frontiers | Frontiers in Nutrition

ORIGINAL RESEARCH
published: 12 May 2022
doi: 10.3389/fnut.2022.899421

The Methanol Extract of *Polygonatum odoratum* Ameliorates Colitis by Improving Intestinal Short-Chain Fatty Acids and Gas Production to Regulate Microbiota Dysbiosis in Mice

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The potential impacts of methanol extract from *Polygonatum odoratum* on (YZM) colonic histopathology, gut gas production, short-chain fatty acids (SCFAs), and intestinal microbiota composition were evaluated with dextran sulfate sodium (DSS)-induced colitis mice in this study. These results indicated that YZM increased colon length and ameliorated colonic histopathology in DSS-induced colitis mice. Moreover, YZM administration reversed intestinal microbiota compositions leading to the inhibition of H_2S-related bacteria (e.g., *Desulfovibrionaceae*) and the lower level of H_2S and higher contents of SCFA-related bacteria (e.g., *Muribaculaceae*). Taken together, the effects of methanol extract from *Polygonatum odoratum* are studied to provide new enlightenment and clues for its application as a functional food and clinical drug. Our study first revealed the relationship between intestinal gas production and key bacteria in ulcerative colitis.

Keywords: ***Polygonatum odoratum*, DSS-induced colitis mice, gas production, SCFAs, microbiota**

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Specialty section:
This article was submitted to Food Chemistry, a section of the journal Frontiers in Nutrition

Received: *18 March 2022*
Accepted: *12 April 2022*
Published: *12 May 2022*

Citation:
Ye X, Pi X, Zheng W, Cen Y, Ni J, Xu L, Wu K, Liu W and Li L (2022) The Methanol Extract of Polygonatum odoratum Ameliorates Colitis by Improving Intestinal Short-Chain Fatty Acids and Gas Production to Regulate Microbiota Dysbiosis in Mice. Front. Nutr. 9:899421. doi: 10.3389/fnut.2022.899421

INTRODUCTION

Inflammatory bowel disease (IBD) is a relapsing non-specificity inflammatory condition that results from a chronic disorder of the gastrointestinal mucosa immunity system, including Ulcerative colitis (UC) and Crohn's disease (CD) (1). Recent investigations indicate that the prevalence rate of IBD has also increased sharply, especially among younger people. Typical clinical manifestations of IBD include abdominalgia, enterorrhagia, hematochezia weight loss, and recurrence due to inflammatory cell infiltration. Some studies have found that the causes of UC include pathogenic microorganism infection, genetic susceptibility, intestinal microbiome imbalance, and intestinal mucosal barrier defect. However, at present, the pathological mechanism is not clear. The current clinical treatments (sulfasalazine and mesalazine) are mainly to relieve the symptoms of the disease

but accompany adverse impacts (2). Thus, developing a safe and high efficacy treatment to remiss IBD is urgently required.

The intestinal mucosal barrier prevents disease-causing substances and bacteria from entering the bloodstream. The microbial barrier composed of a large number of microbial colonies is crucial in the development of IBD. Extensive research has suggested that changes in colon microflora composition caused by an abnormal increase in pathogenetic bacteria or deficiency of probiotics are associated with IBD. Accompanied by intestinal microbiota disturbance, the alteration of metabolites such as short-chain fatty acids (SCFAs) and gas affect colitis's progression, which is intimately related to colon cancer (3). Although the exact mechanisms related to microorganisms remain to be elucidated, emerging evidence suggests that various natural substances contribute significantly to the improvement of IBD by regulating gut microbiota (4).

Dietary intake is closely associated with the pathogenesis and prevention of IBD without adverse influence (5). The interaction between dietary nutrients and intestinal immunity is very complex, referring to the immune response and the regulation of intestinal microflora composition (6). Ingested natural nutrients can accumulate and interact with intestinal microbiota (7, 8). As the sole input resource for intestinal microbiota, dietary intake has a significant impact on the intestinal microbiome composition (9, 10). Therefore, natural nutrients, which are characterized by low toxicity, multiple components, and targets, play an important role in potentially maintaining microbial homeostasis in patients with IBD with long-term use.

Polygonatum odoratum (Mill.) Druce (YZ) is a perennial herbaceous plant in the Liliaceae family that is widespread in East Asia and Europe. The root of YZ is a sweet and light food, and it is also traditional Chinese medicine that can relieve intestinal problems (11). YZ contains a variety of active substances, namely, flavonoids, terpenoids, phenols, coumarin alkaloids, and organic acids (12). Flavonoids, as an antioxidant, can delay aging, inhibit viral activity, inhibit bacterial reproduction, prevent cancer, and enhance the immune system. In addition, flavonoids are considered a functional factor in healthy foods. Resveratrol, a polyphenol, has a protective effect on acute or chronic colitis in different models, downregulating inflammatory biomarkers and reducing clinical symptoms (13).

Methanol extract of *Polygonatum odoratum* (YZM) was prepared to elucidate its protective effect on UC and further explore its related mechanism in our research. We assessed the impacts of YZM on body weight, colon length, colon lesion degree, intestinal microbiota composition, and metabolites of DSS-induced colitis mice. Our investigation provides insights into the influence of YZM on colitis related to the interactions of microbiota and metabolites. This evidence could support the new therapeutic and preventive avenues for IBD.

MATERIALS AND METHODS

Preparation of the YZM

Polygonatum odoratum was derived from Bozhou Zhongyitang Traditional Chinese Medicine Sales Co., Ltd. The crushed medicinal materials were extracted with methanol at room temperature and repeated three times. The extracts were concentrated and named YZM (yield 20%), the methanol extract from *Polygonatum odoratum*. YZM was dried under vacuum conditions (decompress distillation and vacuum desiccation) for biological tests and stored at 4°C.

Compositions Analysis of YZM

Orbitrap MS (Thermo Fisher Scientific, United States) with the ACQUITY UPLC® HSS T3 (150 mm × 2.1 mm, 1.8 μm, Waters) column was applied for UHPLC-MS analyses. The mobile phase flow rate was 0.25 ml/min; solvent A was composed of 0.1% formic acid in the water, and solvent B was composed of 0.1% formic acid in acetonitrile. The elution condition was as follows: 2% B for 1 min, 2–50% B for 8 min, 50–98% B for 4 min, 98% B for 1.5 min, 98–2% B for 1.5 min, and 2% B for 6 min. The electrospray ionization mass spectrometry (ESI-MS) setting was as follows: positive mode (3.5 kV), negative mode (−2.5 kV), auxiliary gas at 30 units, capillary temperature at 325°C (14, 15). The mass spectra were scanned at a resolution of 60,000 from 100 to 1,000 m/z.

