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Effect and mechanism of *Dendrobium chrysotoxum* polysaccharide on the prevention and treatment of inflammatory bowel disease in mice

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Abstract

Inflammatory bowel disease (IBD) has become a global health problem. The breakdown of intestinal barrier and the imbalance of intestinal flora are key factors affecting the occurrence and development of IBD, and are also important targets for prevention and treatment. The preventive effect of *Dendrobium chrysotoxum* polysaccharide (DCP) on IBD was studied. A mouse model of IBD was constructed using Dexosan Sodium Sulfate (DSS) and pretreated with DCP. qPCR and Western Blotting were used to detect the expression of tight junction protein and anti-inflammatory cytokines at mRNA and protein levels. The composition and distribution of intestinal flora and the content of short-chain fatty acids (SCFAs) in each group were observed. The results showed that except the control group, the expression of claudin-2, occludin and ZO-1 in colon tissue of mice in all groups decreased significantly, indicating the impairment of intestinal barrier function. However, DCP restored the integrity of the intestinal mucosa by upregulating the expression of these tight-linking proteins. In addition, the expression of IL-10 in the model group was significantly down-regulated, and after DCP intervention, the expression level was significantly increased. It is suggested that DCP may prevent IBD in mice by protecting intestinal barrier and exerting anti-inflammatory activity. In addition, DCP can regulate the species composition and distribution of intestinal flora in mice, reverse the relative abundance changes of *Escherichia coli* and *Lactobacillus* in IBD mice, and increase the production of acetic acid, propionic acid, butyric acid, valeric acid and isobutyric acid in IBD mice. In general, the newly extracted DCP polysaccharide has a good effect on improving intestinal barrier dysfunction, and is an ideal natural medicine for the treatment of IBD.

Keywords Inflammatory bowel disease, *Dendrobium Chrysotoxum* Polysaccharide, Intestinal flora, Intestinal barrier, SCFAs

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Introduction

Inflammatory bowel disease (IBD) is an autoimmune disease characterized by mucosal structure disorder, abnormal biochemical changes in the body, and changes in intestinal microbial composition [1, 2]. There are two main clinical forms of the disease: Crohn's disease (CD) and ulcerative colitis (UC). According to the data of the Chinese Center for Disease Control and Prevention in 2014, the total number of IBD patients in China from 2005 to 2014 was about 350,000, and it is expected to reach 1.5 million in 2025 [3]. Clinically, IBD patients often present with a range of digestive symptoms, with abdominal pain and diarrhea being the most common clinical manifestations of IBD. In addition, IBD patients may also have severe symptoms such as vomiting, weight loss, and even rectal bleeding [4, 5], and may even have a variety of serious complications, such as anemia, intestinal fibrosis, intestinal stenosis, fistula, intestinal obstruction, and intestinal abscess [6]. At present, there are various treatment options for IBD, and drug therapy is the most widely used treatment strategy. However, the current drug therapy for IBD is not satisfactory, and some patients may even fail to respond to drug therapy [7]. The exploration of natural and effective dietary substances to prevent IBD has very important practical significance, and has attracted more and more attention from researchers at home and abroad.

The intestinal epithelium consists of a single layer of continuously proliferating and differentiated intestinal epithelial cells (IECs) [8, 9], which separates the intestinal mucosa from the intestinal lumen environment and plays an important role in maintaining intestinal fixation and resisting intestinal infections. Intestinal barrier can protect the intestine from external environment by interacting with intestinal microbiota, immune cells and intestinal nervous system, thus maintaining intestinal balance [10]. Disruption of the IECs tight-junction barrier by any pathogen can promote the development of IBD by increasing intestinal permeability [11, 12]. It has been reported that alcoholic liver injury can alter the intestinal microbiota, disrupt the intestinal barrier, and increase intestinal permeability [13, 14]. Just as in patients with alcoholic liver injury, in patients with IBD, tight-junction protein has been found to play an important role in maintaining the integrity and permeability of the mucosal epithelial mechanical barrier. Downregulation of its expression can lead to impairment of the integrity of the intestinal barrier structure and function, resulting in the invasion of intestinal pathogens and toxins into the colon barrier. It is believed to be a key factor in colon inflammation and the pathogenesis of UC [15–17]. The intestinal barrier is essential for immune function, and restoring its integrity is an extremely important goal in

the treatment of IBD. Bacterial communities maintain intestinal homeostasis by regulating the immune system and inhibiting the growth of pathogens and pathogenic bacteria [18, 19]. The imbalance of species composition and metabolic status of intestinal flora will not only cause changes in intestinal epithelial mucosa and damage the structural integrity of intestinal barrier, but also activate inflammatory response and induce colon inflammation by regulating the activity of cytokines [20]. In summary, remodeling the gut microbiota may alleviate symptoms of IBD and improve the therapeutic outcomes of IBD.

Short-chain fatty acids (SCFAs) are products of bacterial fermentation and play an important role in maintaining intestinal homeostasis. Three major SCFAs produced by intestinal bacteria are acetate, propionate and butyrate. In addition, SCFAs also has immunomodulatory activities, including Treg development, cytokine production, and anti-inflammatory effects [21].

Lipopolysaccharide (LPS) plays a crucial role in causing intestinal and systemic inflammatory responses [22, 23]. *Dendrobium chrysotoxum* Lindl (DC) is one of the largest genera of the orchidaceae, which can be used to relieve local inflammation, nourish the stomach, relieve fatigue, prevent cataract, promote body fluid secretion, reduce peripheral vascular obstruction etc. [24, 25]. Polysaccharide is one of the main active components of *Dendrobium* [26]. Previous studies have shown that *D. officinale* polysaccharide (DOP) can not only be utilized by the microbiome, but may be degraded after passing through the intestine, and may also interact directly with intestinal epithelial cells when arriving at the intestinal environment, and DOP has anti-inflammatory activity in colitis mouse models [27]. Like *D. officinale*, *Dendrobium chrysotoxum* has also been used as a medical dendrobium. In this study, a new water-soluble polysaccharide was extracted from *Dendrobium chrysotoxum* and named *Dendrobium chrysotoxum* polysaccharide (DCP). Based on the conclusions of previous studies, we speculated that DCP may have a similar improvement effect on IBD. However, there is no literature report on DCP improving the biological activity of IBD.

