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# Effect of Qishan Formula Granules on Interventing Obesity Intestinal Microflora and Immune-Inflammatory

Wei Yan[1], Hong Yuzhi[2], Hou Pengchao[3]

*[1]Department of Chinese Medicine, The First Affiliated Hospital of Zhejiang University Deputy chief physician of integrated Chinese and western medicine, engaged in clinical and scientific research on endocrine metabolism for 20 years, china*

*[2]Correspondent Author, Chief Physician of Endocrinology and Metabolism, Hangzhou Hospital of Traditional Chinese Medicine, Head of Department, china*

*[3]Department of Endocrinology and Metabolism, Hangzhou Hospital of Traditional Chinese Medicine, China*

*Corresponding author: Wei Yan, Department of Chinese Medicine, The First Affiliated Hospital of Zhejiang University Deputy chief physician of integrated Chinese and western medicine, engaged in clinical and scientific research on endocrine metabolism for 20 years, china

## ABSTRACT

**Objective:** To investigate the effects of Qishan Formula Granule on Simple Obesity and Intestinal Microflora-Inflammatory Immune Pathway. Methods: Eighty patients with simple obesity in our hospital were randomly divided into two groups: traditional Chinese medicine group and placebo group. The Chinese medicine group was treated with lifestyle intervention + Qishan formula granule, while the placebo group was treated with lifestyle intervention + placebo. The therapeutic effect, biochemical indexes, clinical symptoms, the number and composition of bacteria, the proportion of Th17/Treg cells in serum and inflammatory factors were measured before and after treatment. Results: After treatment, the total effective rate of simple obesity patients in Chinese medicine group was significantly higher than that in placebo group. ($P < 0.05$). Compared with the placebo group after treatment, the biochemical indexes and clinical symptoms of the Chinese medicine group improved significantly after treatment. Further tests showed that Qishan Formula Granule could significantly improve the intestinal bacterial abundance, species and quantity of simple obesity patients. The levels of IL-17, TNF-alpha, Th17/Treg and LPS in patients with simple obesity in traditional Chinese medicine group were significantly lower than those in placebo group before and after treatment ($P < 0.05$). Conclusion: Qishan Formula Granule can alleviate clinical symptoms of simple obesity and improve treatment efficiency through intestinal flora-inflammatory immune pathway.

**KEYWORDS:** Qishan formula granule; Obesity; Intestinal flora; Immune inflammatory; Th17/Treg

In recent years, with the change of people's lifestyle, the incidence of obesity has increased rapidly. For the chronic metabolic disorders celected to obesity and overweight, the prevalence of diseases such as diabetes and cardiovascular and cerebrovascular diseases has increased year by year [1]. Obesity cannot only lead to diabetes or high incidence of cardiovascular and cerebrovascular events, but also closely relate to cancer, depression, asthma, apnea syndrome, infertility, osteoarthropathy, fatty liver and many other diseases [2-5]. Therefore, it has become a serious impact on people's health, it's urgent to find reasonable and effective intervention measures. At present, the main drugs of weight loss treatment include non-central drugs, central drugs and hypoglycemic drugs, which have many problems such as low effective response rate, large side effects and weight rebound after stopping [6]. The combination of diet and exercise is often difficult to adhere to for a long time, and compliance is poor [7]. Seeking effective drugs or methods to treat simple obesity has become an important research hotspot in recent years.

It is believed that intestinal flora plays an important role in the regulation of immune inflammation and glycolipid metabolism [8,9]. Studies have shown that there is chronic low-level inflammation in obese people, and chronic low-level inflammation caused by obesity may promote the

occurrence development of metabolic disorders [10]. At the same time, it has been found that the disorder of intestinal flora and its metabolites in obesity patients and the obvious imbalance of proportion can affect the formation and differentiation of immune cells such as Th17 cells and Treg cells, thus leading to chronic low-level immune inflammation and obesity [11-13]. At present, a number of studies have shown that traditional Chinese medicine has an important effect on intestinal flora, berberine, Gegenqinlian decoction, tonifying traditional Chinese medicine and so on have a certain degree of adjustment of bacterial dysbiosis [14-15]. Qishan formula granules from Gegenqinlian modification, is a national famous old Chinese medicine experience prescription. The results of the previous study showed that Qishan formula has the effect of reducing blood sugar, improving insulin resistance and reducing body weight. However, the mechanism is not clear, and the simple obesity population has not been studied. Therefore, this study explores the efficacy of Qishan Formula Granule in the treatment of simple obesity and its effect on intestinal flora immune inflammatory pathway, in order to provide reference for traditional Chinese medicine in the treatment of obesity.