Design of Experiments

Male BABL/c mice (6–8 week old, specific pathogen-free grade, 20 ± 2 g, $n = 30$) were purchased from the Zhejiang Academy of Medical Science and raised at the Zhejiang Academy of Agricultural Sciences. Mice were subjected to an artificial LED light cycle (12-h light/12-h dark) and ambient temperature (24–26°C) indoors. Mice were free to intake standard food and water for 2 weeks under laboratory conditions. The mice were randomly divided into five groups: a control group treated with phosphate-buffered saline (PBS), a model group treated with PBS, a positive control group treated with salicylazosulfapyridine (SASP, 50 mg/kg), a YZM-L group treated with a low concentration of YZM (YZM-L, 200 mg/kg), and a YZM-H group treated with a high concentration of YZM (YZM-H, 400 mg/kg). All drugs were administered by intragastric administration. The control group supplied sterile water. The other groups were supplied with 3% DSS solution for 8 days to induce colitis. All mice were sacrificed on day 9.

Evaluation of Disease Activity Index Score

The disease activity index (DAI) score is a common index to assess the colitis severity of mice. All mice were evaluated for weight loss, stool character, and fecal occult blood. The

TABLE 1 | Criteria for DAI.

DAI score	Weight loss	Dropping consistency	Occult/blood bleeding
0	None	Normal	Normal
1	1–5		
2	5–10	Loose droppings	Occult blood positive
3	10–20		
4	>20	Diarrhea	Blood bleeding

average of these scores was assigned according to DAI criteria (**Table 1**) (5).

Evaluation of Colonic Pathological Changes

Fresh colon tissues were fixed in 4% buffered paraformaldehyde for 48 h and then embedded in paraffin. After stained with hematoxylin–eosin (H&E), photomicrographs were obtained using a microscope for histological examination and histopathological score (**Table 2**) on 4-μm-thick sections (16).

Fermentation With Mice Fecal

Fresh fecal samples (0.24 g) were homogenized with 2.4 ml of 0.1 M PBS (pH 7.0). After filtration by 300 mesh filter sieves, the supernatants were transferred into modified medium (17). The recipe for 1 L was as follows: starch, 8 g; yeast extract 4.5 g; tryptone, 6 g; L-cysteine hydrochloride, 0.8 g; bile salt, 0.4 g; hemin, 0.05 g; NaCl, 4.5 g; $MgCl_2 \cdot 6H_2O$, 0.45 g; $CaCl_2 \cdot 6H_2O$,0.2 g; KCl, 2.5 g; KH_2PO_4, 0.4 g; 1 ml of Tween-80 and 2 ml of a solution of trace elements (g/L, $MgSO_4 \cdot 7H_2O$, 3.0; $MnCl_2 \cdot 4H_2O$, 0.32; $FeSO_4 \cdot 7H_2O$, 0.1; $CoSO_4 \cdot 7H_2O$, 0.18;

TABLE 2 | Histological scoring system.

Histological score	Degree of inflammation	Infiltration of inflammatory cells	Degree of damage to the crypt	Crypt abscesses	Degree of submucosal edema	Reduction of goblet cells	Degree of epithelial hyperplasia
0	Normal	Normal	Normal	Normal	Normal	Normal	Normal
1	Mucosa	Unifocal	Basal 1/3 of crypt	Unifocal	Unifocal	Unifocal	Unifocal
2	Submucosa	Multifocal	Basal 2/3 of crypt	Multifocal	Multifocal	Multifocal	Multifocal
3	Muscular	Suffuse	Entire crypt		Suffuse	Suffuse	Suffuse
4	Serous		Damage to the crypt and ulceration				