Materials and methods

Materials

Male C57BL/6 mice (5–6 weeks old) purchased from Guangdong Experimental Animal Center (license No.:SCXK2018-0002) were selected. This study complies with the Canadian Council on Animal Care guidelines or the Guide for the Care and Use of Laboratory Animals.

Dexosan Sodium sulfate (DSS) was purchased from Guangzhou Sijia Biotechnology Co., LTD., chloral hydrate and PBS were purchased from Guangzhou PythonBio Co., LTD., 4% paraformaldehyde was

purchased from Wuhan Servicebio Co., LTD., Trizol reagent was purchased from American Sigma Company, SYBR Green qPCR kit was purchased from Guangzhou Ruizhen Biotechnology Co., LTD., qPCR primer was purchased from Sangon Biotech Co., LTD., Anti-GAPDH rabbit polyclonal antibody and Goat Anti-Rabbit IgG were purchased from Cell Signaling Co., LTD, Anti-Claudin 2 antibody, Anti-occludin antibody and Anti-IL-10 antibody were purchased from Proteintech, Anti-ZO-1 antibody was purchased from Abmart Biopharmaceutical Co., LTD., TransStart Fastpfu DNA Polymerase was purchased from TransGen. VAHTSTM DNA Clean Beads TruSeq™ from Vazyme, TruSeq Nano DNA LT Library Prep Kit from Illumina, The Quant-iT PicoGreen dsDNA Assay Kit was purchased from Calbiochem.

Establishment and tissue sampling of mouse IBD model

The experimental mice were randomly divided into 5 groups. They were divided into normal control group (NC), model group (DSS), DCP low-dose group (DSS+50 mg/kg·day⁻¹ DCP), DCP medium-dose group (DSS+100mg/kg·day⁻¹ DCP) and DCP high-dose group (DSS+200mg/kg·day⁻¹ DCP), each group consisted of 10 mice(n=10). Mice in each DCP group were given different concentrations of polysaccharide solution intragastric treatment for 7 days, while mice in NC group and DSS group were given equal amounts of normal saline intragastric administration, during which the mice received regular chow diet and normal water. On the 8th day, the drinking water of the model group and each DCP group was changed into 2.7% DSS solution to prepare the IBD model. The modeling cycle was 7 days, during which gavage was continued according to the previous scheme. On the last night of modeling, the DSS solution was replaced with autoclaved water and the mice were fasted for 12 h.

After weighing the mice, they were anesthetized by intraperitoneal injection of 4% chloral hydrate solution. The blood was collected and rested at room temperature for 4 h. Then, samples were centrifuged at 4000 rpm, for 10 min to extract the supernatant. The mice were dissected through the abdomen in a sterile environment and the colon tissue was removed. Then, the colon contents were rinsed with a thick needle syringe with normal saline. The lower colon segment was fixed with 4% paraformaldehyde for the preparation of tissue sections. The remaining intestinal segment was placed in a frozen tube and stored in a refrigerator at -80 °C after rapid freezing with liquid nitrogen. The contents of mouse cecum were collected in frozen tubes, immediately frozen in liquid nitrogen, and stored at -80 °C before being used.

Real-time fluorescence quantitative PCR (RT-qPCR) was used to detect the expression levels of tight junction protein and inflammatory factor mRNA in colon tissues of mice

TRIzol reagent was used to extract total RNA from mouse colon tissue according to the reagent manufacturer's instructions. After the RNA concentration was determined, the RNA sample was diluted to a concentration of 50 ng/μL with enzyme-free water, and a reverse transcription reaction system was prepared for the reverse transcription reaction to synthesize cDNA. The PCR reaction system was prepared according to the operation steps in the instructions of SYBR Green qPCR kit. In this experiment, GAPDH was selected as the internal reference gene, and all primers synthesized in the RT-qPCR experiment were shown in the Table 1.

Western blotting detected the expressions of tight junction proteins and inflammatory factors in colon tissue of mice

In this study, Western blotting was used to detect the expression levels of tight junction proteins claudin-2, occludin and ZO-1 in the colon tissue of mice in each group, so as to explore whether DCP has a protective effect on the intestinal mechanical barrier of IBD mice. Mouse colon tissue homogenates were placed in an ice bath and cleaved with a mixture of RIPA buffer and protease inhibitors for protein extraction. The protein concentration was detected by bicinchoninic acid (BCA) protein assay kit (KGI Biotechnology Co., LTD., China). About 40μg of the protein in each sample was separated using 8% to 15% sodium dodecyl sulphate–polyacrylamide gel electrophoresis (SDS-PAGE) and then transferred to a polyvinylidene fluoride (PVDF) membrane (Millipore, USA). The film was blocked with 5% skim milk powder (dissolved in TBST solution) at room temperature for 2h, then incubated with primary antibody at

Table 1 The primer sequence

Gene	PCR primer sequence
GAPDH	F: AGGTCGGTGTGAACGGATTGG R: GGGGTCGTTGATGGCAACA
Claudin-2	F: GGGTCTCTGACAGCATGAAATTT R: GCCATCATAGTAGTTGGTACGA
Occludin	F: CACACAAGACATGCCTCCAC R: CCATTCACCTTGGCCGTGGA
ZO-1	F: CCACATACATTCCAAGGCCG R: GGGTGGGCTGGTTTGGATA
IL-10	F: CTATGCTGCCTGCTCTTACTGAC R: GAGTCGGTTAGCAGTATGTTGTCCAG

4°C overnight. The membranes were visualized using chemiluminescent reagents and quantified using ImageJ software.

