Pharmacology Mechanism of Polygonum Bistorta in Treating Ulcerative Colitis Based on Network Pharmacology

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Aim. Ulcerative colitis (UC) is a refractory gastrointestinal disease. The study aimed to expound the mechanism of Polygonum bistorta (PB) in treating UC by network pharmacology, molecular docking, and experiment verification. Methods. The compositions and targets of PB and UC-associated targets were obtained by searching the websites and the literature. The potential mechanism of PB in the treatment of UC was predicted by protein-protein interaction network construction, Gene Ontology (GO), and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. Molecule docking was performed by AutoDock. In vitro experiments explored the mechanism of quercetin (Que), the main active composition of PB, in treating UC. Results. Six compositions, 139 PB targets, and 934 UC-associated targets were obtained. 93 overlapping targets between PB and UC were identified, and 18 of them were the core targets. 467 biological processes, 10 cell components, and 30 molecular functions were obtained by GO analysis. 102 pathways were enriched through KEGG analysis. Among them, the IL-17 signaling pathway had high importance. The core targets FOS, JUN, IL-1β, CCL2, CXCL8, and MMP9 could dock with Que successfully. Act1, TRAF6, FOS, and JUN were identified by KEGG as the key proteins of the IL-17 signaling pathway. The expressions of the abovementioned proteins were increased in Caco-2 cells stimulated by Dextran sulfate sodium and decreased after being treated by Que. Conclusion. PB might treat UC by downregulating the IL-17 signaling pathway. It is worth doing further research on PB treating UC in vivo.

1. Background

Ulcerative colitis (UC) is a chronic inflammatory disease of the colon [1] and is characterized by abdominal pain, bloody diarrhea, the passage of mucus, and tenesmus [2]. The extraintestinal organs, including the eyes, mouth, skin, joints, and liver, can be involved in the progression of UC [3–6]. Patients with UC have impaired colorectal function, poor quality of life [7], an increased risk of colon cancer [8], and a higher economic burden [9]. UC is more popular in western countries than in other countries and areas of the world [10–12]. However, the incidence of UC has increased gradually in Asia, the Middle East, and South America in the last two decades [13–16].

5-aminosalicylic acid preparations, corticosteroids, immunosuppressants, biological agents, and small-molecule medications [2, 10] are the main medications used to treat UC. However, due to the side effects, primary failure, or secondary failure of the medications, a proportion of UC patients lack effective treatment [17, 18]. Therefore, it is necessary to develop new medications for UC. There is increasing evidence to support that Chinese herbal medicine can be effective in UC treatment [19–23]. Therefore, Chinese herbal medicines may be a potential source for developing new medications for UC. Polygonum bistorta (PB) is a member of the genus Polygonaceae [24]. In ancient China, it was used to treat dysentery, diarrhea, and hematochezia, which were similar to the symptoms of UC. The
pharmacological studies have shown that PB can inhibit inflammation by reducing the release of proinflammatory cytokines [24] such as interleukin-1β (IL-1β) and tumor necrosis factor-α (TNF-α), which are involved in the inflammation of UC [25–27]. Quercetin (Que), one of the main active compositions of PB, can inhibit inflammation by reducing the release of reactive oxygen species and myeloperoxidase from human neutrophils [28]. Therefore, it is speculated that PB may be effective on UC, and direct evidence from the experiments and the clinical trials is needed.

Andrew L. Hopkins, a pharmacologist at Dundee University, proposed the concept of network pharmacology in 2007. Network pharmacology elucidates the occurrence and the development of diseases from the perspectives of systems biology and biological network balance, understands the interactions between the medications and the body from the holistic perspective of improving or restoring biological network balance, and guides drug discovery. It can effectively screen the bioactive compositions and the potential targets and has an advantage in analyzing the mechanisms of Chinese herbal medicine with multicompositions and multitargets [29]. Therefore, network pharmacology is suitable for developing medications for multifactor and multigene-mediated diseases. Although the pathogenesis of UC has not been clearly elucidated, UC is considered to be caused by the interaction of multiple factors, including genetic susceptibility, immune abnormalities, enteric flora disturbances, and environmental factors [30–32].

In our study, the potential targets and the signaling pathways of PB in treating UC were searched and identified with network pharmacology, molecular docking, and in vitro experiments in order to provide the foundation for conducting animal experiments on treating UC with PB. The workflow of this study is summarized in Figure 1.