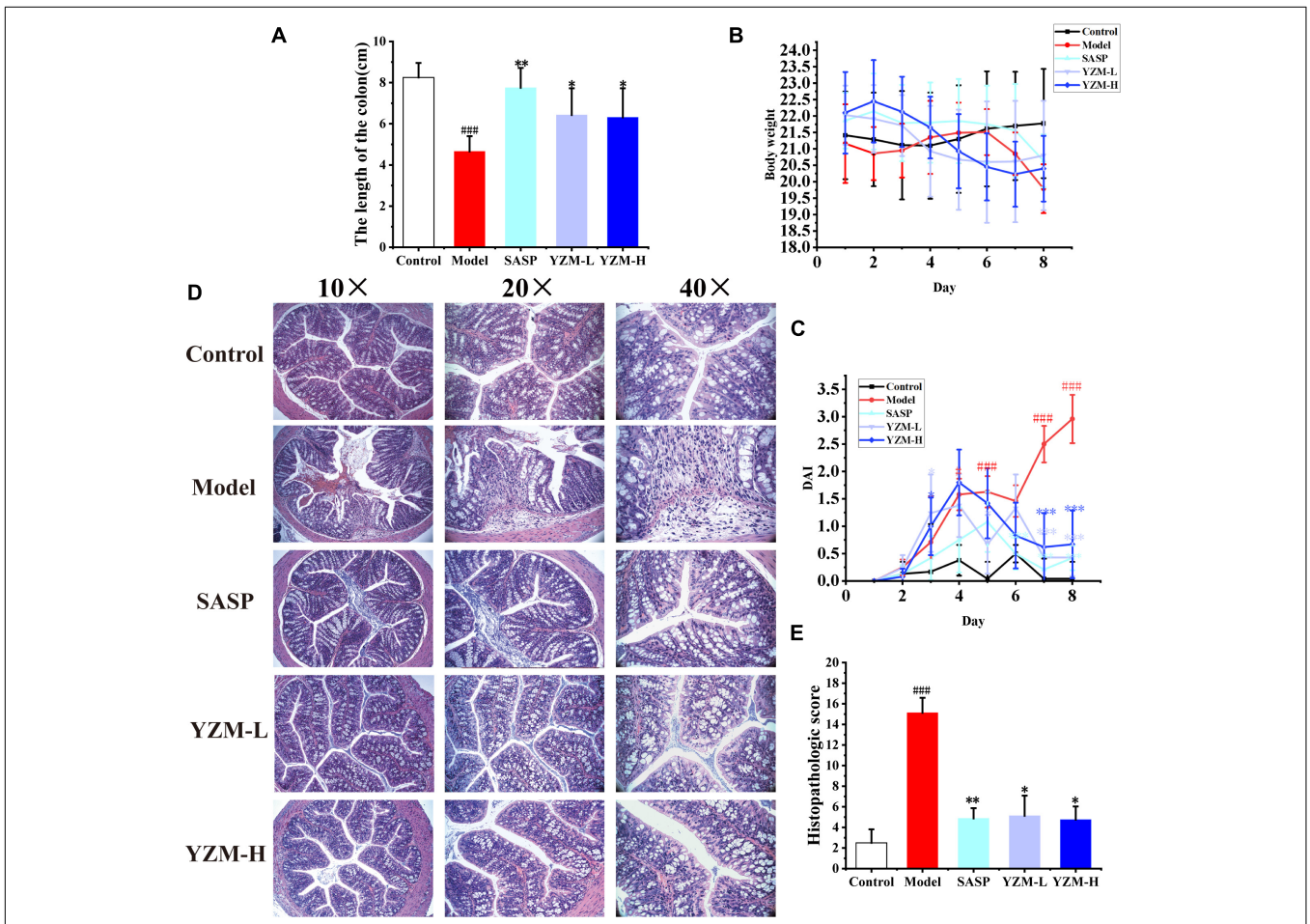

FIGURE 1 | The effect of YZM on colitis mice. **(A)** Analysis of colon length. **(B)** Body weight changes. **(C)** DAI changes. **(D)** Representative images of colon sections. **(E)** Histological score. $^{###}p < 0.001$ vs. control, $^{**}p < 0.01$ vs. model, $^{*}p < 0.05$ vs. model.

$CaCl_2 \cdot 2H_2O$, 0.1; $ZnSO_4 \cdot 7H_2O$, 0.18; $CuSO_4 \cdot 5H_2O$, 0.01; and $NiCl_2 \cdot 6H_2O$, 0.092).

Gas Production

The gas detector measured gas composition after fermentation. Carbon dioxide (CO_2), hydrogen (H_2), methane (CH_4), hydrogen sulfide (H_2S), and ammonia (NH_3) were measured simultaneously after being incubated at 37°C for 24 h (17).

Analysis of Short-Chain Fatty Acids

Gas chromatography (Shimadzu, Japan) with DB-FFAP column (0.32 mm × 30 m × 0.5 μm, Agilent Technologies, United States) was used to quantify the SCFAs. The operation condition was as follows: the flow rate of nitrogen carrier gas: 19.0 ml/min; split ratio: 1:10, the temperature of both detector and injection port: 250°C. Crotonic acid was used as an internal standard (17).

The Intestinal Microbiota Analysis

After the fecal sample's DNA was extracted, and the V3-V4 fragment of the bacterial 16S rDNA gene was amplified with primers (341F/805R). Agilent 2100 Bioanalyzer (Agilent, United States) evaluated the amplicon library. Then, sequencing was performed on the NovaSeq PE250 platform. According to the specific barcode of the sample, the paired-end data were overlapped using the FLASH (v1.2.11). The feature table and sequence, obtained with DADA2 (Divisive Amplicon Denoising Algorithm), were analyzed using QIIME tools (18). Alpha diversity was estimated with the Observed OTUs, Chao 1, Simpson, and Shannon index. Beta diversity was assessed by the Bray–Curtis distance and presented by principal coordinate analysis (PCA) and non-metric multidimensional scaling (NMDS). The differences between groups in taxonomic composition taxa were analyzed using the linear discriminant analysis (LDA) effect size (LEfSe) analysis, and LDA scores > 4 were defined as discriminative taxa. R package (v3.5.2) was utilized to draw diagrams.

Statistical Analysis

Data were reported as means ± SD (n = 6). SPSS 16.0 was conducted to statistically analyze the obtained data. The t-test for unpaired results was used to evaluate differences between two groups. P-value < 0.05 was considered statistically significant. $^{###}p < 0.001$ vs. control, $^{##}p < 0.01$ vs. control, $^{#}p < 0.05$ vs. control; $^{***}p < 0.001$ vs. model, $^{**}p < 0.01$ vs. model, $^{*}p < 0.05$ vs. model.

RESULTS

Identification of Active Components of YZM

A total of fifty-five active compounds were identified through UHPLC-QE-MS, which belonged to the following chemical classes: flavonoids (14), coumarins (8), organic acids (7), phenols (6), terpenoids (4), alkaloids (3), and lactones (3), such as resveratrol, oxyresveratrol, (R)-oxypeucedanin, phloroglucinol, atractylenolide II, neocnidilide maltol, kaempferol, fisetin, isomeranzin, and allocryptopine. The identified active chemical compounds, retention time, experimental mass with positive/negative mode, formula, and class are presented in **Supplementary Table 1**.

YZM Improved the Pathological States of Colitis Mice

Compared to the control group, the model group and drug intervention groups induced with DSS showed significant weight loss, shorter colon length, and decreased stool consistency (**Figure 1** and **Supplementary Figure 1**). The colon length decreased by approximately 43.52, 6.06, 22.06, and 23.52% in the model group, SASP group, YZM-L group, and YZM-H group (**Figure 1A**). The weight loss of YZM-treated mice was recovered from days 5 to 8 (**Figure 1B**). Furthermore, the DAI scores in the SASP and YZM groups were improved (**Figure 1C**).

The structure of the control group was well structured with no damage to the crypt, without prominent inflammatory infiltration. The mucous membrane of the model group was widely absent, and situations of erosion, hyperemia, and edema were observed. Obvious inflammation with considerable lymphocytes infiltrated and gathered between the basal layer and mucosal muscle in the model group. There was edema in the submucosa, and a large number of goblet cells disappeared, showing classic inflammatory changes, and the damaged area of the colon accounted for more than 50% of the entire colon (**Figure 1D**). The histopathological score of the model group was significantly higher than other groups. Compared with the model group, mucosal inflammatory cell infiltration, erosion, and edema in YZM groups (**Figure 1E**) were improved significantly.

YZM Restores the Gut Microbiota and Metabolites

YZM Influenced Gas Production in Fermentation

Intestinal gases produced by the microbiota could take a series of impacts on intestine homeostasis. Gas pressure and composition (CO_2, followed by H_2, H_2S, CH_4, and NH_3) were detected as the indicators of fermentation rate. The pressure increased with the increasing YZM dose (**Figure 2A**), suggesting that YZM stimulated the gas production from bacteria. In **Figure 2B**, CH_4 production of YZM-L was lower than in other groups but increased with the increasing concentration of YZM. The production of NH_3 and H_2S was inhibited in YZM-L and YZM-H groups (**Figures 2C,D**). In addition, H_2 production was inhibited in the YZM-H group (**Figure 2E**). Since CO_2 is the main component of intestinal gas, it shows a similar trend to gas pressure (**Figure 2F**).

