Research Article

Mechanism of Peitu Shengjin Formula Shenlingbaizhu Powder in Treating Bronchial Asthma and Allergic Colitis through Different Diseases with Simultaneous Treatment Based on Network Pharmacology and Molecular Docking

Liying Zeng,1 Shaodan Sun,2 Peiwen Chen,1 Qina Ye,3 Xiaoling Lin,1 Hongjun Wan,1 Yawen Cai,1 and Xiaogang Chen1,4

1The First Clinical College, Guangzhou University of Chinese Medicine, Guangzhou 510405, Guangdong, China
2The Second Affiliated Hospital, Guangzhou University of Chinese Medicine, Guangzhou 510120, Guangdong, China
3Guangzhou Women and Children Medical Center, Guangzhou 510623, Guangdong, China
4The First Affiliated Hospital, Guangzhou University of Chinese Medicine, Guangzhou 510405, Guangdong, China

Correspondence should be addressed to Xiaogang Chen; chenxiaogang1539@gzucm.edu.cn

Received 7 October 2021; Revised 8 March 2022; Accepted 26 March 2022; Published 9 May 2022

Academic Editor: San Jun Shi

Copyright © 2022 Liying Zeng et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Background. Shenlingbaizhu powder (SLBZP), one of the classic Earth-cultivating and gold-generating prescriptions of traditional Chinese medicine, is widely used to treat various diseases. However, the pharmacological mechanisms of SLBZP on bronchial asthma (BA) and allergic colitis (AC) remain to be elucidated. Methods. Network pharmacology and molecular docking technology were used to explore the potential mechanism of SLBZP in treating BA and AC with the simultaneous treatment of different diseases. The potential active compounds of SLBZP and their corresponding targets were obtained from BATMAN-TCM, ETCM, SymMap@TAIWAN, and TCMSP databases. BA and AC disease targets were collected through DisGeNET, TTD, GeneCards, PharmGKB, OMIM, NCBI, and the Human Phenotype Ontology, and DrugBank databases. Common targets for drugs and diseases were screened by using the bioinformatics and evolutionary genomics platform. The analyses and visualizations of Gene Ontology (GO) function and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment of common targets were carried out by R software. The key targets were screened by using the plug-in “cytoHubba” of Cytoscape software, and the “active compound-key target” network was constructed. Molecular docking analysis was performed using AutoDock software. The miRTarBase database was used to predict microRNAs (miRNAs) targeting key targets, and the key target-miRNA network was constructed. Result. Through screening, 246 active compounds and 281 corresponding targets were obtained. Common targets were mainly enriched in 2933 biological processes and 182 signal pathways to play the role of treating BA and AC. There were 131 active compounds related to key targets. The results of molecular docking showed that the important active compounds in SLBZP had good binding ability with the key targets. The key target-miRNA network showed that 94 miRNAs were predicted. Conclusion. SLBZP has played the role of treating different diseases with the same treatment on BA and AC through the characteristics of multicomponent, multitarget, and multipathway of traditional Chinese medicine, which provides a theoretical basis for explaining the mechanism and clinical application of SLBZP treating different diseases with the same treatment in BA and AC.

1. Introduction

Asthma generally refers to bronchial asthma (BA). BA, one of the most common chronic noncommunicable diseases in children and adults, is characterized by variable respiratory symptoms and variable airflow limitation, which is the result of complex gene-environment interactions, and is heterogeneous in clinical manifestations and the type and intensity of airway inflammation and remodeling [1]. The goal of BA treatment is to achieve good asthma control, that is, to
minimize the burden of symptoms and the risk of deterioration [2]. However, asthma attacks and hospitalizations are frequent, and the mortality rate remains high. Strategies need to be developed to change the natural history of BA and prevent serious deterioration and the decline of lung function [1]. Allergic colitis (AC), an inflammatory disease, is characterized by the infiltration of eosinophils into the colon wall and the presence of red blood in the stool of healthy breast-fed or formula-fed infants, which usually develops in the first few weeks or months of life and can be a benign and/or severe disease in infant gastrointestinal diseases [3–4]. To date, the most effective interventions are preventive methods, especially feeding strategies, to reduce the incidence of disease while establishing adequate growth and progression to enteral feeding [5]. However, their pathogenesis has not yet been fully clarified with some allergens unclear or unavoidable, and modern medicine lacks ideal preventive and therapeutic methods [6]. At present, modern medicine adopts allergen avoidance, desensitization, and symptomatic treatment, but some antihistamines and antileukotrienes need to be taken for a long time, which brings certain economic burden and psychological impact to patients and cannot completely cure allergic diseases with some deficiencies, such as side effects of drugs and easy recurrence after withdrawal [7–9]. In recent years, treating allergic diseases with traditional Chinese medicine has been more and more widely used in clinical practice with various methods, remarkable effects, less adverse reactions in long-term application, and good compliance, which is convenient for clinical promotion [10, 11].