2. Materials and Methods
2.1. Network Pharmacology

2.1.1. Screening the Bioactive Compositions and the Potential Targets of PB. The compositions of PB were searched in the Traditional Chinese Medicine Systems Pharmacology Database (TCMSP, https://lsp.nwu.edu.cn/tcmsp.php) [33], the Chinese Network Knowledge Infrastructure (CNKI, https://www.cnki.net/), and PubMed with the keyword Polygonum bistorta. A composition from TCMSP with oral utilization (OB) ≥30% and drug-likeness (DL) ≥0.18 [33] or a composition from CNKI or PubMed with an OB degree of HIGH and at least two terms of DL being YES is defined as having pharmacokinetic activity. The chemical structures of the bioactive compositions were obtained from TCMSP and PubChem (https://pubchem.ncbi.nlm.nih.gov/) [34], then imported into Swiss Target Prediction (https://www.swistargetprediction.ch/) [35] to obtain the potential target proteins. The gene names of the target proteins were obtained from the reviewed human genes in the UniProt Knowledgebase (UniprotKB, https://www.uniprot.org/) [36].

2.1.2. Screening the Target Genes Associated with UC. The UC-associated target genes were searched in GeneCards (https://www.genecards.org/) [37], Online Mendelian Inheritance in Man (OMIM, https://www.omim.org/) [38], Pharmacogenetics and Pharmacogenomics Knowledge Base (PharmGkb, https://www.pharmgkb.org/) [39], Therapeutic target database (TTD, https://dirdblab.org/ttd/) [40], DrugBank (https://www.drugbank.ca/) [41], CNKI, and PubMed with the keyword “ulcerative colitis.”

2.1.3. Identifying the Overlapping Targets of PB and UC. The overlapping targets of PB and UC were identified by importing the targets of PB and UC into the Bioinformatics website (https://www.bioinformatics.com.cn/).

2.1.4. Constructing Protein-Protein Interaction (PPI) Network. The overlapping targets of PB and UC were analyzed by the Search Tool for the Retrieval of Interacting Genes (STRING, https://www.string-db.org/) [42] to construct a PPI network. The species were set as “Homo sapiens.” Cytoscape [43] software was used for visualization. The target whose degree was more than 2 times the median was defined as the core target.

2.1.5. GO and KEGG Pathway Enrichment Analysis. The metascape system (https://metascape.org/) [44] was utilized for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis. The P value was set to less than 0.01.

2.1.6. Constructing PB-Composition-Target-Pathway Network. The bioactive compositions of PB and the corresponding targets and signaling pathways were imported into the Bioinformatics website, and the PB-composition-target pathway network was formed automatically.

2.2. Molecular Docking. The chemical structures of bioactive compositions were processed with ChemOffice software for energy minimization. The protein structures of the core targets were obtained from the RCSB protein database (RCSB PDB, https://www.pdb.org/) and optimized by PyMOL software for ligand extraction, water extraction, and hydrogenation. The molecule docking of bioactive compositions and target proteins was performed by AutoDock Vina 1.1.2 software [45]. The results were visualized by PyMOL software.

2.3. Experiment Verification

2.3.1. Antibodies and Reagents. The antibody against Act1/ TRAF3IP2 (lot: 26692-1-AP) was purchased from Pro- teintech (USA). The antibodies against TRAF6 (lot: bs-2830R), c-FOS (lot: bs-23042R), and c-JUN (lot: bs-0670R) were purchased from Bioss (China). The goat anti-rabbit IgG Alexa Fluor 488 (lot: A0423) was purchased from Beyotime (China). The Que (lot: 211208) was purchased from
Winherb Medical Technology (China). The dextran sulfate sodium (DSS, lot: SR01606) was purchased from MP Biomedicals (USA). The cell counting kit-8 (CCK8, lot: CK04) was purchased from DojinDo (Japan). The Dulbecco’s Modified Eagle’s Medium (DMEM, lot: 8121622) was purchased from Thermofisher (USA). The fetal bovine serum (FBS, lot: C0235) and penicillin-streptomycin (P-S, lot: C0222) were purchased from Beyotime (China).

2.3.2. Cells. Caco-2 cells were provided by the Shanghai Institutes for Biological Sciences and cultured in DMEM containing 20% FBS and 1% P-S.

2.3.3. Defining the Safe Intervening Concentration of Que for Caco-2 Cells. Caco-2 cells were divided into 7 groups and cultured in the medium free of Que and the medium containing 5, 10, 20, 40, 80, and 160 μmol/l Que for 24 h, respectively. The cell proliferation rate of each group was measured by the CCK8 assay. The safe intervening concentration of Que was defined by the results of the cell proliferation rates.