YZM Restored the Production of Short-Chain Fatty Acids

Short-chain fatty acids play crucial roles in human microorganism–host interaction and the pathogenetic mechanism of colitis. In fecal samples, we measured the SCFA (acetic, propionic, isobutyric, butyric, valeric acids, and

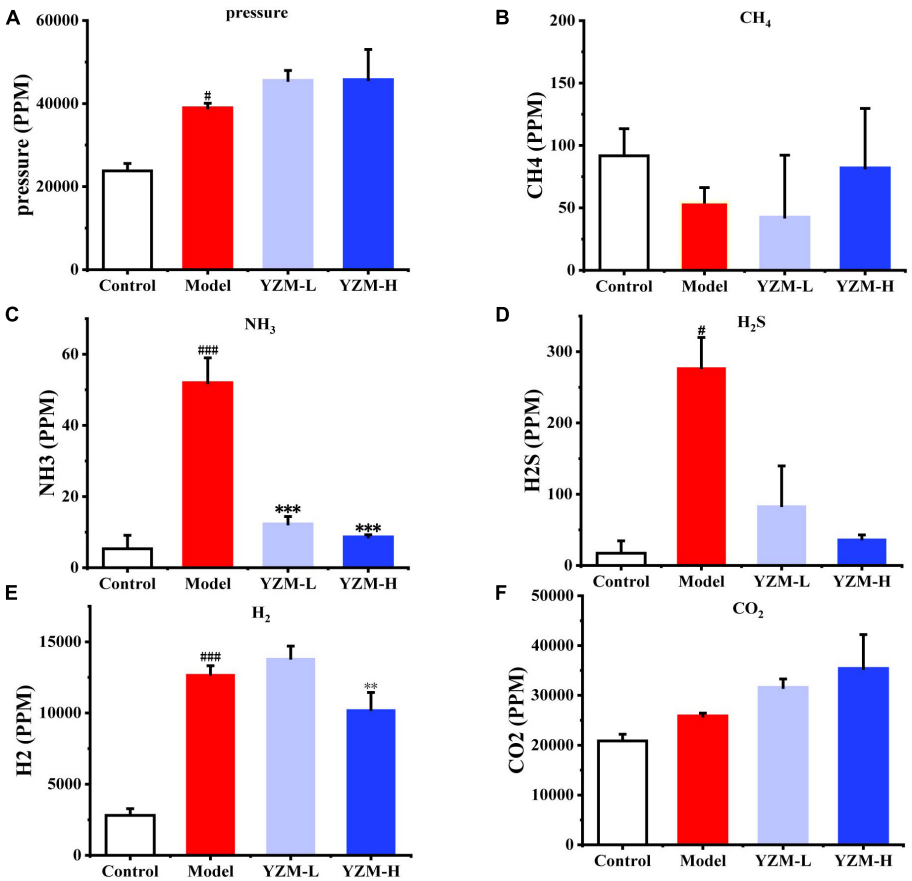

FIGURE 2 | Gas produced by intestinal microbiota. **(A)** The pressure after fermentation. **(B–F)** The abundance of CH_4, NH_3, H_2S, H_2, and CO_2, respectively. $^{###}p < 0.001$ vs control, $^{#}p < 0.05$ vs control; $^{***}p < 0.001$ vs model, $^{**}p < 0.01$ vs model.

isovaleric) level. Compared with the control group, the model group mice showed decreased contents of SCFAs (**Figure 3**). YZM treatment particularly increased the concentrations of acetic and propionic acids (**Figures 3A,B**). The contents of other measured SCFAs displayed similar increasing trends, whereas the changes were not significant in YZM-treated groups (**Figures 3C–F**).

YZM Modulated Intestinal Microbiome Composition

The observed species, Chao 1, Shannon index, and Simpson index of the samples were chosen to represent the alpha diversity of the microbes in the samples (**Table 3**) (19). These indices of YZM groups were higher than that of the model. However, these effects were not significant. These results indicated that the sum of bacterial species in the faces sample of YZM groups was higher than that in the sample of the model, to a certain extent. The microbiota alpha's diversity in the model group was repressed, which was reversed by YZM treatment (**Figures 4A,B**). It was largely improved in observed OTUs and Chao1 indices after the treatment of YZM-H.

Principal coordinate analysis and non-metric multidimensional scaling (NMDS) showed that an apparent clustering division between the control group and model group revealed various differential OTUs (**Figures 4C,D**). Meanwhile, the community structures of the YZM-L group (PCA) and YZM-H (NMDS) were tended to the control group. These results implied that YZM treatment significantly promotes microbial richness.

According to the differences in composition at the phylum level, *Campylobacterota* and *Desulfobacterota* displayed a higher abundance in the model group and a lower abundance of *Actinobacteriota* (**Figure 5A**). The relative abundance of these three taxonomic microbiotas was corrected in SASP and YZM groups (**Figures 5B–D**). The abundance of *Ruminococcus* increased, whereas *Muribaculaceae_unclassified* and *Alloprevotella* decreased in the model group at the genus level (**Figure 5E**). However, YZM-L, YZM-H, and SASP significantly reversed the intestinal bacterial composition (**Figures 5F–H**). This reflected that YZM administration could change the intestinal flora of colitis mice to adjust them to be a healthy biological barrier.

Consistent with other results, linear discriminant analysis effect size (LEfSe) was conducted to identify the differences in the dominant communities (**Figures 6A,B**). *Campylobacteria* was the key bacteria associated with intestinal microbiota disorder in the model group (LDA = 4.14, $p = 0.003$). The