## INFORMATION AND METHODOLOGY

### General Information

In this study, A randomized (randomized digital approach), double-blind (The subjects, researchers, surveyors or data analysts did not know the treatment allocation, placebo-controlled, prospective study approach was selected for simple obese patients through health check-ups, community population screening, and outpatient visits. All patients were treated with lifestyle intervention (In a low sugar diet, 200-350g of main food should be eaten every day, and the ratio of carbohydrate to total calories should be 50% - 65%. Low fat diet, fat intake within 50g, about 30% of the total calories. Protein balance, about 15% of the total heat. Encourage the intake of foods rich in dietary fiber and vitamins. The daily total heat is controlled within 100kj / kg. Adhere to moderate intensity aerobic exercise, i.e., heart rate + 170 age after exercise, at least 3-5 days a week. It lasts for half a year; those with diabetes were treated with glizat sustained-release tablets; and those with hypertension were treated with amlodipine. The study included 80 patients who still met the following criteria after the 1-month elution period. a random number table was established using excel software. the standard 80 patients were randomly averaged into two groups: the traditional medicine group (40) and the placebo group (40). In the group of traditional Chinese medicine,14 cases were male and 26 cases were female; the age was 25-50 years, the average age was 38.74±10.23 years; and the average course of disease was 6.63±3.55 years. in the placebo group,16 men and 24 women; age 25-50 years, mean age 39.61±9.83 years; and mean course of disease 6.17±3.82 years.

### Inclusion and Exclusion Criteria

#### Inclusion Criteria

(1)Patients with simple obesity (male waist ≥90 cm, female ≥85 cm, and BMI≥25 kg/m2) in accordance with the 2011 edition of the Expert Consensus on the Prevention and Control of Adult Obesity in China;(2) age greater than 25 years of age less than 70 years of age;(3) classification of TCM syndrome differentiation as obesity-wet-heat accumulation of spleen syndrome : The body is fat(25kg/m2≤BMI≤28kg/m2 : +1score, 28kg/m2≤BMI≤30kg/m2:+2scores, 30kg/m2≤BMI:+3scores,); the abdomen is full(+1score); the food is little and tired(+1score); the head is heavy as wrap(+1score),The loose stool is not good(+1score); the urine color is yellow(+1score); and the whole body is hot and humid jaundice(+1score);The tongue is fat(+2scores); with yellow and greasy fur(+2scores);and smooth veins(+2scores);(4) discontinuation of drugs affecting weight for 4 weeks; (5) signing of informed consent.

#### Exclusion Criteria

(1)Weight gain due to drugs, endocrine diseases or other diseases;(2) severe liver and kidney dysfunction or other severe primary diseases;(3) history of acute cardiovascular and cerebrovascular events or myocardial infarction within 6 months;(4) stress state or secondary blood glucose elevation or secondary hypertension;(5) weight-loss surgery within one year;(6) severe dyslipidemia;(7) unwillingness of cooperators (who cannot cooperate with dietary control or do not use drugs as prescribed);(8) mental illness, tumor patients;(9) women with or breast-feeding, and women with planned or unplanned contraception;(10) possible allergy to gestational drugs;(11) patients with diabetes who have received medication.

### Treatment

(1) The Chinese medicine group was given lifestyle intervention + qishan formula granules orally, one pack at a time, twice a day. (The formulas are: Pueraria root 15g, Scutellaria baicalensis 10g, Coptis chinensis 10g, Rhubarb 3g, gynostemma pentaphyllum 10g, Shengqi 20g, Huai yam 20g, Atractylodes chinensis 15g, Poria cocos 15g, fried Fructus Aurantii 10g, Raw Hawthorn 10g, Chuanxiong 10g, produced by the preparation room of traditional Chinese medicine in our hospital). (2) The placebo group was given a lifestyle intervention plus a placebo oral dose, twice daily. (The formulas are: starch, pigment and adhesive, which are produced by the traditional Chinese medicine preparation

room of our hospital).