Shelingbaizhu powder (SLBZP), from the Prescriptions of Peaceful Benevolent Dispensary and composed of 10 Chinese medicines including renshen (Panax ginseng C. A. Mey.), fuling (Poria cocos (Schw.) Wolf.), baizhu (Atractylodes macrocephala Koidz.), baibian dou (Lablab Semen), shanyao (Rhizoma Dioscoreae), lianzhi (Semen Nelumbinis), yi yiren (Coicis Semen), sharhen (Amomum aurantiacum H. T. Tsai Et S. W. Zhao), jiegeng (Platycodon grandiflorus), and gancao (licorice), has the effects of replenishing qi, strengthening spleen, excreting dampness, and stopping diarrhea [12]. Previous studies have shown that SLBZP can regulate intestinal water metabolism and intestinal flora, inhibit inflammatory response, repair intestinal mucosal barrier, and enhance colonic motility, which is widely used in the clinical treatment of ulcerative colitis, chronic diarrhea, chronic obstructive pulmonary disease, bronchial asthma, diabetes, eczema, allergic rhinitis, etc. [13, 14].

Network pharmacology, targeting biological networks, analyzes the connections between drugs, targets, and diseases in these networks. A comprehensive and systematic research on network pharmacology conforms to a holistic view, which is the main characteristic of many traditional medicines. Studies have shown that many traditional medicines exhibit synergistic effects by acting on multiple targets and pathways at different levels through network pharmacology [15]. This method effectively bridges the gap between modern medicine and traditional medicine and greatly promotes the research on the synergy of traditional medicine. Different diseases with simultaneous treatment means that the same pathogenesis appears in the occurrence and development of different diseases, and the same treatment can be adopted. SLBZP reinforces Earth to generate metal for treating BA and AC, which is in line with the concept of different diseases with simultaneous treatment. This study comprehensively analyzed and explored the mechanism of SLBZP in treating BA and AC with simultaneous treatment of different diseases from compounds, targets, pathways, biological processes, etc., by network pharmacology and molecular docking, which conforms to the overall function of traditional Chinese medicine theory and provides theoretical bases for clarifying the action mechanism of SLBZP on BA and AC and promoting its clinical application (Figure 1).

2. Materials and Methods

2.1. Screening Compounds and Targets of SLBZP. The active compounds of SLBZP were separately obtained from these databases: BATMAN-TCM (http://bionet.ncpsb.org.cn/batman-tcm/index.php/Home/Index/index) [16], ETCM (http://www.tcmip.cn/ETCM/index.php/Home/Index/) [17], SymMap (http://www.symmap.org/) [18] and Traditional Chinese Medicine Database@TAIWAN (http://tc.mcu.edu.tw/review.php?menuid=3) [19]. Then, the active compounds that had good oral bioavailability (OB) and drug similarity (DL) and their targets of SLBZP were screened out under the conditions of OB≥30% and DL≥0.18 by entering the above obtained active compounds into Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP, http://lsp.nwu.edu.cn/tcmsp.php) [20]. Meanwhile, the active compounds and their targets of SLBZP from the TCMSP database were also obtained with OB≥30% and DL≥0.18. Next, all these obtained active compounds were synthesized to remove duplications. The full names of the targets screened by TCMSP were input into the DrugBank database (https://www.drugbank.ca/) [21] and UniProt database (https://www.uniprot.org/?dsourcetag=s_pcq_q_acioms) [22] to get the gene symbol and UniProt ID, which were all standardized and normalized to ensure accuracy.

2.2. Screening Targets of BA and AC. The target genes related to BA were obtained with the keyword “bronchial asthma” and the species set as “Homo sapiens” from these 8 databases: DisGeNET (http://www.disgenet.org/web/DisGeNET/menu/search) [23], TTD (https://db.idri.lab.org/tdt/) [24], GeneCards (https://www.genecards.org) [25], PharmGKB (https://www.pharmgkb.org/) [26], OMIM (https://omim.org/) [27], NCBI (https://www.ncbi.nlm.nih.gov/gene) [28], The Human Phenotype Ontology (https://hpo.jax.org/app/) [29], and DrugBank. The target genes related to AC were obtained with the keyword “allergic colitis” and the species set as “Homo sapiens” from these 5 databases: TTD, GeneCards, PharmGKB, OMIM, and NCBI. The obtained data were combined separately, and then the duplications
were removed. The full name of the last screened target genes were input into the DrugBank database and UniProt database to get the gene symbol and UniProt ID, which were also all standardized and normalized to ensure accuracy.

2.3. Screening of Common Targets. The targets related to active compounds, BA, and AC were matched and mapped by using the bioinformatics and evolutionary genomics platform (http://bioinformatics.psb.ugent.be/webtools/Venn/). At the same time, a Venn diagram was drawn to obtain the common targets of the active compounds of SLBZP for treating BA and AC.

2.4. GO and KEGG Enrichment Analysis of Common Targets. The enrichment analysis and visualization of Gene Ontology (GO) function and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathways were carried out for the common targets of SLBZP in treating BA and AC with the species set as “Homo sapiens” and the threshold set as \( P < 0.05 \) by the "ggplot2", "enrichplot", "clusterProfiler" [30], and "ggpubr" packages of R software (version 3.6.1).

