Bupi Hewei decoction ameliorates 5-fluorouracil-induced intestinal dysbiosis in rats through T helper 17/T regulatory cell signaling pathway

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Abstract

OBJECTIVE: To observe the effects of the Bupi Hewei (BPHW) decoction on diarrhea and intestinal flora disorder induced by 5-fluorouracil (5-FU) and investigate the possible mechanism underlying these actions.

METHODS: Thirty-five male Sprague-Dawley rats were randomly divided into four groups: normal control, 5-FU, 5-FU + BPHW decoction (10.5 g/kg for 5 consecutive days), and 5-FU + Bacillus licheniformis capsule groups (0.2 g/kg for 5 consecutive days). Animal models were established via the intraperitoneal injection of 5-FU (30 mg/kg for 5 consecutive days). At the end of the treatment period, diarrhea was assessed, and the change of the intestinal flora was examined using 16S rDNA high-throughput sequencing. Interleukin (IL)-17, IL-21, IL-6, IL-10, RAR-related orphan receptor gamma (ROG), and forkhead box P3 (Foxp3) expression in the jejunum was detected using immunohistochemistry, quantitative real-time polymerase chain reaction (PCR), Western blotting, and enzyme-linked immuno sorbent assay.

RESULTS: In this study, the BPHW decoction effectively lowered the diarrhea score, increased the proportions of Bacteroidetes and Prevotellaceae-Allobrevibacter species, and reduced the proportions of Proteobacteria, Escherichia-Shigella, Ruminococcaceae NK4A214, and Ruminococcaceae UCG-005 species in the rat intestine after 5-FU chemotherapy. In addition, the BPHW decoction significantly suppressed the expression of IL-17, IL-21, IL-6, IL-10, RORγt, and Foxp3 in the jejunum.

CONCLUSION: Our findings suggest that the BPHW decoction can improve the intestinal immune balance and reduce intestinal inflammation by targeting T helper cell/T regulatory cell-associated factors.

Keywords: Gastrointestinal microbiome; Fluorouracil; Drug therapy; T-lymphocytes, regulatory; Th17 cells; Bupi Hewei decoction
INTRODUCTION

Chemotoxicity is considered to be associated with intestinal dysbiosis after chemotherapy. In particular, the abnormal differentiation of T cells caused by chemotherapeutic drugs is characterized as the critical causative factor that subsequently promotes the abnormal upregulation of downstream inflammatory factors, including tumor necrosis factor (TNF-α) and interleukin (IL)-1β. In recent years, T helper 17 (Th17) cells/T regulatory cells (Tregs) have been found to maintain T cell immune homeostasis through various pathways, thereby playing an important role in regulating the balance of inflammatory factors. As a central medium for the production of pro-inflammatory cytokines, Th17 cells exert pro-inflammatory effects by releasing IL-17 and other cytokines to upregulate inflammatory factors (including downstream IL-1β and TNF-α) in a cascade-release pattern. Tregs exert multiple effects that can induce immune tolerance, attenuate the immune defense response of Th1 cells, and promote Th17 development, thereby aggravating inflammatory damage. Excessive inflammatory mediators can cause changes in the total amounts and structures of the intestinal flora and induce flora translocation by damaging intestinal homeostasis (via interfering with macrophages, NK cells, and mucosal epithelial barriers). Therefore, it is clear that Th17 cells and Tregs play important roles in maintaining the body’s immune balance, and intestinal immune dysfunction may be the key cause of intestinal dysbiosis after chemotherapy.

Microecological agents are commonly used in the clinical treatment of intestinal dysfunction. Studies have illustrated that they can increase probiotic levels in vivo and inhibit the growth of pathogenic bacteria, thereby alleviating clinical symptoms such as diarrhea and constipation. The pathogenesis of intestinal microecosystem disorder after chemotherapy is complex. The intestinal microecosystem disorders can be treated via supplementation with one or several probiotics. Although some effects have been achieved, probiotics cannot significantly reduce the incidence of gastrointestinal toxicity and side effects after chemotherapy.

The Bupi Hewei (BPHW) decoction is a commonly used Traditional Chinese Medicine (TCM) after chemotherapy, and it has multi-target regulatory effects and can effectively alleviate gastrointestinal adverse reactions such as diarrhea, constipation, and vomiting. Relevant studies indicated that the BPHW decoction can effectively regulate the expression of intestinal probiotic and pathogenic bacteria. Nevertheless, it is unclear whether the effects of the treatment on intestinal dysbiosis are mediated by Th17 and Treg pathways.