16s rRNA gene sequencing

This project commissioned Suzhou PANOMIX Bio-medical Technology Co., Ltd. for sequencing, the specific experimental steps are as follows. The total DNA of bacteria in mouse cecum contents was extracted first. Because the improvement effect of DCP in the medium-dose group was the most obvious, this group was selected as the representative of the intervention group for sequencing, and the control group and model group were also sent for sequencing, and 5 samples were selected in each group. Firstly, total bacterial DNA was extracted from mouse cecum contents, and the DNA was quantified by Nanodrop, and the quality of DNA extraction was detected by 1.2% agarose gel electrophoresis. Subsequently, the target fragment was amplified by PCR and the product was recovered, and then fluorescence quantification was performed. The raw data obtained by high-throughput sequencing were initially screened, and linear discriminant analysis effect size (LEfSe) was used to analyze the community composition of multiple samples. Non-parametric Kruskal–Wallis (KW) and Wilcoxon rank sum tests were used to detect species with significant richness differences between populations, and Tukey's and Dunnett's multiple comparison tests were used to compare the statistical differences.

Quantification of SCFAs profiles

For the quantitative determination of SCFAs in fecal samples, including acetate, propionate and butyrate by ion chromatograph, a 50 mg fecal sample was weighed, dissolved, homogenized, and then centrifuged at 3000xg for 10 min. The supernatant was diluted (1:50), filtered through a 0.22 µm sterile membrane, stored in 2 ml screw cap vials, and then analyzed with an ion chromatography system for SCFAs.

Results and discussion

DCP can improve expressions of tight junction proteins in colon tissue of IBD mice and relieve intestinal inflammation

Studies have found that IBD patients often have impaired intestinal mechanical barriers and downregulated expressions of tight junction proteins. In order to understand whether DCP has a protective effect on the intestinal barrier, RT-qPCR was further performed to detect the mRNA expression level of tight junction proteins in mouse colon tissue. The results showed that compared with the control group, mRNA expression levels

of tight junction proteins claudin-2, occludin and ZO-1 in the colon tissue of IBD mice after DSS induction decreased significantly. However, after intervention with different concentrations of DCP, the mRNA expression level of intestinal compact linking protein claudin-2 in medium and high dose groups was significantly increased ($p < 0.001$). The mRNA expression level of intestinal tight junction protein occludin also increased significantly in medium dose group ($p < 0.001$) and high dose group ($p < 0.01$). The mRNA expression level of intestinal compact junction protein ZO-1 was significantly increased in the DCP low-dose ($p < 0.05$), medium-dose ($p < 0.01$) and high-dose groups ($p < 0.05$) (Fig. 1a,b,c), indicating that DCP may have a protective effect on the intestinal compact junction function of mice. It protected the integrity of the intestinal mechanical barrier. In addition, this study also explored whether DCP has anti-inflammatory effects on IBD mice. We measured the mRNA expression level of anti-inflammatory factor IL-10 in mouse colon tissue, and the results showed that compared with the model group, the mRNA expression level of IL-10 in colon tissue of mice in DCP low-dose ($p < 0.05$), medium-dose ($p < 0.05$) and high-dose groups ($p < 0.001$) was significantly increased, and showed an increasing trend with the increase of intervention concentration. This suggests that DCP may have a alleviating effect on intestinal inflammation in IBD mice (Fig. 1d).

Western blotting results showed that compared with the control group, the expression levels of tight junction proteins and IL-10 in colon tissue of mice in the model group were significantly decreased. After DCP intervention, the expression levels of tight junction proteins and IL-10 were increased compared with the model group, especially in the medium-dose group ($p < 0.05$) (Fig. 1e-j). We found that the intervention effect of high-dose DCP on IBD was not as obvious as that of medium-dose DCP, possibly because excessive dose of DCP may lead to competitive inhibition. Medium-dose DCP is the optimal intervention dose for preventing IBD in mice, and once this dose is exceeded, the effect may decline.

Effects of DCP on intestinal flora diversity

The occurrence and development of IBD are closely related to the composition of intestinal flora. In this study, 16s rRNA gene sequencing was performed to determine the composition of intestinal flora in mouse cecum contents. Fig. 2a, and 2b showed the dilution curves of Shannon index and Simpson index for sample species richness α diversity, indicating that the sequencing depth is qualified.

In order to comprehensively evaluate the α diversity of mouse intestinal flora, the diversity of flora was characterized by Shannon index and Simpson index, and the

