases, combining methods to clear heat and warm the interior, as well as methods to promote bowel movement and astringe diarrhea. Li Guodong et al. [12] believe that it is important to distinguish between the root and branch and the urgency of symptoms, and to select appropriate methods of clearing, warming, and tonifying to protect the spleen and stomach. Therefore, commonly used treatment methods for this disease include clearing heat and detoxifying to resolve dampness, strengthening the spleen and astringing the intestine to stop diarrhea, tonifying deficiency and replenishing qi to strengthen the body's resistance, and regulating qi and blood circulation to promote collateral circulation. Besides traditional oral Chinese medicine or proprietary Chinese medicine (PCM) treatment, various effective treatment methods such as intravenous infusion of PCM, Chinese herbal enemas, acupuncture, auricular point pressing with seeds, acupoint application, preventive health care, and others highlight the advantages of TCM treatment. It can be seen that for the same disease, syndromes may vary due to differences in time, place, or individual factors, leading to differences in treatment, which reflects the concept of syndrome differentiation and treatment in TCM.

#### 4. Research on the Treatment of Radiation Enteritis with Traditional Chinese Medicine

## 4.1 Internal Treatment with Traditional Chinese Medicine

Currently, internal treatment with traditional Chinese medicine (TCM) is widely applied and represents one of the primary methods in TCM for treating diseases. Therapeutic Efficacy Confirmed in a Study on Monotherapy for Radiation Enteritis Using Traditional Chinese Medicine. Evodia rutaecarpa, a Single Chinese Herb, Possesses Effects of Warming Yang to Stop Diarrhea, Dispersing Cold to Relieve Pain, and Lowering Adverse Qi to Stop Vomiting. Its Extract, Primary Evodiamine. the Constituent, **Exhibits** Anti-inflammatory, Analgesic, and Anti-tumor Activities [13, 141. Research Indicates that Evodiamine Reduces Inflammatory Responses in RE by Decreasing the mRNA Expression of IL-6-Related Genes in Mouse RE Tissue and Inhibiting the Expression of Inflammatory Mediators Such as TNF- $\alpha$  and IL-8, While Also Increasing Diamine Oxidase (DAO) Levels in Intestinal Mucosal Villus Cells to Promote Intestinal Mucosal Repair [15]. Additionally, Evodiamine is Found to Enhance the Barrier Protective Effect of the Intestinal Mucosa in RE Mice, Reducing the Side Effects of Radiotherapy, with Mechanisms Related to Regulation of the Toll-like Receptor 4/Nuclear Factor KB Signaling Pathway and Downregulation of NF-kB p65 Protein and TNF-a Expression [16]. Nutmeg Possesses the Effects of Warming the Middle Jiao to Promote Qi Circulation, Astringing the Intestines to Stop Diarrhea, and Its Extract, Nutmeg Volatile Oil, One of Its Main Components, Demonstrates Anti-inflammatory and Antibacterial Pharmacological Effects. Studies Show that Nutmeg Volatile Oil Reduces Radiotherapy-induced Intestinal Mucosal Damage (Decrease in Intestinal Mucosal and Wall Thickness) by Inhibiting the NF-kB Signaling Pathway, Reducing the Release of Inflammatory Cytokines, and Downregulating IL-8 Expression [17]. Rhei Radix et Rhizoma Has Effects of Dispersing Blood Stasis to Promote Menstruation, Clearing Heat to Reduce Fire, and Purging to Relieve Accumulation, While Emodin, Its Main Extract, Displays Anti-inflammatory and Anti-tumor Pharmacological Effects [18, 19]. Wang Yu et al. [20] Found that Emodin Decreases the Expression of TNF-α and the Production of Nitric Oxide (NO) in Intestinal Tissue of RE-Modeled Rats (Higher NO Concentrations Correlate with More Severe Cellular and Tissue Damage), Enhances DAO Activity in Intestinal Tissue, and Thus Improves the Protective Effect of the Intestinal Mucosal Barrier. Chuanxiong, Known as the Qi-Moving Herb in the Blood, Has Effects of Promoting Blood Circulation to Remove Blood Stasis and Dispersing Wind to Relieve Pain, and Tetramethylpyrazine, Its Main Constituent, Demonstrates Anti-inflammatory and Antioxidant Effects According to Modern Pharmacological Research [21]. Gao Chunfang [22] Applied Tetramethylpyrazine to Rats with Acute Radiation Enteritis (ARE) and Observed that It Facilitates the Repair of Damaged Small Intestinal Mucosa, Which is Related to Reduced Synthesis and Secretion of the Inflammatory The Traditional Chinese Mediator NO. Medicine Prescriptions Also Exhibit Significant Therapeutic.