**Indicator Measurements**

Fasting blood glucose (FPG), blood lipids, blood pressure, waist-to-hip ratio, body mass index (BMI), body fat content, tcm symptom score (and other biochemical indicators, clinical symptoms were measured every 4 weeks. HbA1c, fasting insulin (FINS), fecal intestinal flora, proportion of serum th17/treg cells and serum IL-17, TNF-α, liver and kidney function, blood routine, urine routine, electrocardiogram were measured at week 0 and 12.

**Determination of Flora Size and Composition**

Quantitative intestinal excreta were diluted and inoculated into bs medium (bifidobacterium isolate) anaerobic culture for 48 h, bbe medium (bacillus isolates) anaerobic culture for 24h, lactic acid bacteria selective medium for 24h, enterococcal agar for 24h, fs medium (clostridium isolates) for 72h, kf streptococcus agar (streptococcus isolates) anaerobic culture for 24 h, and iridium agar for 24h. After the growth of the colony, the desired target bacteria were identified by colony morphology, Gram staining and biochemical reaction. On a variety of different media, the colonies were identified, and the number of each bacteria was compared with the reference value, and the B/E value was calculated to evaluate the number and composition of intestinal flora in patients with simple obesity after oral intervention of Qishan without sugar.

**PCR-DGGE Analysis Intestinal Flora Composition**

Fecal specimen collection and DNA extraction: The collection of feces of simple obese patients by aseptic method was about 1 g in 2 mL EP tube, and the stool genomic DNA was extracted according to the instructions of the DNA extraction kit.pcr: the v3 section of bacterial 16srdna was amplified by universal primers. the amplification conditions were 94°c for 3 min predenaturation,94° c for 1 min denaturation,55°c for 1 min annealing,72°c for 1 min extension, a total of 36 cycles,72°c for 10 min extension, and 4°c preservation.PCR products were detected by 2% agarose gel electrophoresis and stored at -20°C.dgge: the pcr product was separated on 8% polyacrylamide glue, the gel was stained by gelred after the end, the gs-800 grayscale scanner was imaged, and the correlation analysis of dgge molecular fingerprint was performed by biomerics software.

**Quantitative Quantitative PCR Analysis of Intestinal Microflora**

Fecal specimen collection and DNA extraction: The collection of feces of simple obese patients by aseptic method was about 1 g in 2 mL EP tube, and the stool genomic DNA was extracted according to the instructions of the DNA extraction kit. PCR primer design: according to Bifidobacterium, Lactobacillus, Escherichia coli, Bacillus, Clostridium, Streptococcus 16SrDNA gene sequence, the corresponding bacterial PCR primer was designed, and the specificity of the corresponding bacterial sequence was compared in the BLAST gene bank. Preparation of the standard curve: the PCR products of each bacteria in the control group were purified according to the instructions of the DNA purification kit, and the absorbance (A value) and concentration of the purified product were determined, and the copy number of each standard product 1μl was converted to be used to make the standard curve.

**Detection of Biochemical Indexes**

Blood sugar, blood lipids and other biochemical indicators were determined by the Olimpas 2000 large automatic biochemical instrument. serum insulin, hba1c was determined by our advia centur®xp fully automated chemiluminescence immunoanalyzer. Serum LPS was detected by ELISA. Methods for the determination of intestinal flora and SCFAs:2g of fresh feces of patients were frozen at -20°C refrigerator with a toilet provided by the Institute of Microbiology of Zhejiang Province (containing stabilizer), and the Institute was commissioned to test it. Body fat content was determined by the department's own body fat tester.HOMA-IR is calculated by formula HOMA-IR = FPG × FINS /22.5, HOMA-IS is calculated by formula HOMA-IS =1/HOMA-IR=22.5/ FPG × FINS.

**Anges Of Th17/Treg Cells Before and After Intervention**

The peripheral blood of the two groups of patients was collected, standing for 1 h,2000 rpm,4°c, centrifuged for 10 min, collected and packed into supernatant, and stored at -20°c when not detected in time. the content of serum il-17, tnf- α was determined by double antibody sandwich enzyme-linked immunosorbent assay (elisa), and the specific operation was carried out strictly according to the instructions of elisa kit. cd3-pecy7 and cd4-pe 0.5μg each, after oscillating and mixing evenly, incubated at room temperature for 30 min;300 g centrifuged for 5 min. after washing with cold pbs,1 ml of diluted fixed, membrane-penetrating agent was added. after reaction for 50 min, the concentration of th17 and treg cells was determined by flow cytometry.