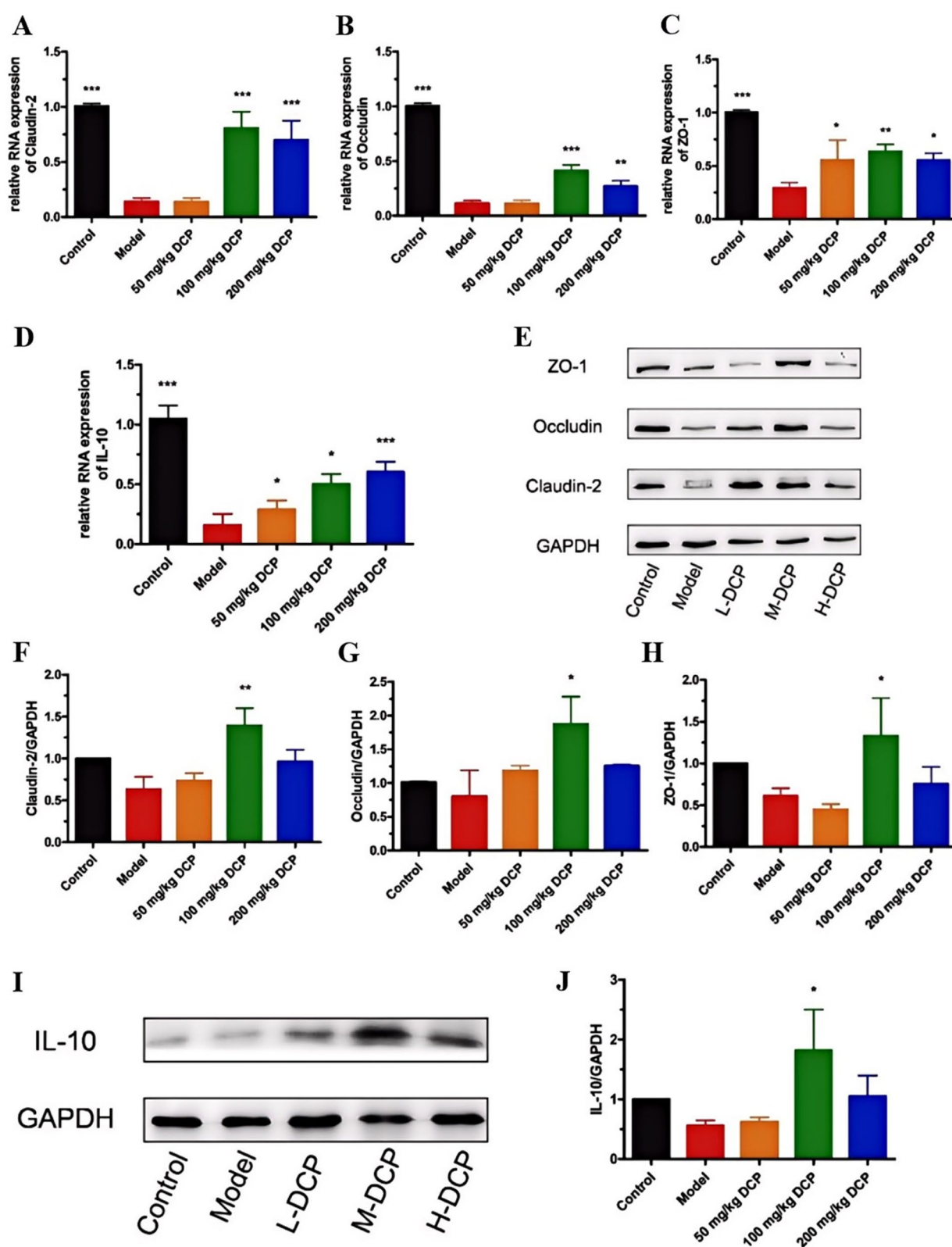


Fig. 1 Ameliorating effect of DCP on colonic tissue tight junction protein and inflammation in IBD mice. Tight junction proteins (a-c); Inflammatory cytokine (d); Protein bands of tight junction protein in each group of mice (e); Tight junction proteins quantification (f-h); Protein bands of inflammatory cytokines in each group of mice (i); inflammatory cytokines quantification (j). ps: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs Model group

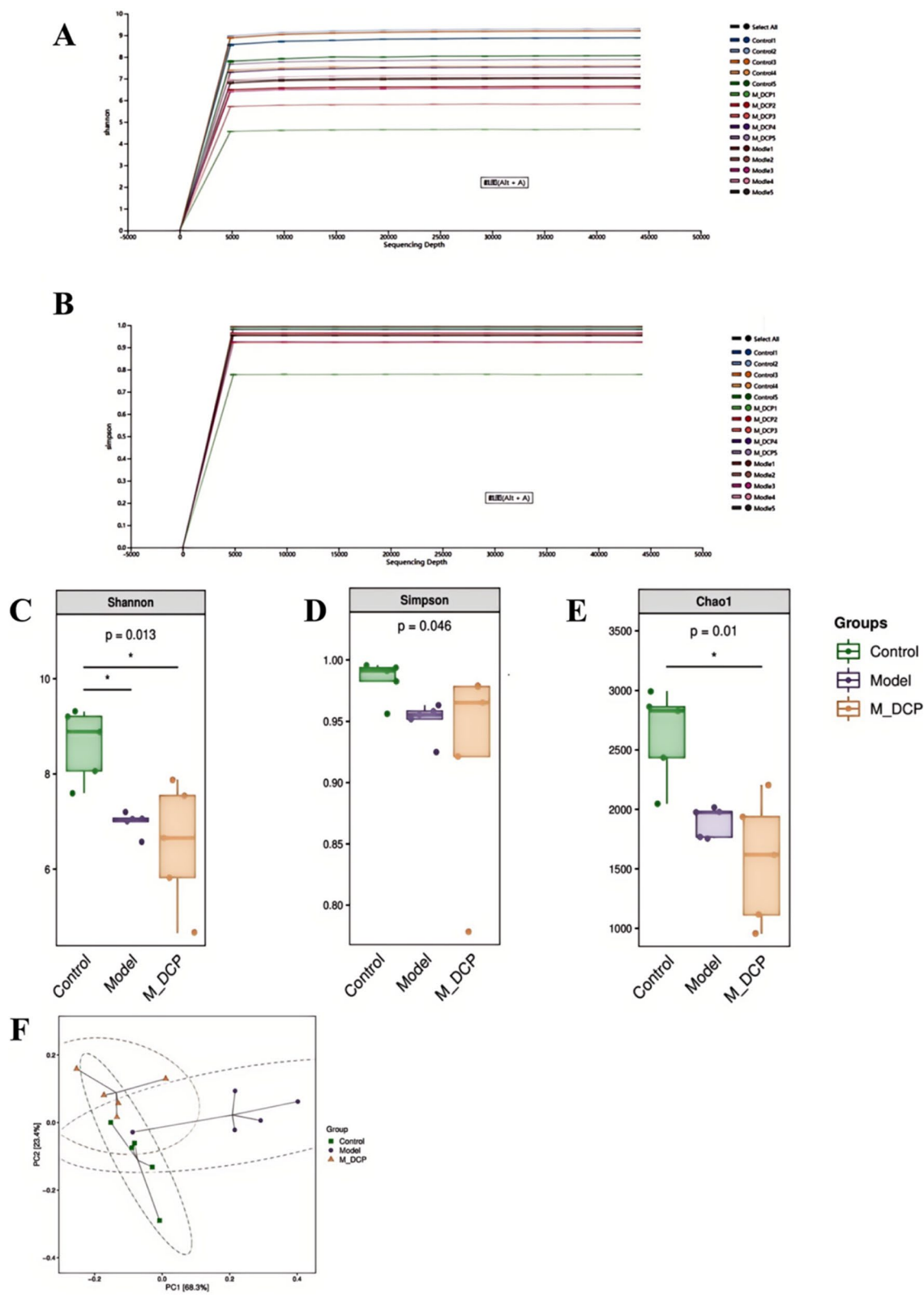


Fig. 2 Effects of DCP on intestinal flora diversity. The rarefaction curve of Shannon index (a); Simpson index (b); Shannon index (c); Simpson index (d); Chao1 index (e); The PCoAnalysis of gut microbiota among groups (Based on Bray–Curtis distance) (f). ps: * $p < 0.05$ vs control group

richness of flora was characterized by Chao1 index. The α diversity analysis results are shown in Fig. 2c-e. Compared with the normal control group, Shannon index ($p < 0.05$), Simpson index and Chao1 index of mice in the model group were all decreased, indicating that the diversity and richness of microflora of mice in the model group were lower than those in the normal control group. The Simpson index of mice in the DCP medium-dose group was slightly higher than that in the model group, while the Shannon index and Chao1 index were lower than that in the model group, but the difference was not statistically significant, suggesting that DCP intervention had no significant effect on the regulation of α diversity of intestinal flora in mice.