Effects in the Treatment of Radiation Enteritis. Lu Xiyan and Zhao Ningxia [23] randomly and double-blindly divided 120 patients with radiation enteritis into a control group and an observation group. The control group received mesalazine enteric-coated tablets, while the observation group was given Wumei Pill combined with Sijunzi Decoction on top of the control group's treatment. The results showed that the total effective rate was 96.7% (58/60), significantly higher than the 85.0% (51/58) in the control group, indicating that Wumei Pill combined with Sijunzi Decoction is effective in treating radiation enteritis, not only improving clinical symptoms but also enhancing the patients' health status. Zhou Tiecheng and Xiang Shengxia [24] also adopted a multicenter, prospective, double-blind, randomized controlled clinical design. The treatment group received abdominal and pelvic radiotherapy while taking Purslane Soup, while the control group received a placebo. The results showed that continuous oral administration of Purslane Soup for 24 days could effectively reduce the severity of radiation enteritis (RE), decrease the frequency of diarrhea, and improve patients' sleep, mood, and general activities, thereby enhancing their quality of life. Gao Ying et al. [25] administered Baitouweng Decoction to 8 mice with radiation enteritis through gavage for 7 days. The results found that Baitouweng Decoction could improve colonic cell apoptosis and reduce inflammation by inhibiting the expression of serum proinflammatory cytokines (IL-6, TNF-α, COX).

## 4.2 External Treatment with Traditional Chinese Medicine

External treatment with TCM has the advantages of few

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adverse reactions, rapid onset of efficacy, simplicity, and ease of administration. It can avoid the gastrointestinal irritation and inactivation of digestive enzymes caused by oral medications, and it offers stable efficacy, economy, and safety [26].

#### 4.2.1 Enema Therapy

TCM enema therapy has certain advantages in tumor-related diseases and is widely used in clinical practice. Jiang Lin et al. [27] used a heat-clearing, blood-cooling, and detoxifying formula for enema therapy to treat 32 patients with acute radiation enteritis caused by cervical cancer radiotherapy. The results showed that the remission rate was 93.75%, significantly higher than the 87.50% remission rate in the control group, with a statistically significant difference (P<0.05). Long Lin et al. [28] used a self-developed Tongluo Enema Solution for retention enema to treat 40 patients with RE. The effective rate was 90.0%, significantly higher than the 60.0% in the conventional western medicine retention enema control group. A follow-up six months later found that the incidence of symptoms such as diarrhea, abdominal pain, tenesmus, purulent bloody stools, and anal burning was 18.9% in the treatment group and 42.9% in the control group, indicating that the long-term efficacy of the treatment group was superior to that of the control group (P<0.05). Li Meng et al. [29] used Jiawei Changfengyin for retention enema to treat 64 patients with acute radioactive proctitis. The total effective rate was 95.31%, higher than the 82.81% in the western medicine enema group (P<0.05). External treatment with TCM, mainly enema therapy, has the characteristics of few adverse reactions, good absorption, and obvious efficacy. Relevant studies have shown that it has better long-term efficacy, but further clinical validation is needed.

#### 4.2.2 Other External Treatments

Besides enema therapy, other external treatments such as acupoint catgut embedding and acupoint injection have also achieved good efficacy. Dai Junjun et al. [30] used acupoint catgut embedding to treat 30 patients with acute radiation enteritis (ARE) caused by cervical cancer radiotherapy. Among them, 15 cases were cured, 13 cases improved, and 2 cases were ineffective, with a total effective rate of 93.3%. The effect was significantly better than the 73.3% in the conventional treatment control group (P<0.05), indicating that acupoint catgut embedding is one of the effective adjunctive treatments for ARE. Zhong Fuqiang et al. [31] observed 20 patients with acute radioactive proctitis treated with compound Kushen injection for acupoint injection combined with retention enema therapy using a famous doctor's empirical prescription "Yuchang Decoction". The total effective rate was 90.91%.