2.5. Construction of Active Compound-Key Target Network. The obtained common targets were imported into Cytoscape software (version 3.8.0; http://www.cytoscape.org) [31], and the “cytoHubba” plug-in was used to screen out the key targets. Then, an active compound-key target network was constructed by Cytoscape software, of which the network topology analysis was carried out by "Network Analysis" in the tool. The network showed the connection between the active compounds and key targets, and the molecular mechanism of SLBZP in treating BA and AC was explored on this basis.

2.6. Molecular Docking Verification. According to the above analysis results, the key target proteins and the important active compounds were molecularly docked. The protein structures of the targets were obtained from the RCSB PDB database (https://www.rcsb.org/) [32]. The 2D structures of the active compounds were obtained from the PubChem database (https://pubchem.ncbi.nlm.nih.gov/) [33] and were optimized to save as 3D structures with Chem3D software. AutoDockTools and AutoDockVina software were used for molecular structure processing and molecular docking. PyMOL and Discovery Studio were used to visualize the docking results.

2.7. Construction of Key Target-microRNA (miRNA) Network. The miR TarBase database (https://mirтарbase.cuhk.edu.cn/%7EminiTarBase/miRTarBase_2019/php/index.php) is used to predict upstream miRNAs targeting key targets [34]. The collected miRNA-mRNA interactions have been verified by different types of experiments including report analyses in miR TarBase, western blot, qPCR, microarray, and next-generation sequencing experiments. In order to make predictions more reliable and accurate, only miRNAs that may interact with the targets were obtained through reporter gene analyses. After selecting “By Target Gene” and the species as “Human”, key targets were entered to predict miRNAs. Then, the key targets and their corresponding predicted miRNAs were organized into an Excel file that was imported into Cytoscape software. Finally, the network of the predicted miRNAs and key targets were constructed by Cytoscape software.