2.3.4. Defining the Optimal Intervening Concentration of Que for Caco-2 Cells. Caco-2 cells were divided into the control group, the model group, and 5 Que intervention groups with different concentrations. Except for the control group, Caco-2 cells were stimulated with 10% DSS [46] for 24 h to promote the expression of Act1 in the interleukin-17 (IL-17) signaling pathway. Then, the cells were treated with 5, 10, 20, 40, and 80 μmol/l Que for 24 h, respectively, and the expression of Act1 in each group was detected by immunofluorescence staining (IF) to define the optimal intervening concentration.

2.3.5. Observing the Effect of Que on the Expressions of TRAF6, FOS, and JUN. Caco-2 cells were divided into the control group, the model group, and the Que intervention group. The model group and Que intervention group were stimulated with DSS for 24 h. Afterwards, the intervention group was treated with the optimal intervening concentration of Que for 24 h. The expressions of TRAF6, FOS, and JUN downstream of Act1 were detected by IF.

3. Results

3.1. Network Pharmacology

3.1.1. Compositions and Target Proteins of PB. Six bioactive compositions and 139 corresponding target proteins are obtained and listed in Table 1 and Table S1, respectively. The other compositions without bioactivity are listed in Table S2.

3.1.2. UC Associated Target Genes. 3,235 UC-associated target genes were collected by GeneCards. The higher the relevance score, the more closely the target gene is associated with UC. We screened the target genes according to the criteria that the relevance score was no less than 2 times the median score, and 804 target genes were obtained. The numbers of the target genes obtained from the other websites were 118 (OMIM), 72 (Drugbank), 50 (TTD), and 15 (PharmGkb), respectively. Finally, 934 targets were obtained after removing the repetition (Figure 2, Table S3).
3.1.3. Overlapping Targets of PB and UC. There were 93 overlapping targets between PB and UC (Figure 3, Table S4) for further analysis.

3.1.4. PPI Network of the Overlapping Targets of PB and UC. The PPI network was constructed by importing the overlapping targets of PB and UC into the STRING website with species set as “Homo sapiens.” The visualization was performed by Cytoscape software. In the PPI network, the core and the extending targets were represented by the nodes, and the connection between the genes was represented by the edges. There were 93 nodes (Figures 3 and 4; Table S4) and 1550 edges (Figure 4) in this network. There were 42 targets whose degree was higher than the median (Figures 3 and 5). Among them, there were 18 core targets whose degree was more than 2 times the median (Figures 5–7, Table 2). There were 153 edges in the network of the core targets (Figure 4).

3.1.5. GO and KEGG Pathway Enrichment Analysis. The biological functions and pathways enriched through GO and KEGG analysis of the core targets could be the potential intervening targets of the newly developing medication.

GO analysis includes a biological process (BP), a cell component (CC), and a molecular function (MF). 467 BP-related functions suggested that these core targets were associated with the inflammatory response, cytokine production, and the response of cells to cytokine stimulation \((P < 0.01,\ \text{Figure 8})\). 30 CC related functions revealed that the targets could respond to the transcription regular complex, transcription repressor complex, nuclear envelope, membrane microdomain, and so on \((P < 0.01,\ \text{Figure 8})\). 30 MF-related functions showed that the targets might have the following functions: cytokine activity, cytokine receptor binding, transcription factor binding, and ubiquitin protein ligase binding \((P < 0.01,\ \text{Figure 8})\). 102 pathways were

<table>
<thead>
<tr>
<th>MOL IDs</th>
<th>Molecule names</th>
<th>Structures</th>
<th>OB (%)</th>
<th>DL</th>
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<td>MOL000492</td>
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<td>0.24</td>
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<tr>
<td>MOL000098</td>
<td>Quercetin</td>
<td><img src="image2.png" alt="image" /></td>
<td>46.43</td>
<td>0.28</td>
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<tr>
<td>MOL001002</td>
<td>Ellagic acid</td>
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<td>0.43</td>
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<tr>
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<td>ZINC04073977</td>
<td><img src="image4.png" alt="image" /></td>
<td>38</td>
<td>0.76</td>
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<tr>
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<td>0.75</td>
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<tr>
<td>MOL000358</td>
<td>Beta-sitosterol</td>
<td><img src="image6.png" alt="image" /></td>
<td>36.91</td>
<td>0.75</td>
</tr>
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</table>

