

# The Therapeutic Effect of Biling Weitong Granules Combined with Oryz-Aspergillus Enzyme and Pancreatin Tablet on Reflux Esophagitis with Functional Dyspepsia

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**Abstract:** *Objective:* To investigate the therapeutic effect of Biling Weitong Granules combined with oryz-aspergillus enzyme and pancreatin tablets on patients with reflux esophagitis with functional dyspepsia. *Methods:* Sixty patients diagnosed with reflux esophagitis with functional dyspepsia who were admitted to the Affiliated Hospital of Hebei University between June 2020 and June 2023 were selected and divided into two groups: the control group and the observation group, each consisting of 30 cases. The control group received oryz-aspergillus enzyme and pancreatin tablets only, while the observation group received Biling Weitong Granules in addition to the tablets. The clinical efficacy, Chinese medicine syndrome points, esophageal kinetic indexes, gastrointestinal hormone levels, and therapeutic safety of both groups were evaluated. *Results:* The total efficiency of the observation group reached 93.33%, significantly higher than the 73.33% of the control group ( $P < 0.05$ ). After treatment, patients in the observation group exhibited significantly lower scores for Chinese medicine symptoms such as early satiety, belching, abdominal distension, abdominal pain, and loss of appetite compared to the control group ( $P < 0.05$ ). Furthermore, the observation group showed significantly higher upper esophageal sphincter pressure, lower esophageal sphincter pressure, and distal esophageal contraction scores compared to the control group ( $P < 0.05$ ). Additionally, levels of gastric motility hormone, vasoactive intestinal peptide, and gastrin were significantly higher in the observation group compared to the control group ( $P < 0.05$ ). Throughout the treatment period, there was no significant difference in the incidence of adverse reactions between the two groups, indicating comparable safety of the two treatment modalities ( $P > 0.05$ ). *Conclusion:* The combination of Biling Weitong Granules with oryz-aspergillus enzyme and pancreatin tablets demonstrates significant efficacy in the treatment of reflux esophagitis with functional dyspepsia, with a better safety profile. This finding warrants further clinical promotion.

**Keywords:** Biling Weitong Granules; Oryz-aspergillus enzyme and pancreatin tablets; Reflux esophagitis; Functional dyspepsia

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## 1. Introduction

Reflux esophagitis represents a prevalent digestive disorder characterized by symptoms such as retrosternal or epigastric pain, burning, and acidity, often accompanied by dyspeptic manifestations like belching, nausea, and vomiting. The condition typically arises from the reflux of gastric acid and bile into the esophagus, primarily affecting the esophageal sphincter and mucosa. Pathological changes, including mucosal inflammation, ulceration, and impaired sphincter function, contribute to a compromised esophageal anti-reflux barrier <sup>[1]</sup>. Diagnostic approaches for reflux esophagitis encompass endoscopy, 24-hour esophageal pH monitoring, and esophageal manometry. Treatment modalities involve medication, dietary adjustments, lifestyle modifications, and surgical interventions.

Oryz-aspergillus enzyme and pancreatin tablet, a medication commonly employed in reflux esophagitis management, combines oryz-aspergillus enzyme extracts with pancreatic enzymes, thereby enhancing gastrointestinal digestive function by supplementing necessary digestive enzymes <sup>[2]</sup>. Nevertheless, some patients may not achieve lasting relief solely with Western medicine, potentially experiencing disease recurrence. In the realm of Chinese medicine, the spleen and stomach play pivotal roles in digestion and absorption. Dysfunction in these organs leads to compromised digestive function and gastric qi reversal, contributing to reflux esophagitis symptoms. Chinese medical theory attributes the etiology of the disease to factors like liver qi stagnation, spleen deficiency, and disharmony between the spleen and stomach.

Treatment strategies in Chinese medicine often revolve around regulating the spleen and stomach, tonifying the qi and meridian, promoting qi circulation, and resolving qi stagnation. Biling Weitong Granules, a traditional Chinese medicine preparation, holds a venerable status in the treatment of gastroepidermal pain. It exhibits efficacy in promoting qi and blood circulation, harmonizing the stomach, and relieving pain, particularly effective against gastroepidermal pain induced by qi stagnation and blood stasis <sup>[3]</sup>.

This study aims to administer Biling Weitong Granules in combination with oryz-aspergillus enzyme and pancreatin tablets to patients suffering from reflux esophagitis with functional dyspepsia, comprehensively evaluating its therapeutic efficacy.