3. Results

3.1. Acquisition of Active Compounds of SLBZP. Preliminarily, a total of 335 active compounds were acquired from the BATMAN-TCM database; a total of 443 active compounds were acquired from the ETCM database; a total
| Code | Molecule ID | Molecule name | OB (%) | DL | Herbs |
|------|-------------|---------------|--------|----|-------|
| P1   | MOL004924   | (-)-Mediocarpin | 40.99  | 0.95 | Gancao |
| P2   | MOL004988   | Kanzonol F    | 32.47  | 0.89 | Gancao |
| P3   | MOL005018   | Xambiona      | 54.85  | 0.87 | Gancao |
| P4   | MOL005458   | Dioscoreside C, qt | 36.38 | 0.87 | Shanyao |
| P5   | MOL007536   | Stigmasa-5, 22-dien-3-beta-y acetate | 46.44 | 0.86 | Sharen |
| P6   | MOL001474   | Sanguinarine   | 37.81  | 0.86 | Sharen |
| P7   | MOL001973   | Sitosterol acetate | 40.39 | 0.85 | Sharen |
| P8   | MOL004948   | Isoglycyrol   | 44.7   | 0.84 | Gancao |
| P9   | MOL008752   | Dihydroverticillatine | 42.69 | 0.84 | Jiegeng |
| P10  | MOL000787   | Fumarine       | 59.26  | 0.83 | Renshen |
| P11  | MOL005357   | Gomisin B     | 31.99  | 0.83 | Renshen |
| P12  | MOL000300   | Dehydroeburicoic acid | (2R)-2-[(5R, 10S, 13R, 14R, 16R, 17R)-6-hydroxy-3-keto-4, 10, 13, 14-pentamethyl-1, 2, 5, 6, 12, 15, 16, 17-octahydrocyclopenta[a]phenanthren-17-y]-5-isopropyl-hex-5-enoic acid | 38.26 | 0.82 | Fuling |
| P13  | MOL00285    | Deoxyharringtonine | 39.27 | 0.81 | Renshen |
| P14  | MOL00276    | Ergosterol peroxide | 40.88 | 0.81 | Fuling |
| P15  | MOL00287    | 3beta-hydroxy-24-methylene-8-lanostane-21-oic acid | 38.7 | 0.81 | Fuling |
| P16  | MOL00276    | 7, 9(11)-Dehydroperoxidic acid | 35.11 | 0.81 | Fuling |
| P17  | MOL00289    | Pachymic acid | 33.63  | 0.81 | Fuling |
| P18  | MOL00546    | Diosgenin     | 80.88  | 0.81 | Shanyao |
| P19  | MOL000275   | Trametenolic acid | 38.71 | 0.80 | Fuling |
| P20  | MOL005376   | Panaxadiol    | 33.09  | 0.79 | Sharen |
| P21  | MOL005401   | Ginsenoside Rg5, qt | 39.56 | 0.79 | Renshen |
| P22  | MOL004971   | Glycosyrol    | 37.25  | 0.79 | Shanyao |
| P23  | MOL000283   | (2R)-2-[(3S,5R,10S,13R,14R,16R,17R)-6-dihydroxy-4, 10, 13, 14-pentamethyl-2, 3, 5, 6, 12, 15, 16, 17-octahydro-1h-cyclopenta[a]phenanthren-17-y]-5-isopropyl-hex-5-enoic acid | 31.07 | 0.78 | Fuling |
| P24  | MOL000280   | (3S,8S,9S,10R,13R,14S,17R)-10,13-dimethyl-17-[2(2R,5S)-5-propan-2-yloctan-2-yl]-2,3,4,7,8,9,11,12,14,15,16,17-dodecahydro-1h-cyclopenta[a]phenanthrene-3, 6-dione | 33.12 | 0.79 | Sharen |
| P25  | MOL005348   | Ginsenoside-Rh4, qt | 31.11 | 0.78 | Renshen |
| P26  | MOL00033    | Perakine      | 82.58  | 0.78 | Fuling |
| P27  | MOL000211   | Mairin        | 55.38  | 0.78 | Gancao |
| P28  | MOL005001   | Gancaolin H   | 50.10  | 0.78 | Gancao |
| P29  | MOL001323   | Sitosterol alpha1 | 43.28 | 0.78 | Yiyiren |
| P30  | MOL000279   | Cerevisterol  | 37.96  | 0.77 | Fuling |
| P31  | MOL005465   | AIDS180907    | 45.33  | 0.77 | Shanyao |
| P32  | MOL000449   | Stigmasterol  | 43.83  | 0.76 | Renshen |
| P33  | MOL000028   | a-Amyrin      | 39.51  | 0.76 | Baizhu |
| P34  | MOL000290   | Poricoic acid A | 30.61 | 0.76 | Fuling |
| P35  | MOL001755   | 24-Ethylcholest-4-en-3-one | 36.08 | 0.76 | Renshen |
| P36  | MOL004355   | Spinasterol   | 42.98  | 0.76 | Jiegeng |
| P37  | MOL004718   | a-Spinasterol | 42.98  | 0.76 | Jiegeng |
| P38  | MOL005440   | Isosucosterol | 43.78  | 0.76 | Shanyao |
| P39  | MOL010625   | 24-Methylenecholesterol | 43.54 | 0.76 | Shanyao |
| P40  | MOL000358   | Beta-sitosterol | 36.91 | 0.75 | Renshen |
| P41  | MOL005399   | Alexynarin, qt | 36.91 | 0.75 | Renshen |
| P42  | MOL001525   | Daucosterol   | 36.91  | 0.75 | Renshen |
| P43  | MOL000296   | Hederagenin   | 36.91  | 0.75 | Fuling |
| P44  | MOL000292   | Poricoic acid C | 38.15 | 0.75 | Fuling |
| P45  | MOL000291   | Poricoic acid B | 30.52 | 0.75 | Fuling |
| P46  | MOL006376   | 7-Dehydroginseng | 37.42 | 0.75 | Fuling |
| P47  | MOL000359   | Sitosterol    | 36.91  | 0.75 | Shanyao |
| P48  | MOL001771   | Pariferast-5-en-3beta-ol | 36.91 | 0.75 | Renshen |
| P49  | MOL013119   | Enhydrin      | 40.56  | 0.74 | Renshen |
Table 1: Continued.