In this study, β diversity analysis was carried out to compare the differences in the distribution of intestinal microbial communities. The test method used is based on the OTU's Principal co-ordinate Analysis (PCoA) and is calculated using the Bray–Curtis distance. The results are shown in Fig. 2f, each color represents a sample group, and different points represent different samples. The closer the distance between the groups, the more similar the community compositions are, and vice versa. The same is true of different samples within the same group, with more clustered indicating more similar composition and more dispersed indicating greater differences. As can be seen from Fig. 2, the normal control group, model group and DCP medium-dose group all have overlapping parts, but the distance between the model group and the control group is longer ($p < 0.05$), indicating that the intestinal flora composition of the two groups is significantly different; on the contrary, the distance between the DCP medium-dose group and the control group is closer, indicating that the intestinal flora composition of the two groups is more similar. The distance difference between the model group and the DCP medium-dose group was statistically significant ($p < 0.05$), indicating that the composition of microflora between the two groups was statistically different. In addition, the distance between the samples in the model group is relatively dispersed, indicating that the differences within the group are large and the similarity between the samples is low.

Species composition and dominant flora analysis of intestinal flora at different taxonomic levels

Using the specific composition information of intestinal flora in different samples at different taxonomic levels, the number of taxon contained in each sample was calculated. The relative abundance histogram was drawn, and the difference of species composition among each group was statistically analyzed, so as to know the regulatory effect of DCP on intestinal flora of IBD mice.

As shown in Fig. 3a, at the genus level, compared with the control group, the relative abundance of *Bacteroides* and *Muribaculum* has increased significantly ($p < 0.01$) *Desulfovibrio* has decreased in the model group. After DCP intervention, the relative abundance of *Bacteroides* and *Muribaculum* has decreased significantly. The relative abundance of *Bacteroides* and *Muribaculum* has decreased significantly ($p < 0.01$), while *Desulfovibrio* has increased.

In addition, at the Phylum level (Fig. S1 a), *Firmicutes*, *Bacteroidetes* and *Proteobacteria* are the main Phylums in the fecal microflora. Compared to the control group, The relative abundance of *Firmicutes* and *Actinobacteria* in the model group was significantly decreased ($p < 0.01$), while the relative abundance of *Bacteroidetes* and *Proteobacteria* was significantly increased ($p < 0.01$). After DCP intervention, compared with the model group, The relative abundance of *Firmicutes* and *Actinobacteria* increased significantly ($p < 0.01$), while the relative abundance of *Bacteroidetes* and *Proteobacteria* decreased significantly ($p < 0.01$).

At the class level (Fig. S1 b), compared to the control group, the relative abundances of *Clostridia*, *Erysipelotrichia* and *Bacilli* in the model group was significantly decreased ($p < 0.05$), while the relative abundance of *Bacteroidia* was significantly increased ($p < 0.01$). After DCP intervention, their relative abundances increased ($p < 0.05$), while the relative abundance of *Bacteroidae* decreased significantly ($p < 0.01$).

At the order level (Fig. S1 c), compared with the control group, the relative abundance of *Clostridiales* was significantly decreased ($p < 0.05$) and that of *Bacteroidales* was significantly increased ($p < 0.01$) in the model group. After DCP intervention, compared with the model group, the relative abundance of *Bacteroidales* was significantly decreased ($p < 0.01$). The relative abundance of *Clostridiales* was significantly increased ($p < 0.05$), while the relative abundance of *Bacteroides* was significantly decreased ($p < 0.01$).

At the family level (Fig. S1 d), compared with the control group, the relative abundances of *Bacteroidaceae* and *Muribaculaceae* were significantly increased in the model group ($p < 0.01$), while the relative abundances of *Erysipelotrichaceae* were decreased. After DCP intervention, compared with the model group, the relative abundances of *Bacteroidaceae* and *Muribaculaceae* decreased significantly ($p < 0.01$), while the relative abundance of *Erysipelothrix* increased.

Different intestinal dominant flora will affect different metabolic pathways in human body. In this study, dominant flora with LDA value greater than 2 was screened by LEfSe analysis (LDA and Effect Size), and their differences among all groups were statistically analyzed. LEfSe