**Safety Evaluation and Adverse Reaction Management**

If there is an alt increase during medication, the principle of adjusting the drug dose or interrupting treatment is:1 If the alt increase is within 2 times the normal value, continue to observe. If ALT rises at 2-3 times the normal level and is

taken in half, continue to observe if ALT continues to rise or remains between 80-120 U.L-1 and interrupt treatment. 3 If ALT rises above 3 times the normal value, stop the drug. After the withdrawal of drugs return to normal can continue to use, and strengthen the treatment of liver protection and follow-up. If leukopenia occurs during medication, the principles for adjusting the drug dose or interrupting treatment are as follows:1 If leukopenia is not lower than 3.0 x 109·L-1, continue to take medication to observe. If the white blood cell drops between (2.0 and 3.0) ×109·L-1, observe in half. Most patients can return to normal during continued medication. If the review of leukocytes is still below 3.0 x 109·L-1, the treatment is interrupted. 3 If leukopenia falls below 2.0 x 109·L-1, interrupt treatment.

## CRITERIA FOR EVALUATION OF SYNDROME EFFICACY

Clinical recovery: TCM clinical symptoms, signs disappear or basically disappear, syndrome score reduction ≥90% and weight lost by ≥ 15%. Remarkable effect: the clinical symptoms and signs of TCM were obviously improved, and the score of syndromes was reduced by more than 70% and weight lost by ≥ 10%. Effective: TCM clinical symptoms, signs are improved, syndrome score reduction≥30% and weight lost by ≥ 5%. Invalid: TCM clinical symptoms, signs are not significantly improved, or even aggravated, syndrome score reduction <30% or weight lost by<5%. Total effective = (clinical recovery + significant + effective)/ total number *100%.

### Statistical Analysis

Statistical software SPSS 17.0 is used to compare and analyze the indexes in this paper. The measurement data are expressed in form, and the measurement data are normally distributed, which meet the t-test standard.T-test to compare the counting data with xs test comparison; the count data are compared by X2 test; when $p < 0.05$, the statistics have significant differences.

### Estimation of Sample Size

Estimation of sample size: according to the estimation method of sample size in clinical experimental research, the sample size of two sample mean comparison is estimated. Check the "sample size table required for two sample mean comparison". According to the bilateral $\alpha = 0.05$, the test efficiency $(1- \beta) = 0.9$, $\mu\ 0.05 = 1.96$, $\mu\ 0.1 = 1.28$, according to the previous research experience, $\sigma$ is the estimated value of the overall standard deviation of two samples = 16, $\delta$ is both samples. The difference of number = 3.0, and the result is n = 34. Considering the loss rate of sample 15%, 40 cases in the experimental group and 40 cases in the control group were preliminarily determined.

## RESULTS

The rate of abscission and baseline were compared between the two groups. In the placebo group, 40 cases were enrolled, 2 cases were dropped, 38 cases were observed, and the drop rate was 5%. In the treatment group of traditional Chinese medicine, 40 cases were enrolled, 3 cases fell off, 37 cases were observed, the rate of falling off was 7.5%. There were 12 diabetic patients in placebo group, 15 hypertensive patients, 13 diabetic patients and 14 hypertensive patients in traditional Chinese medicine treatment group. There was no significant difference between the two groups in the proportion of diabetic and hypertensive patients. The age gender, baseline FPG, total cholesterol, triglyceride, LDL, BMI, body fat content, HbA1c, fins, waist to hip ratio, TCM syndrome score and the number of specific intestinal flora were comparable.

### Groups Comparison of Clinical Effect of Simple Obesity Patients After Treatment

Compared with the placebo group after treatment, the total effective rate of simple obese patients in the traditional chinese medicine group was significantly increased after treatment (81.1% vs 50.0 %), and there was a significant difference in comparison ($p < 0.05$). the clinical efficacy of the two groups was compared in table 1. Further observation found that the two groups of patients did not have liver function, renal function, abnormal white blood cell level and other adverse reactions Table 1.