## 2. Materials and methods

### 2.1. General information

Sixty cases of patients diagnosed with reflux esophagitis with functional dyspepsia were recruited from the Affiliated Hospital of Hebei University as research subjects and randomly allocated into two groups, each comprising 30 cases. Inclusion criteria were as follows: (1) age between 18 and 60 years old; (2) clear diagnosis of reflux esophagitis with functional dyspepsia; (3) absence of related treatment for at least three months or discontinued treatment; (4) willingness and ability to comply with study requirements and sign informed consent. Exclusion criteria included: (1) the presence of other serious digestive system diseases such as gastric ulcer or gastric cancer; (2) severe cardiovascular, liver, or kidney dysfunction; (3) pregnancy or lactation; (4) mental illness or cognitive disorders hindering effective study participation; (5) allergies to treatment regimen components including oryz-aspergillus enzyme and pancreatin tablets, Biling Weitong Granules, or other conditions.

### 2.2. Methods

The control group received treatment with oryz-aspergillus enzyme and pancreatin tablets (enteric-coated tablets) manufactured by Daiichi Sankyo Pharma GmbH, Germany. Each tablet contained 24 mg of mitomycin mycobacterial extract and 220 mg of pancreatic enzyme. Dosage involved oral administration, to be taken

during or after meals, one tablet three times daily.

The observation group underwent combined treatment with oryz-aspergillus enzyme and pancreatin tablets and Biling Weitong Granules (produced by Yangzijiang Pharmaceuticals, 5 g dissolved in boiled water, three times daily). The treatment regimen for oryz-aspergillus enzyme and pancreatin tablets enteric coated tablets was consistent with the control group.

The experiment spanned a duration of two weeks per treatment course, with a total of three treatment courses administered.

## **2.3. Observation indexes**

### **2.3.1. Clinical efficacy observation indexes**

- (1) Obvious effect: Symptoms completely subside, with a decline of more than 80% in Chinese medicine symptoms points, and esophageal dynamics indexes return to normal levels.
- (2) Effective: Symptoms show significant improvement, with a decrease of 30% to 80% in TCM evidence points and significant improvement in esophageal kinetic indexes.
- (3) Ineffective: No significant improvement in symptoms, TCM evidence points, or esophageal kinetic indexes post-treatment.

### **2.3.2. TCM evidence points**

A four-level scoring method is used to evaluate symptoms such as early satiety, abdominal distension, abdominal pain, and loss of appetite:

- (1) 0 point: No relevant symptoms or very mild symptoms.
- (2) 1 point: Mild symptoms with some impact on daily life but not severe.
- (3) 2 points: Moderate symptoms significantly impacting daily life but still tolerable.
- (4) 3 points: Severe symptoms greatly impact daily life and seriously interfere with normal functioning.

Scoring these symptoms provides insight into their severity and serves as a reference index for assessing treatment effectiveness.

### **2.3.3. Esophageal kinetic indexes**

One day before and after each treatment course, the Solar GI type gastrointestinal kinetic examination system (Shanghai Hanfei Medical Devices Co., Ltd.) is employed to compare esophageal kinetic indexes. These indicators include:

- (1) Upper esophageal sphincter pressure (UESP): Assessing the smoothness of food passage through the upper esophageal sphincter, which should have proper contraction and relaxation under normal conditions.
- (2) Lower esophageal sphincter pressure (LESP): Evaluating the smoothness of food passage through the lower esophageal sphincter.
- (3) Distal contractile integral (DCI): Reflecting the motor function of the esophagus, indicating the strength and frequency of distal esophageal contraction.

### **2.3.4. Gastrointestinal hormone indexes**

Before and after treatment, fasting venous blood samples (3 mL) are collected and centrifuged using the TDL-SD-5B type laboratory high-speed centrifuge (Shanghai Anting Scientific Instrument Factory) to separate serum supernatant specimens. Enzyme-linked immunosorbent assay is then utilized to detect motilin (MTL), vasoactive intestinal peptide (VIP), and gastrin (GAS) levels. The PT-3502G automatic enzyme labeling

instrument (Beijing Putian Xinqiao Medical Equipment Company) is used for analysis.

- (1) MTL: Mainly secreted by entero-endocrine (Mo) cells in the upper small intestine, regulating gastrointestinal motility.
- (2) VIP: Secreted by neuroendocrine cells and neurons, promoting peristalsis and increasing gastrointestinal secretion.
- (3) GAS: Mainly secreted by G cells in the lining of the stomach and upper small intestine, which can promote gastric acid secretion and gastric contraction and participate in the regulation of gastrointestinal motility.