| Code | Molecule ID   | Molecule name                          | OB (%) | DL | Herbs          |
|------|---------------|----------------------------------------|--------|----|----------------|
| P52  | MOL000139     | Smitilbin                              | 37.60  | 0.74 | Renshen        |
| P53  | MOL009387     | Didehydrotuberosetemonine             | 51.91  | 0.74 | Baizhu         |
| P54  | MOL004903     | Liquiritin                             | 65.69  | 0.74 | Gancaco        |
| P55  | MOL009154     | Tuberosetemonone                       | 53.90  | 0.73 | Baizhu         |
| P56  | MOL004891     | Shinpterocarpin                        | 80.30  | 0.73 | Gancaco        |
| P57  | MOL009431     | Stemonine                              | 81.75  | 0.72 | Baizhu         |
| P58  | MOL000282     | Ergosta-7, 22e-dien-3beta-ol           | 43.51  | 0.72 | Fuling         |
| P59  | MOL009149     | Cheilanthifoline                       | 46.51  | 0.72 | Fuling         |
| P60  | MOL004805     | (2S)-2-[4-hydroxy-3-(3-methylbut-2-enyl)phenyl]-8, 8-dimethyl-2, 3-dihydropyranol[2, 3-f]chromen-4-one | 31.79  | 0.72 | Gancaco        |
| P61  | MOL005435     | 24-Methylcholest-5-enyl-3beta-O-glucopyranoside,qt | 37.58  | 0.72 | Shanya9        |
| P62  | MOL012254     | Campesterol                            | 37.58  | 0.71 | Renshen        |
| P63  | MOL005438     | Campesterol                            | 37.58  | 0.71 | Renshen, shanya9 |
| P64  | MOL000493     | Campesterol                            | 37.58  | 0.71 | Renshen        |
| P65  | MOL005013     | 18 α-Hydroxyglycyrrhetic acid          | 41.16  | 0.71 | Gancaco        |
| P66  | MOL006070     | Robinin                                | 39.84  | 0.71 | Jiegeng        |
| P67  | MOL011042     | 18Alpha-hydroglycyrrhetic acid         | 38.93  | 0.71 | Baibiandou     |
| P68  | MOL004567     | Isoengelitin                           | 34.65  | 0.70 | Renshen        |
| P69  | MOL007180     | Vitamin-e                              | 32.29  | 0.70 | Sharen         |
| P70  | MOL009953     | CLR                                    | 37.87  | 0.68 | Yiyiren, shanya9 |
| P71  | MOL000554     | Gallic acid-3-O-(6'-O-galloyl)-glucoside| 30.25  | 0.67 | Fuling, sharen |
| P72  | MOL002311     | Glycyrrhiza flavonol A                 | 41.28  | 0.60 | Gancaco        |
| P73  | MOL011455     | 20-Hexdecanoylengol                   | 32.70  | 0.65 | Renshen, fuling |
| P74  | MOL004904     | Licopyranocoumarin                    | 80.36  | 0.65 | Gancaco        |
| P75  | MOL004959     | 1-Methoxyphaseollidin                 | 69.98  | 0.64 | Gancaco        |
| P76  | MOL004071     | Hyndarin                               | 73.94  | 0.64 | Gancaco        |
| P77  | MOL005360     | Malkangunin                            | 57.71  | 0.63 | Renshen, baizhu |
| P78  | MOL004824     | 4, 6-(2, 4-dihydroxyphenyl)-2-(2-hydroxypropan-2-yl)-4-methoxy-2, 3-dihydrofuro[3, 2-g]chromen-7-one | 60.25  | 0.63 | Gancaco        |
| P79  | MOL005008     | Glycyrrhiza flavonol A                 | 41.28  | 0.60 | Gancaco        |
| P80  | MOL005007     | Glyasperins M                         | 72.67  | 0.59 | Gancaco        |
| P81  | MOL004492     | Chrysanthenaxanthin                   | 38.72  | 0.58 | Renshen, fuling |
| P82  | MOL005017     | Phaeol                                 | 78.77  | 0.58 | Gancaco        |
| P83  | MOL005003     | Licoacarpin                            | 58.81  | 0.58 | Gancaco        |
| P84  | MOL002773     | Beta-carotene                          | 37.18  | 0.58 | Baibiandou     |
| P85  | MOL004974     | 3'-methoxyglabridin                   | 46.16  | 0.57 | Gancaco        |
| P86  | MOL004966     | 3'-hydroxy-4'-O-Methylglabridin        | 43.71  | 0.57 | Gancaco        |
| P87  | MOL004806     | Euchrenone                             | 30.29  | 0.57 | Gancaco        |
| P88  | MOL005384     | Suchilactone                           | 57.52  | 0.56 | Renshen, baizhu |
| P89  | MOL005344     | Ginsenoside rh2                       | 36.32  | 0.56 | Renshen        |
| P90  | MOL006982     | Codeine                               | 45.48  | 0.56 | Sharen         |
| P91  | MOL004827     | Semilicoisoflavone B                  | 48.78  | 0.55 | Gancaco        |
| P92  | MOL004884     | Licoisoflavone B                      | 38.93  | 0.55 | Gancaco        |
| P93  | MOL004905     | 3, 22-Dihydroxy-11-oxo-delta(12)-oleane-27-alpha-methoxycaarbonyl-29-oic acid | 34.32  | 0.55 | Gancaco        |