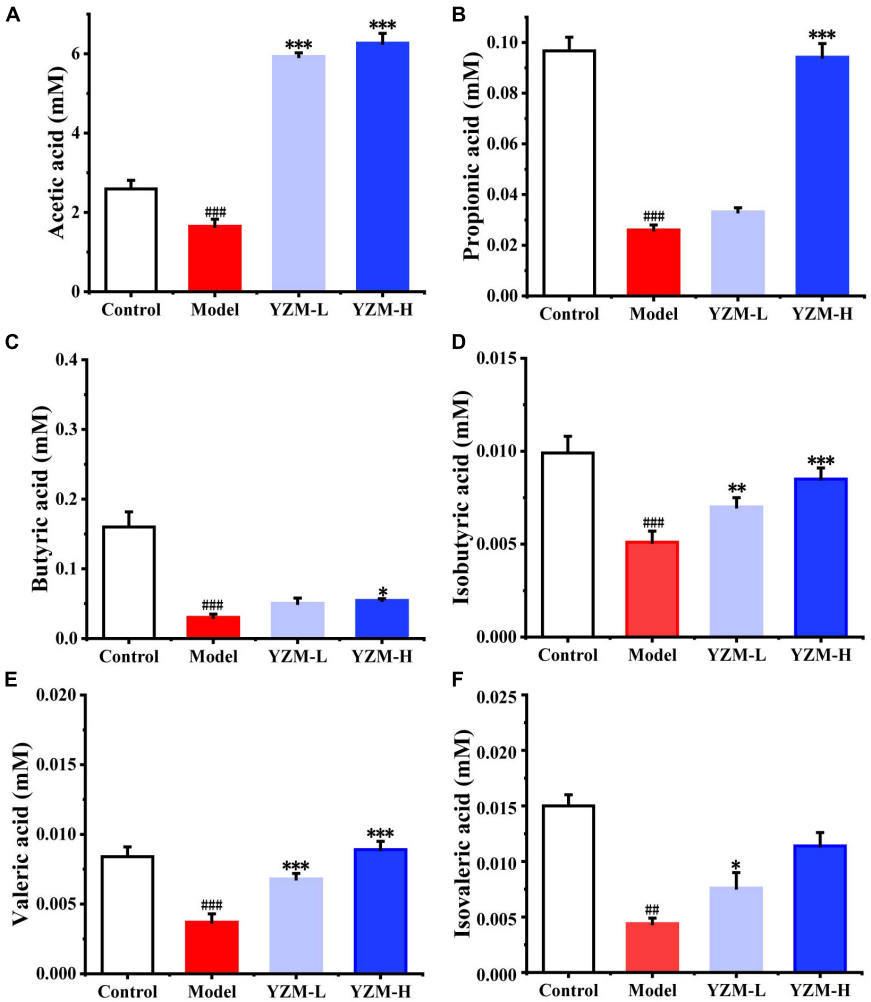

FIGURE 3 | SCFAs produced by intestinal microbiota. **(A–F)** Represents SCFAs amount as acetic acid, propionic acid, butyric acid, isobutyric acid, valeric acid, Isovaleric acid. $^{###}p < 0.001$ vs control, $^{#}p < 0.05$ vs control; $^{***}p < 0.001$ vs model, $^{**}p < 0.01$ vs model, $^{*}p < 0.05$ vs model.

TABLE 3 | Effects of YZM on overall structural modulation of gut microbiota.

	Control	Model	SASP	YZM_L	YZM_H
Observed OTUs	624.50 ± 103.27	505.17 ± 141.76	424.00 ± 142.15	569.83 ± 160.10	609.80 ± 73.15
Shannon	6.77 ± 0.59	6.42 ± 0.32	5.61 ± 0.28*	6.39 ± 0.76	6.59 ± 0.27
Simpson	0.97 ± 0.01	0.96 ± 0.01	0.94 ± 0.01**	0.96 ± 0.02	0.97 ± 0.01
Chao1	632.96 ± 105.22	509.10 ± 145.26	428.15 ± 145.07	572.49 ± 159.29	612.96 ± 74.63

** Indicates significant difference (**p < 0.01 vs. model, *p < 0.05 vs. model).*

strain dramatically decreased once YZM and SASP intervened (**Figure 5B**). In the YZM-H group, *Muribaculaceae_unclassified* at genus level exhibited comparative enrichment (LDA = 5.27, $p = 0.001$). Pearson correlation analysis assessed relationships among intestinal microbiota, microbiota-derived metabolites, and gas production (**Figure 6C**). Potential pathogens, such as *Clostridiales,* were highly correlated with risk factors (high DAI score, HE score, H_2S, and NH_3), whereas beneficial bacteria, including *Prevotellaceae NK3B31*, were negatively associated with these hazard factors.

DISCUSSION

Polygonatum odoratum (Mill.) Druce (YZ) has been widely used as a food source and traditional medicine (20). It has been used to remedy various inflammatory diseases, such as flu virus, diabetes, obesity, and antitumor (21). We identified 46 compounds in YZM, flavonoids, coumarins, alkaloids, terpenoids, phenols, organic acids, and lactones, such as resveratrol. Studies show that resveratrol exerts anti-inflammatory effects within intestinal cells and prevents the onset of DSS-induced colitis (22–24).