4 Evidence-Based Complementary and Alternative Medicine
enriched through KEGG analysis, such as the IL-17 signaling pathway, the colorectal cancer pathway, the TNF signaling pathway, and the nuclear factor kappa-B (NF-κB) signaling pathway \((P < 0.01, \text{Figure 9})\). These pathways were provided with an enrichment score and \(P\) value. The higher the enrichment score and the lower \(P\) value of the pathway are, the
higher its importance is. The enrichment score of the IL-17 signaling pathway was higher, but its $P$ value was lower than those of many other pathways. It suggested that the IL-17 signaling pathway might play an important role in the pharmacology mechanism of PB. Then, we searched the IL-17 signaling pathway diagram through KEGG (Figure 10), and the interaction between several proteins of the IL-17 signaling pathway was identified by the STRING website (Figure 11). The following targets were the overlapping parts of the core targets and IL-17 pathways: FOS and JUN (the main members of activator protein 1 (AP-1)) [47, 48], IL-1$\beta$, MMP9, CXCL8 and CCL2.

3.1.6. PB-Composition-Target-Pathway Network. The compositions and targets obtained by TC MSP and Swiss Target Prediction and the targets and pathways enriched through KEGG were integrated (Table S5). All the information was imported into the Bioinformatics website to build the PB-component-pathway network (Figure 12). Among the bioactive compositions of PB, quercetin (Que) played the most important role in intervening at the overlapping targets of PB and UC. It could intervene in the IL-17 signaling pathway through core targets such as FOS, JUN, IL-1$\beta$, MMP9, CXCL8, and CCL2.

![Figure 4: The PPI network of the overlapping targets of PB and UC.](image)

![Figure 5: The targets with degree higher than the median (the degree of the yellow targets was more than 2 times of the median).](image)
3.2. Molecular Docking. The targets of FOS, JUN, IL-1β, CCL2, CXCL8, and MMP9 in the IL-17 signaling pathway were successfully docked with the bioactive compositions of PB. The active pocket is the area where the medication binds to the protein. The active pockets of the above targets are shown in Figure 13. The binding energy represents the affinity between the targets and the compositions [49, 50]. When the binding energy was negative, stable docking could be achieved. The binding energy of FOS (RCSB PDB: 2WT7), JUN (RCSB PDB: 1JUN), IL-1β (RCSB PDB: 5R8Q), MMP9 (RCSB PDB: 1ITV), CXCL8 (RCSB PDB: 2L8), CCL2 (RCSB PDB: 1DON), and Que were −5.4, −5.5, −5.9, −7.2, −7.8, and −7.2 kcal·mol⁻¹, respectively. The binding energies of FOS, JUN, and (+)-catechin were −5.1 and −5.1 kcal·mol⁻¹, respectively (Table 3). Molecular docking sites, hydrogen bond lengths, and amino acid residues of PB compositions and proteins are shown in Figure 14.

3.3. Experiment Verification. As shown in Figures 11 and 12, IL-17A, B, C, E, and F can bind to Act1/TRAF3IP2 and TRAF6 through different IL-17 receptors (IL-17RA, B, C, and E) and further regulate AP-1(Fos/Jun) to promote the release of proinflammatory cytokines and chemokines. DSS can induce colitis in mice [51–53] and rats [54–56]. The expressions of Act1/TRAF6/FOS/JUN of the IL-17 signaling pathway in Caco-2 cells were increased after being stimulated with DSS in our experiment. Que is the main active composition of PB according to the results of network pharmacology and molecular docking. It may act on the proteins in the IL-17 signaling pathway. Therefore, we further observed the effect of Que on the IL-17 signaling pathway.