| P94  | MOL003648     | Inermine                               | 65.83  | 0.54 | Renshen        |
| P95  | MOL004810     | Glyasperin F                          | 75.84  | 0.54 | Gancaco        |
| P96  | MOL001484     | Inermine                               | 75.18  | 0.54 | Gancaco        |
| P97  | MOL004885     | Licoisoflavone                        | 52.47  | 0.54 | Gancaco        |
| P98  | MOL005461     | Doradexanthin                          | 38.16  | 0.53 | Shanya9        |
| P99  | MOL004914     | 1, 3-Dihydroxy-8, 9-dimethoxy-6-benzofuran [3, 2-c]chromenone | 62.90  | 0.53 | Gancaco        |
| P100 | MOL004820     | Kanzonols W                           | 50.48  | 0.52 | Gancaco        |
| P101 | MOL004978     | 2-[1(3R)-8, 8-Dimethyl-3, 4-dihydro-2h-pyranol [6, 5-f]chromen-3-yl]-5-methoxyphenol | 36.21  | 0.52 | Gancaco        |
| P102 | MOL003851     | Isoramanone                            | 39.97  | 0.51 | Gancaco        |
| P103 | MOL004912     | Glabrone                               | 52.51  | 0.50 | Gancaco        |
| P104 | MOL005314     | Celabenzine                            | 101.88 | 0.49 | Renshen        |
| P105 | MOL005012     | Licoagroisoflavone                    | 57.28  | 0.49 | Gancaco        |
| P106 | MOL004855     | Licoricone                            | 63.58  | 0.47 | Gancaco        |
| P107 | MOL004908     | Glabridin                              | 53.25  | 0.47 | Gancaco        |
| Code | Molecule ID | Molecule name | OB (%) | DL | Herbs |
|------|-------------|---------------|--------|----|-------|
| P108 | MOL004879   | Glycyrin      | 52.61  | 0.47 | Gancao |
| P109 | MOL009436   | Stemotinine   | 38.69  | 0.46 | Baizhu |
| P110 | MOL004857   | Gancaonin B   | 48.79  | 0.45 | Gancao |
| P111 | MOL004833   | Phaseolislavon| 32.01  | 0.45 | Gancao |
| P112 | MOL004808   | Glysasperin B | 65.22  | 0.44 | Gancao |
| P113 | MOL004911   | Glabrene      | 46.27  | 0.44 | Gancao |
| P114 | MOL010002   | Ellagic acid  | 43.06  | 0.43 | Fuling, sharen |
| P115 | MOL004849   | 3-(2, 4-Dihydroxyphenyl)-8-(1, 1-dimethylprop-2-enyl)-7-hydroxy-5-methoxy-coumarin | 59.62 | 0.43 | Gancao |
| P116 | MOL004913   | 1, 3-Dihydroxy-9-methoxy-6-benzofurano [3, 2-c]chromenone | 48.14 | 0.43 | Yiyiren |
| P117 | MOL008118   | Coixenolide   | 32.40  | 0.43 | Yiyiren |
| P118 | MOL004949   | Isolicoflavonol | 45.17  | 0.42 | Gancao |
| P119 | MOL004883   | Licoisoflavone| 41.61  | 0.42 | Gancao |
| P120 | MOL004814   | Isotrifoliol  | 31.94  | 0.42 | Gancao |
| P121 | MOL002372   | (6Z, 10E, 14E, 18E)-2, 6, 10, 15, 19, 23-Hexamethyltetraacosa-2, 6, 10, 14, 18, 22-hexaene | 33.55 | 0.42 | Yiyiren |
| P122 | MOL004863   | 3-(3, 4-Dihydroxyphenyl)-5, 7-dihydroxy-8-(3-methylbut-2-enyl)chromone | 66.37 | 0.41 | Gancao |
| P123 | MOL004866   | 2-(3, 4-Dihydroxyphenyl)-5, 7-dihydroxy-6-(3-methylbut-2-enyl)chromone | 44.15 | 0.41 | Gancao |
| P124 | MOL004989   | 6-Prenylated eriectyol | 39.22 | 0.41 | Gancao |
| P125 | MOL004935   | Sigmodin-B     | 34.88  | 0.41 | Gancao |
| P126 | MOL004864   | 5, 7-Dihydroxy-3-(4-methoxyphenyl)-8-(3-methylbut-2-enyl)chromone | 30.49 | 0.41 | Gancao |
| P127 | MOL005890   | Pachypodol    | 75.06  | 0.40 | Fuling |
| P128 | MOL004993   | 8-Prenylated eriectyol | 53.79 | 0.40 | Gancao |
| P129 | MOL004856   | Gancaonin A   | 51.08  | 0.40 | Gancao |
| P130 | MOL004811   | Glyasperin C  | 45.56  | 0.40 | Gancao |
| P131 | MOL007213   | Nuciferine    | 34.43  | 0.40 | Lianzi |
| P132 | MOL012537   | Spinoside A   | 41.75  | 0.40 | Jiegeng |
| P133 | MOL008406   | Spinoside A   | 39.97  | 0.40 | Jiegeng |
| P134 | MOL002879   | Diop          | 43.59  | 0.39 | Renshen |
| P135 | MOL005000   | Gancaonin G   | 60.44  | 0.39 | Shanyao |
| P136 | MOL005430   | Hancione C    | 59.05  | 0.39 | Shanyao |
| P137 | MOL004838   | 8-(6-Hydroxy-2-benzofuranyl)-2, 2-dimethyl-5-chromenol | 58.44 | 0.38 | Gancao |
| P138 | MOL006980   | Papaverine    | 64.04  | 0.38 | Sharen |
| P139 | MOL000322   | Kadsurenone   | 54.72  | 0.38 | Shanyao |
| P140 | MOL000310   | Denuudatin B  | 61.47  | 0.38 | Shanyao |
| P141 | MOL005020   | Dehydroglyasperins C | 53.82 | 0.37 | Gancao |
| P142 | MOL003656   | Lupiwighteone | 51.64  | 0.37 | Gancao |
| P143 | MOL004915   | Eurycaprin A  | 43.28  | 0.37 | Gancao |
| P144 | MOL009172   | Pronuciferin  | 32.75  | 0.37 | Lianzi |
| P145 | MOL005429   | Hancinol      | 64.01  | 0.37 | Shanyao |
| P146 | MOL004882   | Licocoumarone | 33.21  | 0.36 | Gancao |
| P147 | MOL003673   | Wighteone    | 42.80  | 0.36 | Gancao |
| P148 | MOL004907   | Glyzaglabrin | 61.07  | 0.35 | Gancao |