In this study, intraperitoneal injection of 5-fluorouracil (5-FU) was used to induce intestinal dysbiosis in rats. By assessing the diarrhea score, fecal microbiota counts, and the expression of Th17/Treg-related factors in the jejunum, we aimed to investigate the effects of the BPHW decoction on post-chemotherapy intestinal dysbiosis and the mechanism of its effects.

MATERIALS AND METHODS

Rats

Thirty-five male Sprague-Dawley rats [weight, (200 ± 10) g] were provided by the Experimental Animal Center of the 302 Military Hospital (animal certificate number: SYXX [Army]-2012-0010). All rats were housed on a 12-h/12-h light/dark cycle in a temperature- and humidity-controlled room and maintained on a standard diet and water ad libitum. Animal experimental procedures were conducted in accordance with the Guidance Suggestions for the Care and Use of Laboratory Animals formulated by the Ministry of Science and Technology of China, and the protocols were approved by the Animal Ethics Committee of Chinese PLA General Hospital (Beijing, China).

Preparation of the BPHW decoction and Bacillus licheniformis solution

The BPHW decoction consisted of Huangqi (Radix Astragali Mongolici) 20 g, Baizhu (Rhizoma Arctacylodis Macrocephalae) 15 g, Zhiqiao (Fructus Auranti Subnatura) 10 g, Banxia (Rhizoma Pinelliae) 10 g, Shenqu (Massa Medicata Fermentata) 15 g, Maiya (Fructus Hordei Germinatus) 15 g, Fuling (Poria) 15 g. Herbs were proved and identified by the Chinese Pharmacy of Chinese PLA General Hospital (Beijing, China). The components were mixed, added to a 1.5-fold volume of water, immersed twice, mixed, filtered, and concentrated in a constant temperature water bath at 80℃ to a crude drug concentration of 5 g/mL, and the solution was stored at 4℃ for further application.

Bacillus licheniformis capsules were purchased from Northeast Pharmaceutical of China (Shenyang, China). Product lot number: S10950019, specification: (0.25 g/ g), and 0.2 g/kg Bacillus licheniformis capsules in physiological saline were prepared for use. The doses of the aforementioned drugs were converted according to the clinical dose for adults.

Reagents and instruments

A TRIzol® RNA extraction kit was purchased from Sigma (Palo, CA, USA). High-Capacity cDNA Reverse Transcription Kits (Cat. No. 4368814) were purchased from Thermo Fisher (Waltham, MA, USA). A LightCycler® 480 SYBR Green I Master real-time PCR kit (Cat. No. 04707516001) was purchased from Roche Applied Science (Basel, Switzerland). RAR-related orphan receptor gamma (RORYt) and forkhead box P3 (Foxp3) antibodies were purchased from Abcam (Boston, MA, USA).

The following instruments were used in this study: real-time PCR amplifier (Applied Science 384, Basel, Switzerland).
Model establishment and grouping
The random number method was utilized to divide all rats into blank control (N, n = 8), model (M, n = 9), BPHW decoction (BPHW, n = 9), and Bacillus licheniformis capsule groups (BLC, n = 9). Rats in the N group were intraperitoneally injected with 10 mL of normal saline, and rats in the other groups were intraperitoneally injected with the same volume of 5-FU (Shanghai Xudong Haipu Pharmaceutical Co., Ltd.) at 30 mg·kg⁻¹·d⁻¹ for 5 consecutive days to establish the chemotherapeutic rat model.

Rats in the N and M groups were gavaged with 2 mL of normal saline daily starting on the day of model establishment (for 5 consecutive days). Rats in the BPHW group were gavaged with 10.5 g/kg BPHW decoction daily for 5 consecutive days. Rats in the BLC group were gavaged with 0.2 g/kg Bacillus licheniformis capsules (2 mL dissolved in normal saline) daily for 5 consecutive days. The dose was equivalent to the adult dose. On the sixth day 24 h after the final gavage, 0.5 g of feces from rats in each group were collected into sterile EP tubes and stored at −80 °C for further use. Finally, all rats were sacrificed via spinal dislocation, and the small intestine (jejunum) tissues were removed from rats and stored at −80 °C for further experiments.