## 2.4. Statistical methods

Measurement information is expressed as mean  $\pm$  standard deviation (SD). Comparison between groups is conducted using the two-sample mean *t*-test or chi-squared test. Data analysis is performed using SPSS software, with significance considered at  $P < 0.05$ .

## 3. Results

### 3.1. Comparison of general information

As shown in **Table 1**, the difference between the two groups of patients' gender, age, average duration of disease, and average body mass index (BMI) data comparison was not statistically significant ( $P > 0.05$ ).

**Table 1.** Comparison of general data of patients in two groups (mean  $\pm$  SD)

Group	Gender		Mean age (years)	Mean duration of illness (month)	Mean BMI
	Male	Female			
Control group ( $n = 30$ )	16	14	43.61 $\pm$ 9.73	8.88 $\pm$ 2.89	23.16 $\pm$ 2.69
Observation group ( $n = 30$ )	15	15	42.52 $\pm$ 9.89	8.67 $\pm$ 2.86	23.14 $\pm$ 2.81
$\chi^2 / t$	0.067		0.426	0.283	0.028
<i>P</i>	0.800		0.671	0.778	0.978

### 3.2. Comparison of clinical efficacy between the two groups

**Table 2** shows that the observation group has a higher total effective rate ( $n = 28, 93.33\%$ ) as compared to the control group ( $n = 22, 77.33\%$ ,  $P = 0.038$ ).

**Table 2.** Comparison of clinical efficacy between the two groups ( $n$ )

Group	Obvious effect	Effective	Ineffective	Total effective
Control group ( $n = 30$ )	13	9	8	22
Observation group ( $n = 30$ )	16	12	2	28
$\chi^2$				4.320
<i>P</i>				0.038

### 3.3. Comparison of Chinese medicine symptoms points between the two groups

Before treatment, there was no difference in the TCM symptom scores of both groups ( $P > 0.05$ ). However, after treatment, the TCM symptom points of the observation group were significantly lower than those of the control group ( $P < 0.05$ ), as seen in **Table 3**.



**Table 3.** Comparison of TCM evidence points between the two groups before and after treatment (mean ± SD, points)

Group (n)	Early satiety		Bloating and abdominal pain		Loss of appetite	
	Before	After	Before	After	Before	After
Control group (n = 30)	2.57 ± 0.43	0.75 ± 0.16	2.48 ± 0.46	0.85 ± 0.23	2.47 ± 0.49	0.95 ± 0.26
Observation group (n = 30)	2.53 ± 0.45	0.65 ± 0.14	2.43 ± 0.48	0.71 ± 0.21	2.41 ± 0.48	0.72 ± 0.23
<i>t</i>	0.352	2.576	0.412	2.462	0.479	3.629
<i>P</i>	0.726	0.013	0.682	0.017	0.634	0.001

### 3.4. Comparison of esophageal kinetic indexes between the two groups

As shown in **Table 4**, there was no difference between the esophageal kinetic indexes of both groups before treatment ( $P > 0.05$ ). After treatment, the esophageal kinetic indexes of the observation group were significantly higher than those of the control group ( $P < 0.05$ ).

**Table 4.** Comparison of esophageal kinetic indexes between the two groups before and after treatment (mean ± SD)

Group (n)	UESP (mmHg)		LESP (mmHg)		DCI (mmHg/s/cm)	
	Before	After	Before	After	Before	After
Control group (n = 30)	35.67 ± 5.73	44.75 ± 5.46	7.68 ± 2.12	10.28 ± 3.13	269.45 ± 29.49	352.95 ± 41.81
Observation group (n = 30)	34.81 ± 5.45	49.81 ± 5.54	7.43 ± 2.18	13.95 ± 3.19	266.21 ± 29.48	387.41 ± 45.15
<i>t</i>	0.596	3.563	0.450	3.272	0.426	3.067
<i>P</i>	0.554	0.001	0.654	0.002	0.672	0.003

### 3.5. Comparison of gastrointestinal hormone levels between the two groups

**Table 5** shows that there were no differences between the gastrointestinal hormone levels of both groups before treatment ( $P > 0.05$ ). After treatment, the gastrointestinal hormone levels of the observation group were significantly higher than those of the control group ( $P < 0.05$ ).