| P149 | MOL004828   | Glepidotin A  | 44.72  | 0.35 | Gancao |
| P150 | MOL004815   | (E)-1-(2, 4-dihydroxyphenyl)-3-(2, 2-dimethylchromen-6-yl)prop-2-en-1-one | 39.62 | 0.35 | Gancao |
| P151 | MOL005321   | Frutinone A   | 65.90  | 0.34 | Renshen |
| P152 | MOL004829   | Glepidotin B  | 64.46  | 0.34 | Gancao |
| P153 | MOL002565   | Medicarpin    | 49.22  | 0.34 | Gancao |
| P154 | MOL011072   | Quinicine     | 75.44  | 0.33 | Fuling, baibiandou |
| P155 | MOL004961   | Quercetin der. | 46.45  | 0.33 | Gancao |
| P156 | MOL004980   | Inflacoumarin A | 39.71  | 0.33 | Gancao |
| P157 | MOL004848   | Licochalcone G | 49.25  | 0.32 | Gancao |
| P158 | MOL004945   | (2S)-7-hydroxy-2-(4-hydroxyphenyl)-8-(3-methylbut-2-enyl)chroman-4-one | 36.57 | 0.32 | Gancao |
| P159 | MOL005356   | Girinimbin    | 61.22  | 0.31 | Renshen |
| P160 | MOL000021   | 14-Acetyl-12-senecioyl-2E, 8E, 10E-atractylentriol | 60.31 | 0.31 | Baizhu |
| P161 | MOL004910   | Glabranin     | 52.90  | 0.31 | Gancao |
| Code | Molecule ID | Molecule name                                  | OB (%) | DL  | Herbs                |
|------|-------------|-----------------------------------------------|--------|-----|----------------------|
| P162 | MOL000354   | Isorhamnetin                                   | 49.60  | 0.31| Gancao, baibiandou   |
| P163 | MOL004898   | (E)-3-[3, 4-dihydroxy-5-(3-methylbut-2-enyl)phenyl]-1-(2, 4-dihydroxyphenyl)prop-2- en-1-one | 46.27  | 0.31| Gancao               |
| P164 | MOL000022   | 14-Acetyl-12-senecioyl-2E, 8Z, 10E-atriactylentriol | 63.37  | 0.30| Baizhu               |
| P165 | MOL005016   | Odoratin                                       | 49.95  | 0.30| Gancao               |
| P166 | MOL002882   | [(2R)-2, 3-dihydroxypropyl] (Z)-octadec-9-enoate | 34.13  | 0.30| Yiyiren              |
| P167 | MOL000239   | Jaranol                                        | 50.83  | 0.29| Gancao               |
| P168 | MOL000497   | Licochalcone a                                 | 40.79  | 0.29| Gancao               |
| P169 | MOL007206   | Armeapavine                                    | 69.31  | 0.29| Lianzi               |
| P170 | MOL008121   | 2-Monoolein                                    | 34.23  | 0.29| Yiyiren              |
| P171 | MOL009135   | Ellipticine                                    | 30.82  | 0.28| Fuling, sharen       |
| P172 | MOL000098   | Quercetin                                      | 46.43  | 0.28| Gancao, sharen, baibiandou |
| P173 | MOL004576   | Taxifolin                                       | 57.84  | 0.27| Renshen              |
| P174 | MOL004990   | 7, 2', 4'-Trihydroxy - 5-methoxy-3-arylcoumarin| 83.71  | 0.27| Gancao               |
| P175 | MOL004860   | Licorice glycoside E                            | 32.89  | 0.27| Gancao               |
| P176 | MOL005575   | Gentiacaulein                                  | 72.82  | 0.27| Gancao               |
| P177 | MOL001735   | Dinatin                                        | 30.97  | 0.27| Gancao               |
| P178 | MOL004580   | cis-Dihydroquercetin                            | 66.44  | 0.27| Jiegeng              |
| P179 | MOL001736   | (-)-Taxifolin                                  | 60.51  | 0.27| Shanyao              |
| P180 | MOL005267   | Elymoclavine                                    | 72.87  | 0.27| Shanyao              |
| P181 | MOL004991   | 7-Acetoxy-2-methylisoflavone                   | 38.92  | 0.26| Gancao               |
| P182 | MOL011093   | Apohysosine                                    | 59.68  | 0.25| Renshen              |
| P183 | MOL003617   | Isogosferol                                    | 30.07  | 0.25| Gancao               |
| P184 | MOL000006   | Luteolin                                       | 36.16  | 0.25| Jiegeng              |
| P185 | MOL005996   | 2-O-methyl-3—O-β-D-glucopyranosyl platycogenate A | 45.15  | 0.25| Jiegeng              |
| P186 | MOL000626   | Dimethyl 2-O-methyl-3-O-α-D-glucopyranosyl platycogenate A | 39.21  | 0.25| Jiegeng              |
| P187 | MOL000422   | Kaempferol                                     | 41.88  | 0.24| Renshen, gancao, baibiandou |
| P188 | MOL000417   | Calycosin                                      | 47.75  | 0.24| Gancao               |
| P189 | MOL005573   | Genkwanin                                      | 37.13  | 0.24| Gancao               |
| P190 | MOL000492   | (+)-Catechin                                    | 54.83  | 0.24| Sharen, baibiandou   |
| P191 | MOL001689   | Acacetin                                       | 34.97  | 0.24| Jiegeng              |