*Table 1: Comparison of clinical efficacy between the two groups*

*Remark: *: P <0.05 compared to placebo group (Chi square test)*

| Subgroup | Number of cases | Cure | Significant effects | Effective | Invalid | Total efficiency |
|---|---|---|---|---|---|---|
| TCM Group | 37 | 4 | 13 | 13 | 7 | 81.1%* |
| Placebo Group | 38 | 1 | 4 | 14 | 19 | 50.00% |

### Two Groups Comparison of Biochemical Indexes of Simple Obesity Patients Before and After Treatment

Compared with the previous treatment, the indexes of the patients with simple obesity in placebo group did not change significantly after treatment, and there was no significant statistical difference ($P > 0.05$). The scores of FPG, total cholesterol, triglyceride, low-density lipoprotein, BMI, body fat, HbA1c, FINS, waist-to-hip ratio and TCM syndromes were significantly lower in patients with simple obesity than before and after treatment group of placebos, whereas HDL was significantly higher than that before and after treatment placebo group, there was a significant difference in comparison ($P < 0.05$); the comparison of biochemical indexes before and after treatment in the two groups was shown in Table 2.

**Table 2:** *Comparison of biochemical indexes between the two groups before and after treatment*

| Factors | Traditional Chinese Medicine Group | | Placebo Group | |
|---|---|---|---|---|
| | Before Treatment | After Treatment | Before Treatment | After Treatment |
| FPG (mmol/L) | 6.65±0.86 | 5.54±0.32*# | 6.51±0.91 | 6.22±0.75 |
| Total cholesterol (mmol/L) | 5.63±1.39 | 4.26±0.48*# | 5.65±1.28 | 5.24±1.07 |
| Triglycerides (mmol/L) | 2.38±0.75 | 1.52±0.64*# | 2.40±0.77 | 2.01±0.42* |
| Low-density lipoprotein (mmol/L) | 3.72±0.63 | 2.41±0.58*# | 3.69±0.59 | 3.35±0.55 |
| High-density lipoprotein (mmol/L) | 0.80±0.27 | 1.31±0.36*# | 0.82±0.23 | 0.97±0.31 |
| B MI | 29.61±3.14 | 24.05±2.97*# | 29.53±3.08 | 28.57±3.11 |
| Body fat content | 41.35±6.84 | 34.26±5.39*# | 41.21±6.54 | 38.79±5.82 |
| HbA1c % | 6.23±1.04 | 5.76±0.95*# | 6.19±1.01 | 5.94±0.87 |
| FINS (mU/L) | 10.41±3.78 | 6.54±1.46*# | 10.53±2.34 | 9.48±2.01 |
| Waist to hip ratio | 0.85±0.13 | 0.76±0.09*# | 0.86±0.15 | 0.82±0.09 |
| TCM Syndrome Points | 17.35±1.35 | 11.18±1.29*# | 17.41±1.40 | 15.25±1.32 |

*Remark: *: P <0.05 Compared with the group before treatment;*

*#: P <0.05; comparision of difference between the two groups before and after treatent;*

**Table 3:** *Comparison of intestinal flora between the two groups before and after treatment*

| Factors | Traditional Chinese Medicine Group | | Placebo Group | |
|---|---|---|---|---|
| | Before Treatment | After Treatment | Before Ttreatment | After Treatment |
| Bifidobacteri um | 6.33±1.12 | 8.29±1.07*# | 6.28±1.24 | 6.30±1.19 |
| Fragile Pseudomonas | 8.45±1.37 | 9.68±1.14*# | 8.77±1.10 | 8.93±1.24 |
| Lactic acid bacteria | 5.04±3.36 | 6.96±2.49*# | 6.45±3.71 | 6.51±3.01 |
| Enterococcus | 8.78±1.27 | 6.29±1.31*# | 8.73±1.25 | 8.66±1.17 |
| E. coli | 8.01±0.64 | 6.73±0.55*# | 9.57±0.58 | 9.41±0.53 |

*Remark: *: P <0.05 Compared with the group before treatment;*

*#: P <0.05; comparision of difference between the two groups before and after treatment;*

**Groups Patients with simple obesity before and after treatment Comparison of intestinal flora**

The colony numbers of Bifidobacterium, Bacillus fragilis, Lactobacillus, Enterococcus and Escherichia coli in the placebo group were not significantly different after treatment compared with that before and after treatment (P >0.05). The colony numbers of Bifidobacterium and Bifidobacterium in the traditional Chinese medicine group were significantly higher than those in the comfort group before and after treatment (P <0.05). A similar result was found for the detection of bacterial copy number of each stool by real-time fluorescence quantitative PCR, and the real-time fluorescence quantitative PCR is shown in Table 4.