The CCK8 assay showed that the maximum non-cytotoxic concentration of Que was 80 μmol/l (Figure 15). Act1 expression was used as the effect indicator to determine the optimal intervention concentration of Que in the IL-17 signaling pathway. 10 μmol/l Que could maximally reduce Act1 expression in Caco-2 cells stimulated by DSS (Figures 16(a) and 16(e)). Therefore, 10 μmol/l was used as the optimal concentration of Que to intervene in the expressions of the downstream proteins (TRAF6, FOS, and JUN) in the IL-17 signaling pathway. 10 μmol/l Que could also effectively reduce the expressions of TRAF6 (Figures 16(b) and 16(f)), FOS (Figures 16(c) and 16(g)), and JUN (Figures 16(d) and 16(h)) in Caco-2 cells stimulated by DSS.
<table>
<thead>
<tr>
<th>Gene names</th>
<th>Protein name</th>
<th>UniProt ID</th>
<th>Degree</th>
<th>Compositions of PB</th>
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<tr>
<td>MMP2</td>
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<td>50</td>
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<td>MMP9</td>
<td>Matrix metalloproteinase-9</td>
<td>P14780</td>
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<td>Quercetin, ellagic acid</td>
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<tr>
<td>NFKB1A</td>
<td>NF-kappa-B inhibitor alpha</td>
<td>P25963</td>
<td>48</td>
<td>Quercetin, ellagic acid</td>
</tr>
<tr>
<td>CXCL8</td>
<td>Ubiquitin carboxyl-terminal hydrolase 17</td>
<td>Q6R6M4</td>
<td>60</td>
<td>Quercetin, ellagic acid</td>
</tr>
<tr>
<td>PTGS2</td>
<td>Prostaglandin G/H synthase 2</td>
<td>P35354</td>
<td>64</td>
<td>(±)-catechin, quercetin, ellagic acid, ZINC04073977, beta-sitosterol</td>
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<td>JUN</td>
<td>Transcription factor AP-1</td>
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<tr>
<td>CASP3</td>
<td>Caspase-3</td>
<td>P42574</td>
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<td>PPARγ</td>
<td>Peroxisome proliferator-activated receptor gamma</td>
<td>P37231</td>
<td>57</td>
<td>Quercetin, poriferast-5-en-3beta-o, beta-sitosterol</td>
</tr>
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<td>EGFR</td>
<td>Epidermal growth factor receptor</td>
<td>P00533</td>
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<td>AKT1</td>
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<td>Proto-oncogene-Fos</td>
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<td>TP53</td>
<td>Cellular tumor antigen p53</td>
<td>P04637</td>
<td>75</td>
<td>Quercetin</td>
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<td>HIF1A</td>
<td>Hypoxia-inducible factor 1-alpha</td>
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<td>MYC</td>
<td>Myc proto-oncogene protein</td>
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<td>C-C motif chemokine 2</td>
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<td>55</td>
<td>Quercetin</td>
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</table>
**Figure 8:** The results of GO analysis.

**Figure 9:** The results of KEGG analysis.
4. Discussion

The immune inflammatory response is crucial in the pathogenesis of UC. Some proinflammatory factors released in immune inflammation are closely related to intestinal mucosal injury [57]. IL-17 is a proinflammatory factor and plays an important role in the pathogenesis of various autoimmune diseases [58, 59]. The IL-17 cytokine family consists of IL-17A (usually called IL-17), IL-17B, IL-17C, IL-17D, IL-17E (also called IL-25), and IL-17F [60]. The IL-17 receptor family consists of IL-17RA, IL-17RB, IL-17RC, IL-17RD, and IL-17RE [60]. Among the proteins of the IL-17 signaling pathway, NF-κB activator 1 (Act1/TRA2IP2) [61, 62], tumor necrosis factor receptor-associated factor 6 (TRAF6) [63], and AP-1 play important roles. After IL-17 combines with IL-17R, IL-17R binds to Act1 through a domain called similar expression to fibroblast growth factor genes and IL-17Rs (SEFIR) [62, 64, 65]. Then, Act1 binds to TRAF6 and activates the signaling pathway of MAPK/AP-1 to stimulate the secretion of proinflammatory cytokines and enhance the inflammatory response [60, 66–76]. MAPK family includes extracellular signal-regulated kinase (ERK) [77], Jun N-terminal kinases (JNK) [78], and p38 MAPK [79] and can activate and regulate AP-1. AP-1, which is mainly composed of FOS and JUN protein family members, plays a major role in cell inflammation, proliferation, and apoptosis [80]. It can increase the expression of proinflammatory cytokines such as IL-1β, IL-6, and TNF-α [81].

Many studies have confirmed that the IL-17 signaling pathway is involved in the pathogenesis of UC [82–84]. Nanki et al. found that the IL-17 signaling pathway was
activated in colonic epithelial cells of UC patients, and the expressions of downstream target genes ACT1, NF-kB, PIGR, CXCL1, and LCN2 were increased [82]. Zhang et al. compared the serum levels of IL-17, IL-17R, and CRP in the colonic mucosa of 36 UC patients with those of 60 healthy controls [83]. The results showed that the serum levels of IL-17 in UC patients were significantly higher than those in healthy controls. Besides, the levels of IL-17 in active UC patients were higher than those of patients in remission and were correlated with CRP levels. The mRNA expression of IL-17R in the colonic mucosa of patients with active UC was also higher than that in healthy controls. Zhou et al. confirmed that IL-17A, IL-17RA, Act1, p-ERK, p-JNK, p-p38, and other proteins in the IL-17 signaling pathway were involved in the pathogenesis of UC in HT29 cells and DSS-induced colitis mice [84]. The expressions of these proteins in the model group were higher than those in the control group. After TCM intervention, the inflammation of the colon mucosa was alleviated, and the levels of the above signaling proteins were also decreased. These studies suggested that the IL-17 signaling pathway might be involved in the pathogenesis of UC and be related to disease activity. Therefore, it may be a potential target for treating UC.