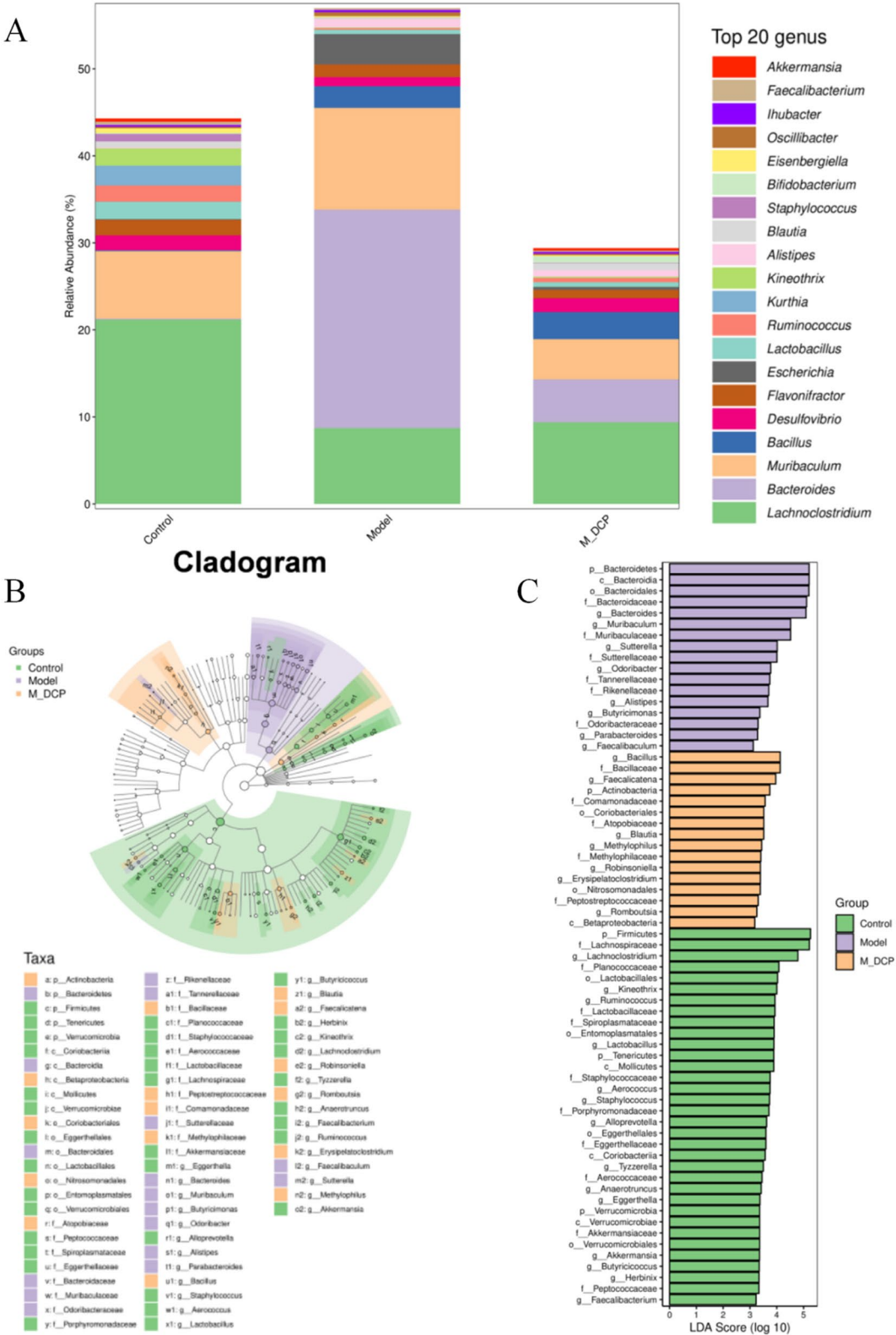


Fig. 3 Effect of DCP on Bacteria composition at the Genus (a) level Cladogram generated by the LEfSe analysis (b); Histogram of LDA value distribution of discriminative taxa (c)

analysis combined Wilcoxon rank sum test and non-parametric Kruskal–Wallis with LDA Effect size. Fig. 3 b is the taxonomic Cladogram, which revealed the taxonomic hierarchical distribution of different groups of marker species. Fig. 3c showed the histogram of LDA value distribution of significantly different species, and the longer the length of taxon, the more significant the difference. In the control group, 34 dominant strains were selected, among which *Firmicutes*, *Lachnospiraceae* and *Lachnospiraceae* contributed the most. *Bacteroidetes*, *Bacteroidia*, *Bacteroidales*, *Bacteroidaceae* and *Bacteroides* were the main dominant strains in the model group. A total of 16 dominant bacteria were identified in the DCP medium-dose group. *Bacillus* and *Bacillaceae* contributed

the most, followed by *Faecalicatena* and *Actinobacteria*. These results suggested that DCP may alter the dominant microflora in the intestinal microflora of IBD mice, resulting in changes in the composition of the intestinal microflora of mice.

Effects of DCP on intestinal short-chain fatty acids in mice

People with IBD may have changes in their microbiome composition. Principal component analysis (PCA) provided the overall difference in metabolite profiles between the control group, model group, and the DCP medium-dose group. PCA of mice in each group is shown in Fig. 4a. PCA1 was 61.8%, PCA2 was 22.2%, and the composition of feces in the same group was similar. The