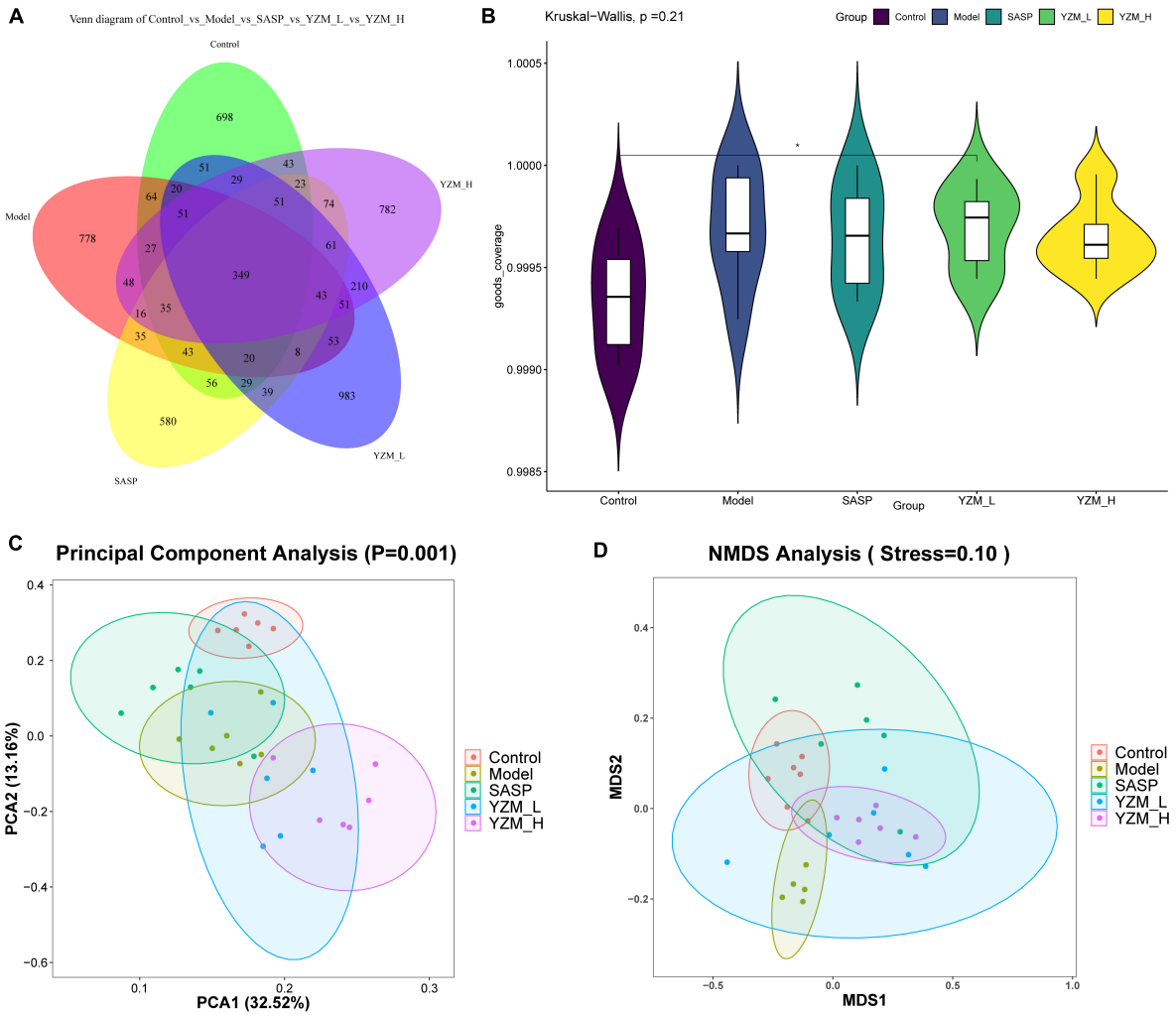

FIGURE 4 | Effects of YZM on intestinal microbiota. **(A)** The cluster analysis. **(B)** The alpha diversity, **(C)** PCA. **(D)** NMDS. *$p < 0.05$ vs. model.

Furthermore, human clinical trials of resveratrol indicated that it improves the quality of life in patients with IBD by lowering inflammation and oxidative stress (25). Increasing evidence demonstrates that flavonoids play a critical role against IBD by modulating the gut microbiota and the metabolites (13, 26). Further studies provided an adequate theoretical basis for the anti-IBD effect of YZM. It is the first time demonstrating that *Polygonatum odoratum* could be a potential treatment for colitis. Our present results suggested that YZM, the methanol extract from *Polygonatum odoratum*, could remarkably improve colon shortening, body weight reduction, and decreased DAI score in colitis mice. H&E staining indicated that the intestinal tissue of the YZM group was similar to the control group. YZM could improve the integrity of the intestinal epithelium layer and prevent mucosal damage in DSS-induced mice. Our study lays the groundwork for developing the *Polygonatum odoratum*, a new treat from nature food and traditional Chinese medicine. In addition, an in-depth research is being developed in our laboratory.

Subsequently, we demonstrated that YZM efficiently influenced gut gas production, SCFAs synthesis, and gut microbiota composition.

The gases generated from the gut are becoming increasingly intrigued. Various gases, including H_2, CH_4, CO_2, H_2S, and NH_3, work as the modulator of human health. In the gut, these gases are generated via the metabolic actions of resident microbiota in the colon. CO_2 is the main product of gut microbiota and is rapidly excreted via breath, whereas it is a noble gas with volume-related mechanical stimuli (27). H_2 is the major gas marker of carbohydrate fermentation, which is used to diagnose poor carbohydrate absorption. Studies are highlighting emerging links between H_2 and *Ruminococcus* spp., but it is still inconclusive (28, 29). CH_4 is generated from the metabolism of CO_2 and H_2 by archaea in the colon. The value of the CH_4 profile in the breathing is more controversial than for H_2 in clinical diagnostic tests (29). H_2S is produced during the fermentation of proteins and has toxic impacts at high concentrations in human tissues (29). A high concentration of NH_3 is a precipitating factor causing

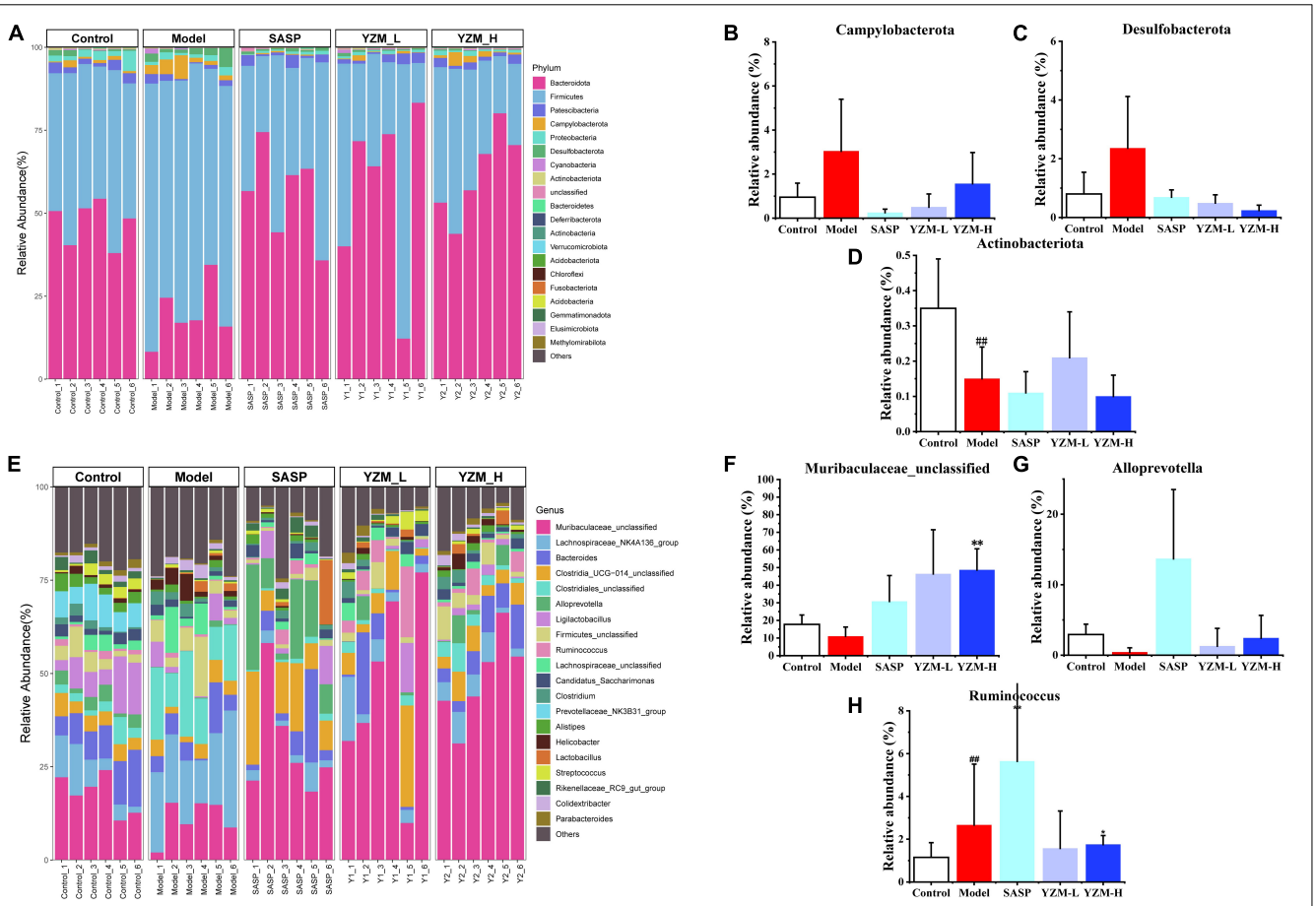

FIGURE 5 | Impacts of YZM at *phylum* and *genus* level. **(A)** The proportion of intestinal microbiota at *phylum* level **(B–D)**. Relative abundance of *Campylobacterota*, *Desulfobacterota*, *Actinobacteriota*. **(E)** The proportion of intestinal microbiota at *genus* level. **(F–H)** Relative abundance of *Muribaculaceae unclassified*, *Alloprevotella*, *Ruminococcus*. $^{\#\#}p < 0.01$ vs. control; $^{**}p < 0.01$ vs. model, $^{*}p < 0.05$ vs. model.