In our study, GO and KEGG enrichment analysis showed that intervention of the cytokines and regulation of the inflammatory response might be the mechanism of PB in the treatment of UC. Among the inflammation-related pathways enriched by KEGG, the importance of the IL-17 signaling pathway was high. The core targets FOS, JUN, IL-1β, MMP9, CXCL8, and CCL2 were all involved in the IL-17
Figure 13: The active pockets of the targets.

Table 3: Molecules docking information between compositions and targets.

<table>
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<tr>
<th>Compositions</th>
<th>Core targets</th>
<th>PDB</th>
<th>Degree</th>
<th>Binding energy (kcal mol$^{-1}$)</th>
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<tr>
<td>Quercetin</td>
<td>FOS</td>
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<td>(++)-catechin</td>
<td>FOS</td>
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<td>-5.1</td>
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<td>Quercetin</td>
<td>JUN</td>
<td>1JUN</td>
<td>67</td>
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<td>Quercetin</td>
<td>IL1β</td>
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Figure 14: The molecular docking information. (a) 2WT7-Que. (b) 1JUN-Que. (c) 2WT7- (++)-catechin. (d) 1JUN- (++)-catechin. (e) 5R8Q-Que. (f) 1ITV- Que. (g) 2IL8-Que. (h) 1DON-Que.
**Figure 15:** The safe intervening concentration of Que of Caco2 cells. Compared to the control group, $$***P < 0.001.$$
signaling pathway. These targets could successfully dock with the active compositions of PB. Molecular docking is an effective method to verify the binding of natural compounds to the target proteins [49, 50, 85]. The hydrophobic interaction and hydrogen bond interaction between compounds and amino acids of target proteins can promote stable binding [49, 50, 85]. In addition, the active sites assist the compounds to form sufficient contacting points and stably bind to target proteins by maintaining optimal catalytic microenvironments [85]. It was verified in vitro experiments that the expressions of Act1, TRAF6, and AP-1(Fos/Jun) in the IL-17 signaling pathway increased in the cells stimulated by DSS and decreased in Que-treated cells. Therefore, the IL-17 signaling pathway could enhance the inflammatory response and aggravate UC. PB and its main active composition Que could treat UC by inhibiting the IL-17 signaling pathway. The possible mechanism of Que treating UC is shown in Figure 17.

Figure 16: The expressions of the proteins in the IL-17 signaling pathway of Que of Caco2 cells ((a) Act1; (b) TRAF6; (c) FOS; (d) JUN). The average IF intensity of the proteins of each group ((e) Act1; (f) TRAF6; (g) FOS; (h) JUN). Compared to the control group, ***P < 0.001. Compared to the model group, ###P < 0.001.
5. Conclusion

PB has been used to treat diarrhea and hematochezia effectively for hundreds of years in ancient China. It might be a potential source for developing new medications for UC. The results of network pharmacology, molecular docking, and in vitro experiments demonstrated that PB might treat UC via downregulating the IL-17 signaling pathway. It is worth conducting further research on PB treating UC in vivo.

Data Availability

The datasets generated or analyzed during the current study are available from the corresponding author upon reasonable request.

Conflicts of Interest

These authors declare that there are no conflicts of interest.

Authors’ Contributions

Jun Liu contributed to the design of the study, performed network pharmacology, and wrote and edited the manuscript. The in vitro experiments were carried out by Suxian Liu and Hui Cao. Bei Shi and Qiaodong Li contributed to collecting data. Jingyi Shan contributed to the performance of the statistical analysis. Jiang Lin and Jiangye Yuan contributed to the conception of the study and reviewed the manuscript. All authors read and approved the final manuscript.

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Supplementary Materials

Table S1: The potential targets of PB. Table S2: The compositions of PB without bioactivity. Table S3: The UC-associated targets. Table S4: The overlapping targets of PB and UC. Table S5: The information on the PB-composition-target-pathway network. (Supplementary Materials)

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