Diarrhea score
The defecation of rats in each group was observed before and after the experiment, and the diarrhea score was calculated using the method of Kurita et al. Normal stool or absent records 0 point, Slightly wet and soft stool records 1 point, Wet and unformed stool with moderate perianal of the coat records 2 point, Watery stool with severe perianal staining of the coat records 3 point.

High-throughput sequencing
Five samples were randomly selected from each group for detection. The genomic DNA of the samples was extracted using the CTAB method, and sequencing library preparation and high-throughput sequencing were conducted at Novogene, Inc. (Beijing, China). Briefly, 30-50 ng of DNA were used to generate amplions using the V3 and V4 hypervariable regions of prokaryotic 16S rDNA. The sequences of the forward and reverse primers for the V3 and V4 regions were “CCTAYGGGRBGASCAG” and “GGAC-TACNNGGATATCTAAT,” respectively. An Ion Plus Fragment Library Kit (Thermo Scientific) was used to construct the library, and high-throughput sequencing was conducted after quantification using a Qubit 2.0 fluorometer.

Immunohistochemistry
Jejunal tissue was fixed in 4% paraformaldehyde for 24 h at 4 °C, embedded in paraffin, and sectioned at a thickness of 4 mm. The sections were then heated in a constant temperature oven (60 °C) for 4 h, deparaffinized with xylene, and hydrated using a graded ethanol series (85%, 95%, 100%). The sections were then washed with PBS, blocked with 3% H₂O₂ for 10 min, and heated in citrate buffer (pH 6.0) in a microwave. The sections were washed with PBS again and incubated with RORγt (1: 300 dilution) and Foxp3 polyclonal antibodies (1: 200 dilution) overnight at 4 °C, and negative control sections were incubated in PBS (0.01 mol/L) instead of the primary antibody. On the following day, after three washes with PBS, the sections were incubated with biotinylated secondary antibodies for 30 min, stained with DAB, and lightly counterstained with hematoxylin. Finally, after hydration in a graded ethanol series (85%, 95%, 100%), the sections were sealed with neutral gum, and then observed under a microscope. The Image-Pro Plus 5.1 image analytical system was used to measure the integrated optical density.

RNA extraction and Quantitative real-time PCR
According to the gene sequence in the GenBank database, Primer 5.0 software was used to design primers (Table 1). Total RNA was extracted according to the
manufacturer’s instructions, followed by analysis using a micro-ultraviolet spectrophotometer (NanoDrop 2000, Thermo Scientific) to determine the concentration and purity of RNA. Afterward, RNA was reverse-transcribed into cDNA according to the manufacturer’s instructions. The PCR reaction mixture (10 μL) consisted of 5 μL of 2 × Master Mix (PCR polymerase), 0.5 μL each of forward and reverse primers, 1 μL of cDNA template, and 3 μL of RNase-free water. We used the following PCR reaction conditions: initial denaturation at 95 °C for 5 min followed by 40 cycles of denaturation at 95 °C for 10 s, annealing at 55 °C for 15 s, and extension at 72 °C for 20 s. The SYBR green fluorescent signals were acquired at 72 °C. Standard curves were constructed from PCR reactions using 10-fold serial dilutions of known bacterial DNA. The relative gene expression was converted and shown as fold changes ($2^{ΔΔCt}$).

**Western blot analysis**

Total protein was extracted using protein lysate according to the relevant protocols, followed by protein quantitation via the BCA method. The aforementioned supernatant (containing approximately 80 μg of protein) was subjected to 12% SDS-PAGE, and proteins were subsequently transferred to nitrocellulose filter membranes. The blots were probed with appropriate antibodies against RORγt, Foxp3, and β-actin, followed by incubation with secondary antibodies conjugated with horseradish peroxidase (Thermo Fisher). Milli-pore ECL (Millipore, MA, USA) was used for chemiluminescence, which was analyzed using grayscale values with Image Lab Software (Bio-Rad).

**Enzyme-linked immuno sorbent assay**

According to the manufacturer’s instructions, the levels of IL-17, IL-21, IL-6, and IL-10 in small intestinal tissues were determined using ELISA. A microporous plate spectrophotometer was used to measure the optical density at 450 nm, and the calculated results were based on the standard curve.

**Results of 16S rDNA high-throughput sequencing of intestinal flora**

A total of 42 796 valid sequences were obtained from 20 samples, and the average length of the sequences ranged 409-424 bp. After leveling, a total of 1257 operational taxonomic units (OTUs) were found out, and the similarity of bioinformatics in each out group reached 97%. Each type of OTU can be approximately considered one species.