hepatic encephalopathy. After fermentation, the production of H_2S and NH_3 was inhibited considerably. The production of H_2S and NH_3 was significantly inhibited in YZM groups; this may be because YZM inhibited the gas-producing bacteria or modulated the microbiome composition, which inhibited the H_2S and NH_3 production in samples. An increase in the *Desulfobacterota* phylum has been associated with rising toxins production and bacterial genes attached to virulence agents (30). Interestingly, *Desulfobacterota* phylum's abundance was dramatically decreased in YZM-treated compared with the model group. It is similar to H_2S production. YZM may contribute to the decrease of H_2S by reducing the abundance of bacteria that produce H_2S.

Polygonatum odoratum on recovered the production of SCFAs in colitis mice. SCFAs are the main metabolites produced by gut microbiome fermentation and have anti-inflammatory properties and immunomodulatory effects. For the reasons mentioned above, SCFAs are critical in maintaining colon health. Studies showed that low concentrations of SCFAs were observed in colitis mice (31). In this study, the contents of measured SCFAs in model mice showed a decrease compared to control group mice. On the other hand, the high dose of YZM administration dramatically increased valeric and acetic acids. Our results suggested that YZM reversed the abundance of beneficial symbiotic and SCFA-related bacteria, such as *Muribaculaceae* (32), *Ruminococcus* (33), and *Alloprevotella* (34). The changes in SCFA-related bacteria caused by YZM might contribute to and restore SCFAs and ameliorate DSS-induced colitis.

Dextran sulfate sodium-treated mice were usually associated with the changes in the gut microbial composition as the increase in the pernicious microbe and the decrease in beneficial microorganisms (3). Our results indicated a large shift in the microbial community and changes in abundance or dominance of microbial groups under YZM treatments. *Campylobacter jejuni* disorder the protective toll-like receptor 9 (TLR9) signaling in intestinal epithelial cells and aggravated colitis in mice treated with DSS (35). *Desulfobacterota*, as a toxin bacteria, can accelerate the generation of inflammatory factors and exacerbations of colitis (30). YZM observably restored the microbiota composition by modulating phylum *Campylobacterota*, *Desulfobacterota,* and *Actinobacteriota* in DSS-treated mice. The results suggest that the *Actinobacteria* changed with YZM administration compared to the model

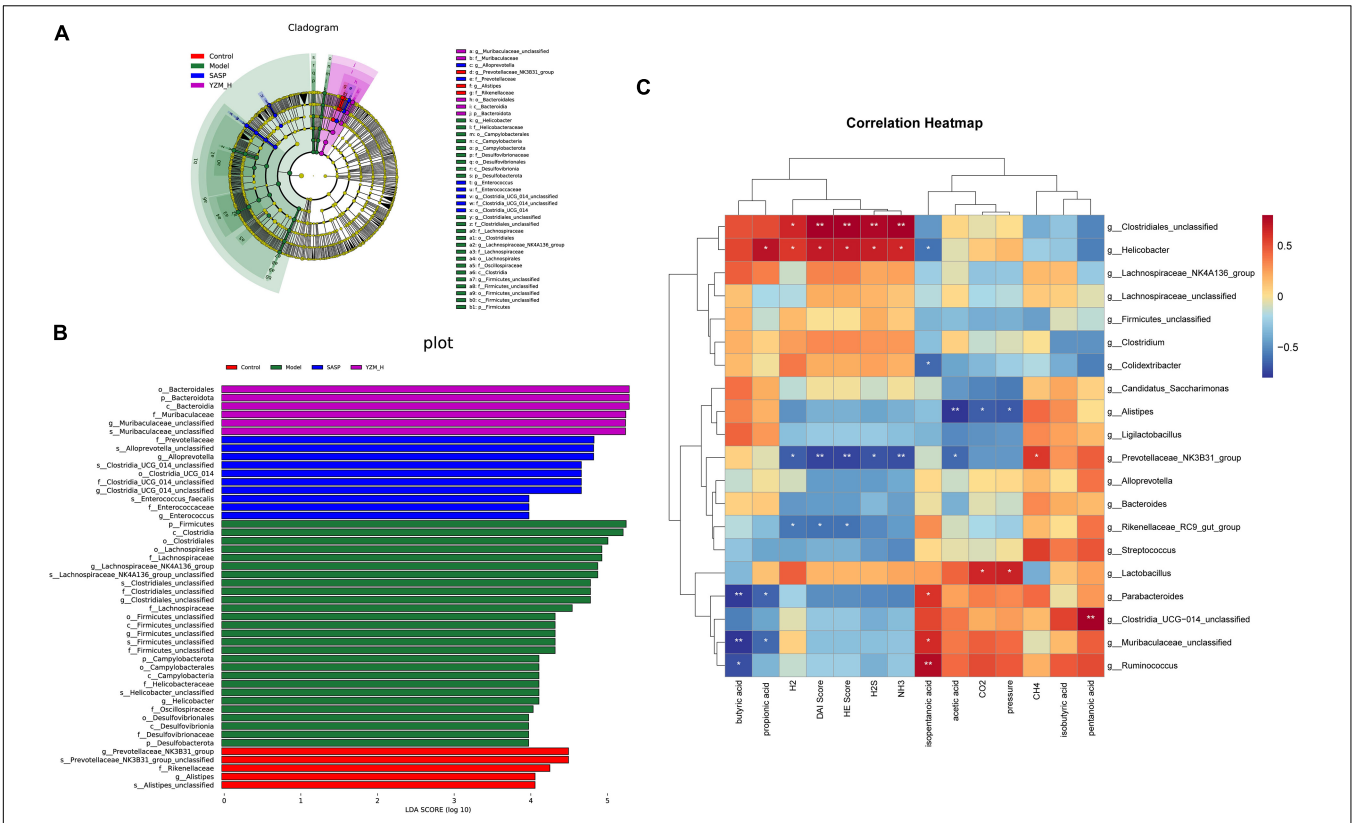

FIGURE 6 | LEfSe analysis and correlation analysis. **(A)** LEfSe analysis. **(B)** LDA scores (LDA) >4, $p < 0.05$. **(C)** Heatmap of Pearson correlation analysis, Red-white-blue color: positive correlation-no correlation-negative correlation. $^{**}p < 0.01$, $^{*}p < 0.05$.