## **4.3 Combined Internal and External Treatment with Traditional Chinese Medicine**

Comprehensive treatment combining internal and external treatment with TCM has also achieved good results. Liu Keshen et al. [32] randomly divided 62 patients with RE occurring within one month during or after radiotherapy into two groups of 31 patients each. The treatment group received orally administered self-prepared Qingre Cuyu Fang

combined with Kangfuxin Liquid for enema therapy, while the control group only received Kangfuxin Liquid for enema therapy. The total remission rate in the treatment group was 96.77%, higher than the 93.55% in the control group (P < 0.05), and the EORTC (European Organization for Research and Treatment of Cancer) grade of radiation injury after treatment was better in the treatment group (P<0.05). Lei Miao et al. [33] randomly divided 106 patients with radioactive proctitis into a routine Western medicine group and an observation group using a random number table. The observation group received Guchang Zhixie Fang combined with catgut embedding at shu-mu acupoints on the basis of conventional Western medicine treatment. The total effective rate was 98.11%, higher than the 86.79% in the control group (P<0.05). Xu Ying et al. [34] used Huaihua San plus Baitouweng Decoction for oral administration combined with Mayinglong Hemorrhoids Ointment plus Sanqi Powder for local external application to treat 30 patients with acute radioactive proctitis. The total effective rate was 86.7%, significantly higher than the 66.7% in the conventional symptomatic treatment control group (P<0.05).

#### 4.4 Integrated Chinese and Western Medicine Treatment

Zou Changpeng et al. [35] used modified Shaoyao Decoction for enema combined with Western medicine to treat 40 patients with RE. The results showed that the total effective rate in the treatment group was 92.50%, higher than the 75.00% in the control group receiving conventional Western medicine therapy (P<0.05). He Meibo et al. [36] used modified Changpi Fang combined with conventional Western medicine to treat 43 patients with RE caused by cervical cancer radiotherapy. Among them, 26 cases were markedly effective, 14 cases were effective, and 3 cases were ineffective, with a total effective rate of 93.02%. Ge Dongxu et al. [37] used Rumo Tang for enema combined with oral Western medicine to treat 30 patients with acute radioactive proctitis. After four weeks of treatment, the total effective rate was 90.0%, and the scores for TCM syndromes and the grade of radiation injury were better than those in the conventional oral Western medicine treatment group (P<0.05). Hu Yue and Huang Ai [38] randomly divided 108 patients with acute radioactive proctitis caused by cervical cancer radiotherapy into two groups using a random number table. The control group received Western medicine for enema, while the observation group received additionally self-prepared Changfeng Cuyu Yin. The results showed that the total effective rate in the observation group was as high as 90.74%. Therefore, combined Chinese and Western medicine treatment is more effective than Western medicine alone, and its safety is worthy of recognition.

## 5. Conclusion

Traditional Chinese Medicine (TCM) holds promising application prospects in the treatment of radiation enteritis, encompassing various methodologies such as internal treatment, external treatment, and a combination of both. In recent years, research on purely oral TCM medications for this condition has been relatively scarce. Instead, external TCM therapies, particularly traditional Chinese medicine enemas, have demonstrated certain advantages. Furthermore, comprehensive internal and external treatments, as well as integrated traditional Chinese and Western medicine therapies, have achieved notable efficacy. However, these treatments still possess certain.

### 6. Limitations

(1) Limitations in Research Methodology: Most studies have been observational in nature, lacking multicenter, large-sample studies and randomized controlled trials. This limits the reliability and generalizability of the research results, making it difficult to comprehensively and accurately assess the efficacy of TCM in treating radiation enteritis.

(2) Lack of In-depth Mechanism Research: Although TCM has achieved good therapeutic effects in treating radiation enteritis (RE), the underlying mechanisms have not been thoroughly explored. Future research should strengthen the investigation of these mechanisms to provide a more solid basis for clinical application.

(3) Single Evaluation Index for Treatment Effectiveness: The evaluation index for the treatment effectiveness of radiation enteritis is relatively limited, primarily focusing on effectiveness rates, which cannot fully reflect clinical outcomes. Therefore, further exploration of optimal treatment regimens and evaluation indices for RE is needed to guide clinical practice and benefit patients.

TCM can effectively alleviate the clinical symptoms of radiation enteritis and improve patients' quality of life. Future research and clinical validation are essential to promote the popularization and application of TCM in the treatment of radiation enteritis.

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