**Statistical analysis**

16S rDNA data were analyzed using the QIME data package (Denver, CO, USA) and R programming language (R, Auckland, New Zealand). The MetaStat software package (SPSS Inc., Released 2008. SPSS Statistics for Windows, Version 17.0, Chicago, IL, USA) was used to analyze other data. Data with a normal distribution and homogeneity of variances were presented as the mean ± standard deviation ($\bar{x} \pm s$) and analyzed via analysis of variance. Data without a normal distribution or homogeneity of variances were analyzed using the rank sum test. $P < 0.05$ was considered statistically significant.
Taxonomic analysis revealed that the 20 samples contained 18 phyla. In the N group, Firmicutes was the most common genus, followed by Bacteroidetes and Proteobacteria (Figure 2). Compared with the findings in the N group, Firmicutes comprised a smaller portion of the intestinal flora in the M group (46.5% vs 62.7%), albeit without statistical significance ($P > 0.05$). In addition, the proportion of Bacteroidetes was significantly increased in the M group (34% vs 10.4%, $P < 0.05$) whereas that of Proteobacteria was significantly decreased (41.8% vs 1.1%, $P < 0.01$). The BPHW decoction effectively reversed the changes observed in the M group, as indicated by the significantly increased levels of Bacteroidetes (46.9%) and decreased levels of Proteobacteria (11.9%). Despite the lack of statistical significance, the recovery tendencies were more obvious in the BPHW group than in the BLC group ($P > 0.05$, Figure 3).

Further analysis was performed to examine the strain changes in each group at the species level. Using data from the SILVA database, 201 strains were detected in the 20 samples. The intestinal flora of the different samples was significantly different, indicating the diversity of intestinal flora (Figure 2). Compared with the findings in the N

![Figure 2](image-url)
group, the proportions of Escherichia-Shigella (36% vs 0.1%), Ruminococcaceae NK4A214 (6.1% vs 0.8%), and Ruminococcaceae UCG-005 (2.1% vs 0.5%) were significantly increased in the M group (all \( P < 0.05 \)), whereas that of Prevotellaceae-Alloprevotella was significantly decreased (0.2% vs 3%, \( P < 0.05 \)). The proportion of Lactobacillus was reported to be significantly altered in previous studies. However, we failed to observe any significant differences (12% vs 17%, \( P > 0.05 \)). The BPHW decoction could significantly decrease the content of Escherichia-Shigella (9.2% vs 36%, \( P < 0.05 \)). Additionally, compared with the findings in the M group, the BPHW decoction obviously decreased the proportions of Ruminococcaceae NK4A214 (0.8% vs 6.1%) and Ruminococcaceae UCG-005 (1.2% vs 2.1%) and increased that of Prevotellaceae-Alloprevotella (0.5% vs 0.2%), albeit without statistical significance (Figure 4).

Effects of the BPHW decoction on the expression of ROR\(\gamma\)t and Foxp3 in the jejunum of 5-FU-treated rats

As shown in Figure 5, the positive protein expression of ROR\(\gamma\)t and Foxp3 was indicated by brown staining, and some staining was observed in jejunal tissue of the N group rats. By contrast, jejunal ROR\(\gamma\)t and Foxp3 expression was significantly higher in the M group (\( P < 0.01 \)). Compared with the findings in the M group, ROR\(\gamma\)t and Foxp3 expression in the jejunum was reduced in the BPHW and BLC groups (\( P < 0.01, P < 0.05 \)), and no significant difference was found between the BPHW and BLC groups (\( P > 0.05 \)).
Effects of the BPHW decoction on the mRNA expression of IL-17, IL-21, IL-10, ROR\(\gamma\)t, and Foxp3 in the jejunum of 5-FU-treated rats

As shown in Figure 6, compared with the findings in the N group, the expression of IL-17, IL-21, IL-10, ROR\(\gamma\)t, and Foxp3 was significantly increased in the jejunum of rats in the M group \((P < 0.05)\). Compared with the M group levels, the expression of these factors in the jejunum was reduced by BPHW treatment \((P < 0.01)\), and IL-17, IL-10, and ROR\(\gamma\)t expression was significantly lower in the BPHW group than in the BLC group \((P < 0.05)\).