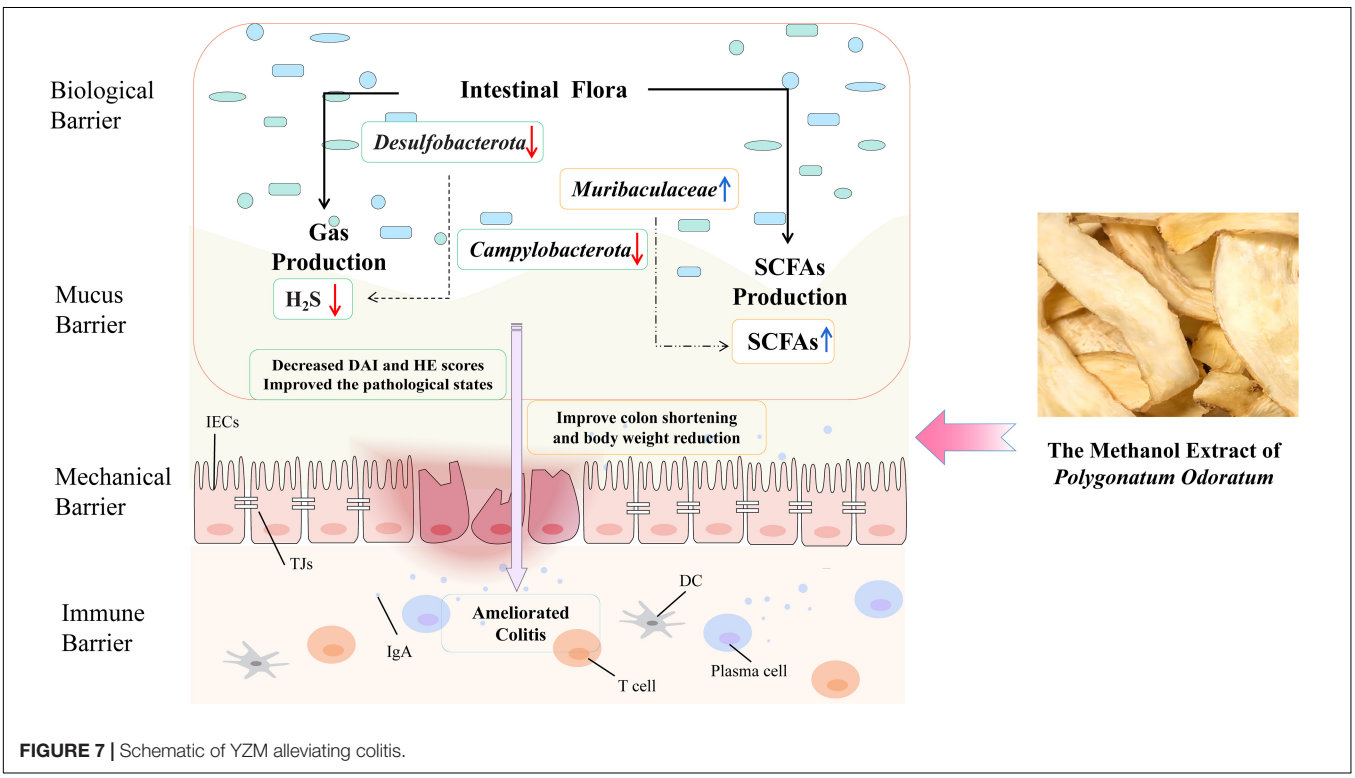

FIGURE 7 | Schematic of YZM alleviating colitis.

group (36, 37). Similarly, *Actinobacteria* was raised sharply after the colitis-associated colon cancer mice were replenished with probiotics. Meanwhile, *Muribaculaceae* was related to SCFAs to tolerate immunity stimulation (38). YZM also could increase the abundance of *Muribaculaceae*. *Clostridiales* contributed to the enhanced colitis severity in chronic colitis observed in mice, and in our experiment (39), it also can increase the production of harmful gases (H_2S and NH_3). *Prevotellaceae* of the gut can degrade polysaccharides and high carbohydrates and benefit the disease status (40, 41). It is similar to our results, which could reverse the production of harmful gases. Altogether, we had shown that YZM evidently could alleviate colitis via reversed intestinal microbiota disorder in colitis mice.

Taken together, we found that *Polygonatum odoratum* might be a multi-targeted resource as food and medicine, for protecting against IBD (**Figure 7**). YZM ameliorates colonic pathological damage to relieve inflammation injure. Moreover, YZM has a modulation affection on the gut microbiome community to decrease the maleficent bacteria associated with gas production (H_2S and NH_3). On the other hand, it improved the intestinal microbiota's composition and metabolites (such as SCFAs) to benefit the gut.

In summary, the methanol extract of *Polygonatum odoratum* (YZM), a plant resource used in food and medicine, was confirmed to alleviate mice colitis and is considered a novel intestinal microecological modifier with bright development prospects. The complex mechanism of YZM regulatory modulation of the intestinal immune response through microbiota needs further study.

DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/**Supplementary Material**, further inquiries can be directed to the corresponding authors. All consensus sequence data of mice were submitted to the National Center for Biotechnology Information Short Read Archive under accession no. PRJNA817426.

ETHICS STATEMENT

The animal study was reviewed and approved by the Ethics Committee of Zhejiang Academy of Agricultural Sciences (No. 2021ZAASLA82). Written informed consent was obtained from the owners for the participation of their animals in this study.

AUTHOR CONTRIBUTIONS

LL, XY, and WL contributed to the study design. XY, XP, WZ, YC, and JN conducted animal experiments. KW and LX analyzed the samples and data. All authors contributed to the article, read, and approved the submitted version.

FUNDING

This work was supported by the National Key Research and Development Program of China (2018YFC2000500), start-up funds from Zhejiang Shuren University (2018R006), National Innovation and Entrepreneurship Program for College Students (202011842025), Zhejiang Public Welfare Project (LGN22C030008), and Hangzhou Agricultural and Society Development Project (202004A20).

SUPPLEMENTARY MATERIAL

The Supplementary Material for this article can be found online at: https://www.frontiersin.org/articles/10.3389/fnut.2022.899421/full#supplementary-material

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