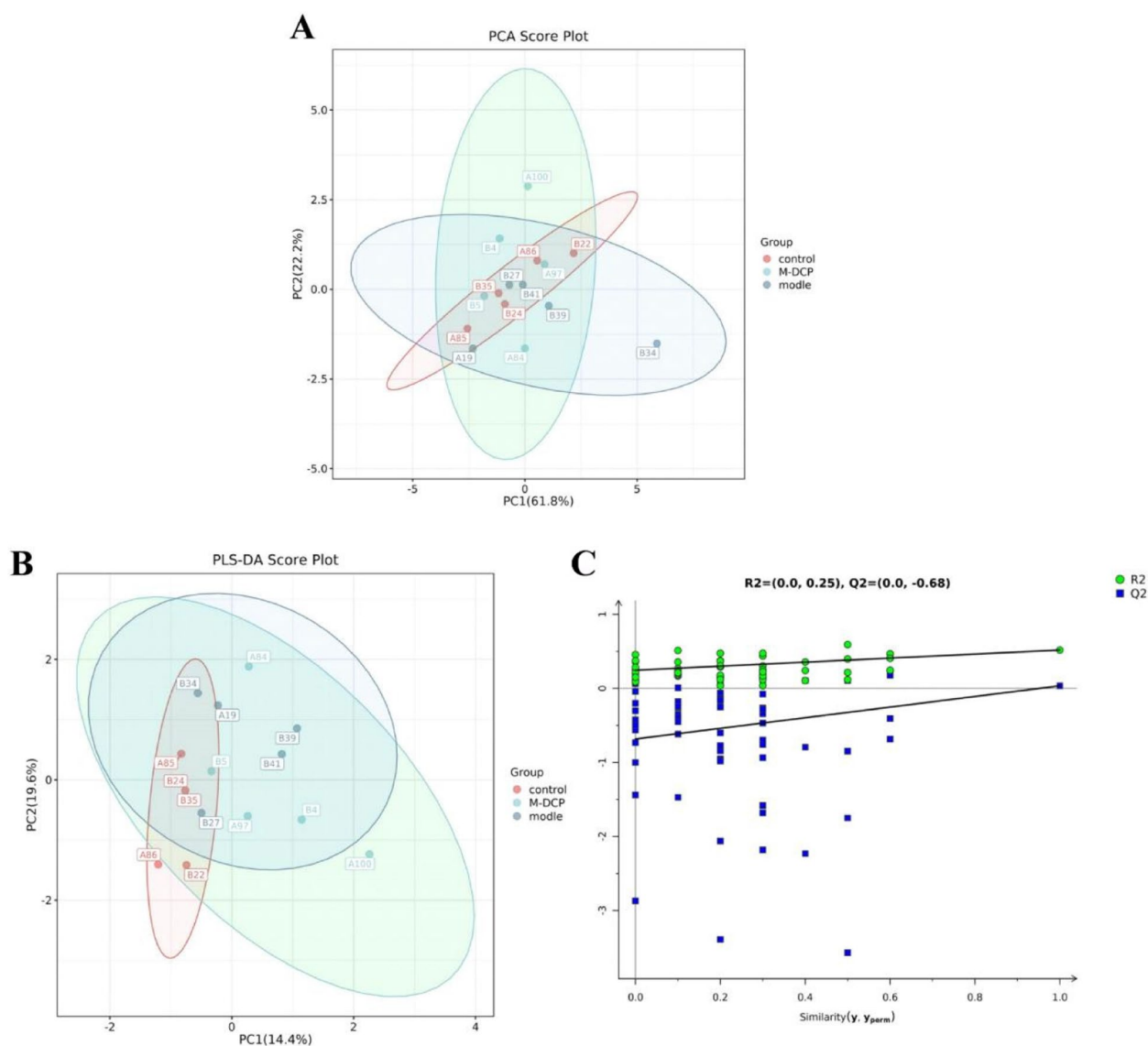


Fig. 4 PCA and PLS-DA analysis of fecal metabolomics. **a** PCA score chart, **b** PLS-DA score chart, **c** PLS-DA permutation test chart

data were processed by PLS-DA. PLS-DA scores in fecal samples showed differences in metabolite distribution in the control, model, and DCP medium-dose groups (Fig. 4b). The model parameter R2X (cum) is expressed as the cumulative interpretation rate for the X-matrix of the model. As shown in Table 2, the R2X (cum) value of the model is >0.5, indicating that it has high predictive power. Reaction alignment test was used to verify the accuracy of PLS-DA model. A value of Q2 < 0 in the response permutation test indicated that the PLS-DA model was not overpopulated (Fig. 4c).

Studies have shown that the level of SCFAs in the gut of IBD patients is different from that of normal individuals, and the SCFAs measured in the stool of IBD patients were lower than that of healthy individuals [28]. Different SCFAs in mouse feces were quantitatively analyzed, including acetic acid, propionic acid, butyric acid,

valeric acid and isobutyric acid (Fig. 5). After DSS treatment, the contents of acetic acid, propionic acid, butyric acid, isobutyric acid and valeric acid were decreased, and after DCP intervention, the acetic acid level of mice was significantly increased ($P < 0.05$), while the levels of propionic acid, butyric acid, isobutyric acid and valeric acid were increased, but there was no significant difference. These results indicated that DCP can increase the productions of acetic acid, propionic acid, butyric acid, valeric acid and isobutyric acid in colitis mice, and restored them to relatively normal levels.

Discussion

IBD is an autoimmune disease that has two main clinical forms: CD and UC. In recent years, the number of patients with IBD has been increasing year by year, and patients often suffer from hematostasis and diarrhea due to digestive tract inflammation and injury. The infiltration of inflammatory cells in the lamina propria and submucosa leads to cryptinitis and crypt abscess, resulting in epithelial degeneration and necrosis [29, 30]. Current clinical treatments can produce a variety of serious side effects, so it is important to develop safe and effective interventions to prevent and treat IBD. In this study, we successfully established a mouse model of IBD using DSS. The model was successfully established by the expression

Table 2 PCA model validation parameters

Group	pre	R2X(cum)
DCP medium-dose vs Model vs Control	2	0.84
DCP medium-dose vs Control	2	0.804
Model vs Control	2	0.863
DCP medium-dose vs Model	2	0.906

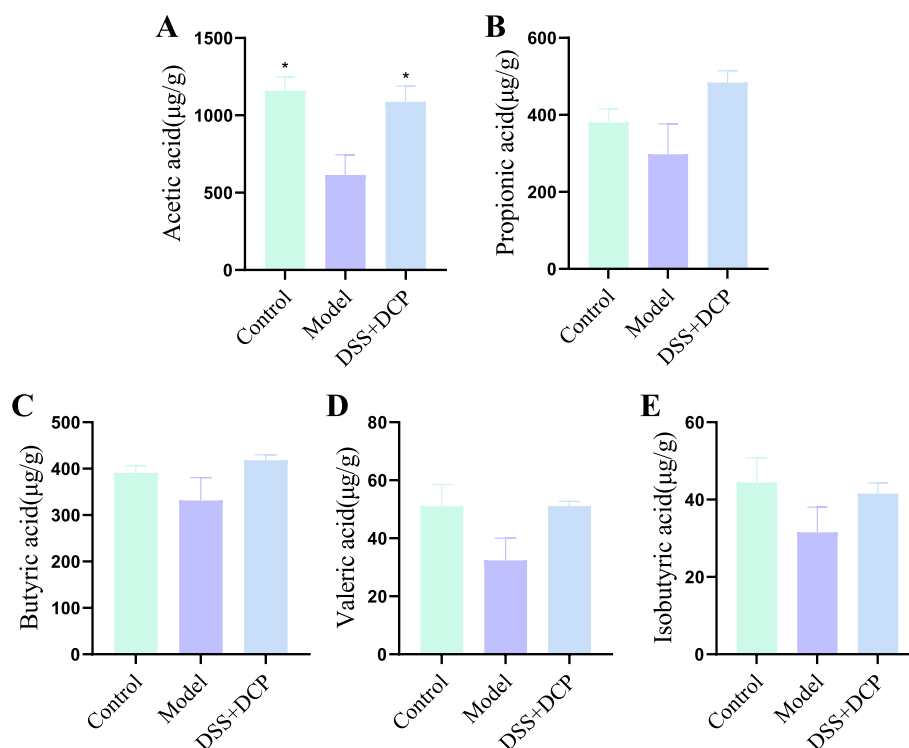


Fig. 5 Effect of DCP on SCFAs content in mice with DSS induced IBD. **a** acetic acid, **b** propionic acid, **c** butyric acid, **d** valeric acid, **e** isobutyric acid. ps: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ vs model group