Effects of the BPHW decoction on the protein expression of ROR\(\gamma\)t and Foxp3 in the jejunum of 5-FU-treated rats

As shown in Figure 7, compared with the findings in
the N group, RORγt and Foxp3 expression was significantly increased in the jejunum of rats in the M group ($P < 0.01$). The BPHW decoction effectively regulated the immune balance by suppressing RORγt and Foxp3 expression relative to that in the M group ($P < 0.05$, $P < 0.01$).

**Effects of the BPHW decoction on IL-17, IL-21, IL-6, and IL-10 levels in intestinal mucosa of rats treated with 5-FU**

As shown in Figure 8, compared with the levels in the N group, the levels of IL-17, IL-21, IL-6, and IL-10 were significantly increased in the jejunum of rats in the M group ($P < 0.01$). Compared with the M group levels, the jejunal levels of these factors were reduced by BPHW treatment ($P < 0.01$), and the expression of IL-17, IL-21 and IL-10 as lower in the BPHW group than in the BLC group ($P < 0.05$, $P < 0.01$).

**DISCUSSION**

Patients undergoing chemotherapy often experience gastrointestinal side effects such as diarrhea and vomiting, which are generally considered to be closely associated with intestinal dysbiosis after chemotherapy. The normal intestine is dominated by Firmicutes and Bacteroidetes. Chemotherapeutic drugs can lead to significantly decreased total amounts of intestinal flora, especially probiotics in anaerobic genera, whereas the numbers and proportions of pathogenic bacteria both in-
crease during chemotherapy. For example, methotrexate can decrease the total size of the intestinal flora by approximately 29.6% in children with leukemia; meanwhile, the numbers of bifidobacteria, lactobacilli, and E. coli were significantly decreased during chemotherapy. The BEAM regimen increased the levels of E. coli and Bacteroides and significantly reduced those of Enterococcus faecalis and bifidobacteria in the intestines of patients with non-Hodgkin’s lymphoma. Although different chemotherapeutic drugs exert certain effects on the intestinal flora, 5-FU and irinotecan are the most common causes of side effects such as obvious chemotherapy-induced diarrhea, which is believed to be associated with severe intestinal dysbiosis.

In TCM, intestinal dysbiosis caused by chemotherapeutic drugs is attributable to the dysfunction of transportation and transformation in the spleen. In addition, the BPHW decoction is an effective approach to prevent and treat intestinal dysbiosis after chemotherapy in clinical practice. Hai et al. found that the Jianpi Shenshi decoction increased the proportions of bifidobacteria and lactobacilli in patients with advanced colorectal cancer who underwent chemotherapy, exerting a regulatory effect of intestinal flora with a total effective rate of 86.7%. Wang et al. confirmed that spleen-deficient rats exhibited disorder and dysbiosis of intestinal flora via diversity analysis using ERIC-PCR fingerprinting, and the Sijunzi decoction significantly improved the intestinal flora diversity in spleen-deficient mice, especially concerning the recovery of bifidobacteria and lactobacilli.

Recent studies illustrated that the intestinal flora and intestinal immune barrier interact with each other. On the one hand, the colonization of intestinal probiotics activates intestinal immune function. In artificially reared germ-free mice, T cells and immune factors are deficient, the number of dendritic cells in the lymph nodes of intestinal mucosa lamina propria is decreased, and the levels of secretory immunoglobulin A (sIgA) and antimicrobial peptide are decreased. The low antibody levels of aseptic mice indicate that the intestinal flora plays an important role in promoting intestinal immune system activity. On the other hand, the intestinal immune barrier plays an important role in regulating the normal development and maintenance of intestinal microecology. The intestinal immune system secretes many immune factors to induce the regular distribution of intestinal microorganisms in different layers in the intestinal cavity, inhibit the excessive reproduction of harmful bacteria, and maintain the intestinal microecological balance. It has been reported that the absence or dysfunction of sIgA and human defensin will lead to the loss or mutation of activation-inducible cytidine deaminase, thus inhibiting intestinal immune function and leading to the proliferation of harmful bacteria and imbalance of the intestinal flora.