**Table 5.** Comparison of gastrointestinal hormone levels between the two groups before and after treatment (mean ± SD, ng/L)

Group (n)	MTL		VIP		GAS	
	Before	After	Before	After	Before	After
Control group (n = 30)	104.08 ± 12.13	173.75 ± 18.16	60.84 ± 6.45	95.06 ± 9.38	32.45 ± 5.44	48.25 ± 5.98
Observation group (n = 30)	105.53 ± 12.43	190.64 ± 17.28	59.23 ± 6.64	102.34 ± 11.39	32.41 ± 5.41	53.18 ± 5.97
<i>t</i>	0.457	3.690	0.953	2.702	0.029	2.742
<i>P</i>	0.649	0.001	0.345	0.009	0.977	0.008

### 3.6. Comparison of treatment safety between the two groups

The treatment safety of both groups showed no significant differences ( $P = 0.754$ ), as shown in **Table 6**.

**Table 6.** Comparison of treatment safety between the two groups of patients (*n*)

Group ( <i>n</i> )	Nausea and vomiting	Bloating and abdominal pain	Dry mouth	Rash	Total
Control group ( <i>n</i> = 30)	3	2	1	1	7
Observation group ( <i>n</i> = 30)	2	2	1	1	6
$\chi^2$					0.098
<i>P</i>					0.754

#### 4. Discussion

Reflux esophagitis, often accompanied by symptoms of functional dyspepsia such as gastric distension, pain, nausea, and vomiting, is commonly viewed through the realms of traditional Chinese medicine as a manifestation of disharmony in the liver-spleen relationship and spleen deficiency. These conditions lead to spleen and stomach qi imbalance, disrupting the spleen qi flow, triggering stomach qi stagnation, and exacerbating symptoms [4]. Poor dietary habits, such as skipping breakfast, overeating, or consuming spicy, high-fat, or high-sugar foods, further burden the spleen and stomach, worsening their function and potentially leading to spleen and stomach deficiency. Psychological stressors can also impact gastrointestinal function, aggravating symptoms like loss of spleen tonicity and gastrointestinal control.

Chinese medicine treatment strategies aim to address these imbalances by promoting liver detoxifying, spleen strengthening, stomach harmonization, and qi regulation [5]. Biling Weitong Granule, a traditional Chinese medicine formulation, contains ingredients including tailed pepper, Chinaberry, *Corydalis yanhusuo* vinegar, Rhubarb liquor, *Coptis chinensis*, and more, known for their ability to promote qi, relieve pain, strengthen the spleen, and harmonize the stomach [6]. This combination effectively clears heat, detoxify toxins, resolves phlegm, dispel dampness, relieve turbidity, activates blood circulation, eliminates qi stagnation, harmonizes the stomach, and alleviates pain [7,8], particularly beneficial for gastric pain and chronic gastritis.

In contrast, oryz-aspergillus enzyme and pancreatin tablet, a digestive medicine, alleviate dyspeptic symptoms by supplementing digestive enzymes, improving pancreatic function, and relieving bloating, stomach pain, nausea, and vomiting. However, there are varying opinions among Chinese medicine scholars regarding the etiology and treatment of functional dyspepsia: (1) Ye posited that the root cause of functional dyspepsia lies in spleen and stomach deficiency, exacerbated by dampness, phlegm, and stasis, which disrupt the organs' receptive and transporting functions. Treatment strategies should vary based on different stages of deficiency and solidity, emphasizing the traditional Chinese medicine principle of "qi transportation and adjustment" [9]. (2) Huang highlighted the impact of acquired dietary habits and emotional factors on functional dyspepsia. Impairment in the spleen and stomach's ability to receive and transport qi leads to imbalances, resulting in the manifestation of functional dyspepsia symptoms [10]. (3) Li proposed that the disease's pathogenesis stems from an imbalance in qi elevation within the Middle Jiao. Treatment focuses on four principles: regulating liver qi to promote elevation of the spleen and stomach qi; balancing cold and heat to regulate qi; harmonizing and transporting qi within the Middle Jiao for balance; and regulating lung qi to support spleen qi elevation and qi clearance [11].

In this study, 60 patients with reflux esophagitis and functional dyspepsia were randomly assigned into two groups: the control group receiving oryz-aspergillus enzyme and pancreatin tablets alone, and the observation group receiving additional Biling Weitong Granules. The combined treatment effectively improved symptoms, enhanced quality of life, and demonstrated safety and reliability without significant side effects. These promising outcomes suggest the potential for clinical application. Future research will delve deeper into the treatment mechanism of this combination therapy, aiming to provide more scientifically

sound and effective clinical interventions. Additionally, efforts will focus on improving patient quality of life and enhancing overall patient care.

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## Disclosure statement

The authors declare no conflict of interest.

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