of tight junction proteins in colon tissue. These findings suggest that IBD mice are characterized by impaired intestinal mechanical barrier and downregulation of tight junction protein expression, accompanied by intestinal microbiota disturbances and changes in short-chain fatty acid levels. Previous studies have shown that polysaccharides can prevent and treat a variety of inflammatory diseases, including UC, and can be used to study the prevention and treatment of IBD. The DCP used in this study is a kind of natural plant active substance, which has the advantages of safety, wide source and low cost.

The intestinal mucosal barrier, which consists of intestinal epithelial cells and tight intercellular connections, plays an important role in maintaining intestinal fixation and resisting intestinal infections. The loss of a fully functional intestinal barrier can lead to bacterial translocation, resulting in ecological dysregulation [31]. In order to understand whether DCP has a protective effect on intestinal barrier, gene expression levels of claudin-2, occludin and ZO-1 were detected in the experiment. The intestinal barrier is a sturdy barrier that protects the gut from the external environment, thereby maintaining balance throughout the body. Loss of a fully functioning intestinal barrier can lead to bacterial translocation, which can lead to ecological dysregulation. The mRNA expression level of compact connectin in colon tissues of mice in model group was significantly reduced, and it recovered after different concentrations of DCP. Further study found that compared with the model group, IL-10 mRNA expression level in colon tissue of mice in low, medium and high dose DCP groups was significantly increased, and showed a gradual increasing trend with the increase of intervention concentration. This suggests that DCP may also have a soothing effect on intestinal inflammation in mice with IBD.

The gut microbiome is critical for maintaining the integrity of the intestinal epithelial barrier [32]. Multiple studies have demonstrated differences in the composition of the gut microbiota between IBD patients and healthy individuals, particularly in terms of microbial diversity and the relative abundance of specific bacterial taxa. When the intestinal barrier is damaged, *Bacteroides* invading the mucus layer inside the intestine will cause a series of intestinal inflammation and eventually lead to IBD, so *Bacteroides* is an important target for anti-IBD treatment [33]. At the same time, this study observed an increase in the abundance of *Proteus* in mice in the model group, which was consistent with the increase in the abundance of *Proteus* in the fecal flora of IBD patients in clinical studies [34]. The study results showed that the intestinal flora of IBD mice induced by DSS decreased butyrate bacteria, such as ruminococcus and Clostridium etc. [35, 36], while the relative abundance of both

increased after DCP intervention. In addition, we also found that DCP can reverse the DSS induced changes in the relative abundances of *Escherichia coli* and *Lactobacillus* in IBD mice. *Escherichia coli* is an adherent invasive bacterium that increases in relative abundance in IBD mice and aggravates the development of colitis. *Lactobacillus* has been developed as a probiotic that helps improve intestinal inflammation. This study observed that DCP had a good regulating effect on both of them. Therefore, it confirmed that DCP can effectively regulate intestinal flora, and plays a regulatory role mainly by changing the species composition and distribution of intestinal flora, so as to effectively improve IBD.

At present, the domestic research on the improvement of IBD activity by DCP is not comprehensive enough and needs further research. In this study, the point of view analysis is not thorough enough, only in vivo to explore the improvement in IBD mice treated with DCP, it is hoped that in the future more in-depth and comprehensive research will be carried out, and constantly improve the application value of DCP.

Polysaccharide is one of the main components of *Dendrobium drumstick*. In this study, the DCP components obtained by self-extraction and separation were used to conduct a preliminary study on DCP. In the future, more preparations and more activity exploration experiments will be conducted on its effect on improving inflammatory bowel disease, which will provide references for further development and application of *Dendrobium* and its polysaccharide components.

Conclusion

This study found that the intestinal barrier function was impaired in the DDS treated mice, but not the control ones. DCP restored the integrity of the intestinal mucosa by up-regulating the expression of tight junction proteins, thereby improving the pathological changes related to IBD. In addition, the prevention of IBD in mice by DCP may be achieved by protecting the intestinal barrier and playing an anti-inflammatory role. Therefore, this study provides evidence for the potential application of DCP as a novel intervention for IBD. In order to understand whether DCP has a regulatory effect on the intestinal flora of mice, 16s rRNA sequencing was performed on the cecum contents of mice in this study, and the results showed that DCP has a good regulatory effect on the intestinal flora. In addition, we found that DCP can reverse DSS induced changes in the relative abundance of *E. coli* and *Lactobacillus* in IBD mice. In this study, we found that DCP increased the production of acetic acid, propionic acid, butyric acid, valeric acid, and isobutyric acid in colitis mice and restored it to relatively normal levels. Based

on these results, we suggest that DCP promotes the low abundance of other microorganisms in the normal control group, thereby improving colitis.

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1007/s44403-025-00031-2>.

Supplementary Material 1.

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Not applicable.

Authors' contributions

Mengting Wu: Writing- Original draft preparation, Software, Data curation, Visualization. Zijun Xia: Writing- Original draft preparation, Investigation, Validation. Yuting Hao: Writing- Reviewing and Editing. Dongliang Feng: Conceptualization, Writing- Reviewing and Editing, Supervision, Project administration, Funding acquisition. Hongji Liu: Software, Data curation, Visualization. Chuqiao Xiao: Investigation, Validation. Wenzhen Liao: Methodology, Formal analysis, Writing- Reviewing and Editing, Supervision, Project administration, Funding acquisition.

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Data availability

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

Male C57BL/6 mice (5–6 weeks old) purchased from Guangdong Experimental Animal Center (license No.:SCXK2018-0002) were selected. This study complies with the Canadian Council on Animal Care guidelines or the Guide for the Care and Use of Laboratory Animals.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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