The mechanism underpinning the effects of chemotherapeutic drugs on the intestinal immune barrier is complex. In recent years, with the clarification of the role of Th17 cells/Tregs in intestinal immune regulation, regulating the Th17 cell/Treg balance has become a research hotspot for maintaining the intestinal immune balance. Th17 cells are the central mediators of pro-inflammation, and RORγt is the signature factor of Th17 cells. IL-17, as its main effector molecule, exerts a strong pro-inflammatory effect and induces the secretion of IL-6, IL-21, IL-22, and TNF-α, subsequently producing a strong inflammatory response and causing tissue damage. In addition, Th17 cells can recruit and activate neutrophils by inducing CXC chemokines via the mitogen-activated protein kinase and nuclear factor-kB pathways to exert their biological effects. Tregs comprise a subset of CD4+CD25+ T cells that can act as negative regulators. Foxp3 is the main regulator of Tregs, and it promotes the secretion of inhibitory cytokines such as IL-10, thereby playing an important role in the negative regulation of body immunity.

Tregs can affect the production of Th1, Th2, and Th17 cells and their immune balance. For example, an increase in the number of Tregs can attenuate the expression of interferon-γ, thereby inhibiting the bactericidal ability of macrophages. On the contrary, Tregs drive Th2-type immune responses and induce immune tolerance. Tregs have a dual role in regulating Th17 expression. It is generally believed that Tregs exert an antagonistic effect on Th17 cells, which mainly depends on the common regulation of IL-6. Meanwhile, Tregs can promote Th17 transformation, which can both promote the preferential expression of Th17 cells via the suppression of Th1 and Th2 factors and induce the differentiation into Th17 cells. Studies revealed that Th17 cells and Tregs express the same cell surface markers, suggesting that they are derived from the same precursor cells, and they could differentiate according to the cytokines in the environment, permitting them to transform into each other. Taken together, the imbalance of Th17 cells/Tregs could aggravate Th17-mediated inflammatory responses, thereby interfering with the body immune balance.

The results of this experiment indicated that the diarrhea severity score of the M group was significantly higher than that of the N group. In addition, the proportions of Firmicutes and Bacteroidetes tended to increase in the M group, whereas that of Proteobacteria was significantly increased. Additionally, at the species level, Escherichia-Shigella, Ruminococcaceae NK4A 214, and Ruminococcaceae UCG-005 were significantly more prevalent in the M group, whereas Prevotellaceae-Alloprevotella was significantly less prevalent. Among them, symbiotic bacteria such as Prevotellaceae-Alloprevotella can effectively prevent the intestinal colonization of E. coli, Shigella, and other pathogens. Conversely, Escherichia-Shigella are typical intestinal pathogenic bacteria associated with diarrhea, and they can suppress the growth of probiotics and cause disor-
order of the intestinal flora. The increased diarrhea score in the M group confirmed that the animal model of intestinal flora disorder after 5-FU chemotherapy was successfully prepared, and the changes of intestinal flora may be the key factor. Further analyses illustrated that the severity of diarrhea in the BPHW group was significantly lower than that in M group. The proportion of Bacteroides was effectively increased in the BPHW group, whereas that of Proteobacteria was effectively reduced, especially the levels of Escherichia-Shigella, which were significantly lower in the BPHW group than in the M and BLC groups. However, levels of Lactobacillus, for which obvious changes were reported in the literature, were not improved, suggesting that the elimination of pathogenic bacteria may be the first step by which TCM reverses microecological damage caused by chemotherapy.

In addition, the imbalance of intestinal mucosal immunity induced by Th17 cells/Tregs is an important factor causing chemotherapy-induced intestinal flora disorder. In this study, we found that the expression of IL-17, IL-21, IL-6, and RORγt was significantly increased, which caused intestinal microecological disorder after 5-FU chemotherapy. Interestingly, unlike the antagonistic effects of Th17 cells and Tregs in chronic inflammatory bowel disease, we found that Foxp3 and IL-10 expression was also significantly increased in the M group, which may be related to the transformation of Th17 cells and Tregs mediated by IL-6, IL-23, ATRA, and the response to acute intestinal stress. Further studies illustrated that the levels of IL-17, IL-21, IL-6, and RORγt were decreased in the BPHW group, indicating that the BPHW decoction inhibited IL-17 expression and reduced the immune inflammatory response, and its effects were superior to those of BLC. In conclusion, the BPHW decoction can inhibit the proliferation of intestinal pathogens in rats undergoing chemotherapy and alleviate the symptoms of diarrhea. The underlying mechanism might be that the effects of the BPHW decoction involve Th17/Treg signaling pathways. However, the effects of TCM compounds are rather complicated. Therefore, the exact active components require further investigation.

REFERENCES