**Two Groups Comparison of Inflammatory Indexes in Simple Obesity Patients Before and After Treatment**

Compared with pre-treatment, the inflammatory indexes of patients with simple obesity in placebo group did not change significantly after treatment (P >0.05)The levels of IL-17, TNF-α and Th17/Treg were significantly lower in

**Table 4:** *Real-time fluorescence quantification of bacterial copies of PCR feces*

| Genus of Bacteria | (Log10copies/g) Traditional Chinese Medicine Group | | | | Placebo Group | | | |
|---|---|---|---|---|---|---|---|---|
| | Before Treatment | | After meridian | | Before Treatment | | After meridian | |
| | Median | O R | Median | O R | Median | O R | Median | O R |
| Bifidobacter ium | 3.58 | 2.91-4.63 | 4.65*# | 3.74-5.24 | 4.21 | 3.42-5.01 | 4.68 | 3.78-5.31 |
| Fragile Pseudomonas | 6.7 | 6.37-7.25 | 6.03*# | 5.48-7.02 | 6.57 | 6.34-7.01 | 6.45 | 6.12-6.98 |
| Lactic acid | 3.74 | 3.01-4.60 | 4.32*# | 3.79-4.91 | 3.77 | 3.05-4.68 | 3.96 | 3.34-3.82 |
| bacteria Enterococcus | 4.62 | 4.30-5.54 | 4.05*# | 3.49-4.76 | 4.64 | 4.36-5.62 | 4.55 | 4.18-5.40 |
| E. coli | 3.42 | 2.93-4.51 | 2.09*# | 0.68-2.24 | 3.37 | 2.58-4.29 | 2.97 | 1.64-3.21 |

*Remark: *: P <0.05 Compared with the group before treatment;*

*#: P <0.05; comparision of difference between the two groups before and after treatment;*

**Table5:** *Comparison of inflammatory indexes between the two groups before and after treatment*

| Microflora | Traditional Chinese Medicine Group | | Placebo Group | |
|---|---|---|---|---|
| | Before Treatment | After Treatment | Before Treatment | After Treatment |
| IL-17(ng/L) | 16.48±2.33 | 11.16±1.98*# | 16.52±2.17 | 15.01±1.76 |
| TNF-α(ng/L) | 8.26±1.31 | 6.20±0.95*# | 8.31±1.21 | 7.94±1.06 |
| Th17 (%) | 1.81±0.34 | 1.46±0.25*# | 1.83±0.31 | 1.76±0.29 |
| Treg (%) | 3.14±0.28 | 3.26±0.33*# | 3.11±0.31 | 3.19±0.35 |
| Th17/Treg (%) | 0.58±0.11 | 0.45±0.08*# | 0.59±0.12 | 0.55±0.10 |

*Remark: *: P <0.05 Compared with the group before treatment;*

*#: P <0.05; comparision of difference between the two groups before and after treatent;*

patients with simple obesity than those before and after treatment placebo group, there was a significant difference in comparison (P <0.05); the comparison of biochemical indexes before and after treatment in the two groups was shown in Table 5.according to the relationship between th17/treg level and normal range after treatment of qishan formula granules, it was divided into normal group (th17/treg level was within normal range) and high level group (th17/treg level was higher than normal range). Further statistics found that the total amount of intestinal flora after treatment in the normal group was significantly higher than that in the high-level group (P <0.05, Fig.1) Table 3.

## DISCUSSION

In recent years, with the rapid development of today's society, people's life style and diet, nutrition structure has undergone great changes, so the incidence of obesity remains high, and the incidence of diabetes, cardio-cerebrovascular diseases and other diseases caused by obesity is increasing year by year. Several studies have shown that Qishan formula granules play an important role in reducing body weight. Therefore, this study discussed the effect of Qishan formula granule on simple obesity and further discussed its mechanism.

This study found that the total effective rate of simple obesity patients was significantly increased after the intervention of qishan formula granules. at the same time, the intervention of qishan formula granules could improve the clinical symptoms and biochemical indexes such as blood sugar and blood lipids in simple obesity patients. The application of Qishan formula granules is

beneficial to the treatment of simple obese patients. The theory of traditional Chinese medicine believes that obesity is due to dietary fat, inactivity,dysfunction of spleen in transportation, accumulation of phlegm and dampness cream. Body diseases characterized by obesity and fatigue. Its most common symptom is damp-heat accumulation spleen syndrome [16,17]. Qishan formula granules from Gegenqinlian decoction and six gentleman decoctions reduced. Raw astragalus, huai yam, poria qi invigorating spleen, Scutellaria baicalensis, Coptis chinensis Qingzhongjiao dampness and heat, rhubarb, gynostemma pentaphyllum to remove dampness, Atractylodes aromatization and dampness, Fructus Aurantiii, Hawthorn Qi digestion, phlegm elimination, Pueraria, Chuanxiong heat Qingjin Qi Huoxue. Thus, it has the effect of invigorating qi and invigorating spleen, clearing away heat and removing dampness and removing turbidity. It can make temper health transport and water Tianjin four cloth, phlegm turbidity inside the heat clear and fat in the full elimination. The purpose of removing Glycyrrhiza in the original prescription of Gegen Qinlian decoction is to prevent the rise of blood sugar and the storage of water and sodium.Therefore, the application of Qishan formula granules can significantly improve the total effective rate of patients and significantly improve clinical symptoms, blood sugar, blood lipids and other biochemical indicators. However, the mechanism of cell biology and molecular biology has not been elucidated Table 5.

Several studies have pointed out that differences in the composition of the intestinal flora are one of the most important causes of obesity, and their mechanisms mainly involve activating inflammatory responses, promoting energy absorption and regulating intestinal permeability [18,19] Studies have shown that obese patients are often accompanied by inflammatory signaling pathway activation, immune cell infiltration and other pathological changes [20]. therefore, stopping from the intestinal flora-inflammatory immune pathway will be helpful to elucidate the mechanism of qishan formula granules to improve simple obesity. this study examined the number and composition of intestinal flora and found that the colony numbers lactic acid bacteria, bifidobacterium and bacteroides were significantly higher in patients with simple obesity than in the placebo group before and after treatment after treatment after treatment with qishan formula granules. The results showed that Qishan formula could significantly affect the intestinal flora of simple obese patients. He Xuyun and other studies have found that Astragalus polysaccharide, the main ingredient of Astragalus membranaceus, can significantly inhibit the formation of obesity in mice and significantly restore intestinal flora disorders [21]. At the same time, several studies have pointed out that Radix Puerariae, Scutellariae, Coptis, Huai yam, Ligusticum chuanxiong, Poria cocos and Astragalus membranaceus It can affect the composition and richness of intestinal flora [22-25]. thus further confirming the effect of Qishan formula granules on intestinal flora. Intestinal flora plays an important regulatory role in the balance of immune cells. Fang Qian et al found a linear positive correlation between Bifidobacterium/ Escherichia coli ratio and Treg/Th17 in children with asthmatic bronchitis [26]. At the same time, numerous studies have found that berberine regulates the intestinal flora and the balance of Th17/Treg cells in rats, while the disruption of the balance between pro-inflammatory Th17 cells and inhibitory Treg cells is a key factor in many immune and metabolic diseases [27-29]. Therefore, the effect of Qishan formula granules on inflammatory cells and inflammatory factors was further examined. the results showed that il-17, tnf-α, th17/treg and levels were significantly reduced in patients with simple obesity after intervention of qishan formula granules, indicating that qishan formula granules could affect the inflammatory response in patients with simple obesity. further exploring the relationship between th17/treg levels and intestinal flora found that the total amount of intestinal flora in patients with th17/treg levels in the normal range was significantly higher than that of patients with th17/treg levels than normal, indicating a association between intestinal flora and treg/th17 values in patients with simple obesity. In summary, Qishan formula granules can improve the symptoms of obesity by increasing the richness and diversity of intestinal flora in simple obese patients and inhibiting the inflammatory response.

To sum up, this study found that Qishan formula granules can alleviate the clinical symptoms of simple obesity and improve the treatment efficiency through the intestinal flora-inflammatory immune pathway. Qishan formula granules can regulate the proportion of Th17, Treg cells and the secretion level of inflammatory factors by influencing the composition and richness of intestinal flora, so as to reshape the body shape and improve the biochemical index, and then achieve the purpose of treating simple obesity. However, there are still some shortcomings in this study, and it is necessary to further explore the main components of its efficacy and how the intestinal flora affects the inflammatory response.

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