| P192 | MOL005463   | Methylcimicificugoside_qt                      | 31.69  | 0.24| Shanyao              |
| P193 | MOL007514   | Methyl icosa-11, 14-dienoate                    | 39.67  | 0.23| Sharen               |
| P194 | MOL003975   | Icosa-11, 14, 17-trienolic acid methyl ester    | 44.81  | 0.23| Sharen               |
| P195 | MOL005308   | Aposiopalamine                                 | 66.65  | 0.22| Renshen              |
| P196 | MOL000049   | 3β-acetoxy atracyctlyone                       | 54.07  | 0.22| Baizhu               |
| P197 | MOL000020   | 12-Senecioyl-2E, 8E, 10E-atriactylentriol       | 62.40  | 0.22| Baizhu               |
| P198 | MOL000072   | 8β-ethoxy atracylenolide III                   | 35.95  | 0.21| Baizhu               |
| P199 | MOL010586   | Formononetin                                   | 66.39  | 0.21| Baizhu               |
| P200 | MOL000500   | Vestitol                                       | 74.66  | 0.21| Gancao               |
| P201 | MOL000392   | Formononetin                                   | 69.67  | 0.21| Gancao, baibiandou   |
| P202 | MOL004328   | Naringenin                                     | 59.29  | 0.21| Gancao, yiyiren, jiegeng |
| P203 | MOL004957   | HMO                                            | 38.37  | 0.21| Gancao               |
| P204 | MOL002419   | Demethylcoclarine(R)-norcoclarine              | 82.54  | 0.21| Lianzi               |
| P205 | MOL005320   | Arachidonate                                   | 45.57  | 0.20| Renshen              |
| P206 | MOL005318   | Diantramine                                    | 40.45  | 0.20| Renshen              |
| P207 | MOL003896   | 7-Methoxy-2-methyl isoflavone                  | 42.56  | 0.20| Gancao               |
| P208 | MOL004985   | Icos-5-enolic acid                             | 30.70  | 0.20| Gancao               |
| P209 | MOL004996   | Gadelaidic acid                                | 30.70  | 0.20| Gancao               |
| P210 | MOL000230   | Pinocembrin                                    | 57.56  | 0.20| Gancao               |
| P211 | MOL004841   | Licochalcone B                                 | 76.76  | 0.19| Gancao               |
| P212 | MOL004835   | Glypallichalcone                               | 61.60  | 0.19| Gancao               |
| P213 | MOL001494   | Mandenol                                       | 42.00  | 0.19| Yiyiren              |
| P214 | MOL004058   | Khell                                           | 33.19  | 0.19| Shanyao              |
| P215 | MOL004941   | (2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one | 71.12  | 0.18| Gancao               |
| P216 | MOL001792   | DFV                                             | 32.76  | 0.18| Gancao               |
| P217 | MOL001559   | Piperlonguminine                               | 30.71  | 0.18| Shanyao              |
of 1182 active compounds were acquired from the SymMap database; a total of 352 active compounds were acquired from the Traditional Chinese Medicine Database@TAIWAN database; and a total of 171 active compounds were acquired from the TCMSP database. At last, 217 eligible unique active compounds of SLBZP in total were retrieved from the TCMSP database under the conditions of OB ≥ 30% and DL ≥ 0.18, which are all shown in Table 1.

3.2. Collection of BA and AC Disease Targets. 4795 BA-related target genes were collected based on DisGeNET, TTD, GeneCards, PharmGKB, OMIM, NCBI, The Human Phenotype Ontology, and DrugBank databases. Duplicate targets were excavated and deleted, and 3388 BA disease action targets in total were collected. 1828 AC-related target genes were collected based on TTD, GeneCards, PharmGKB, OMIM, and NCBI databases. And 1640 AC disease action targets in total were collected by mining and deleting duplicate targets. The obtained target information was standardized for gene symbol and UniProt ID.

3.3. Acquisition of Targets of Active Compounds of SLBZP for Treating BA and AC. After searching the above-mentioned qualified potential active compounds of SLBZP in the TCMSP database, and removing the repeated targets, 281 targets of active compounds of SLBZP were obtained. The bioinformatics and evolutionary genomics platform was used to match the potential targets of drugs with disease targets, and a Venn diagram was drawn (Figure 2). 149 common targets were obtained (Table 2).

3.4. GO and KEGG Pathway Enrichment Analysis. GO enrichment analysis revealed 2933 biological functions with remarkable significance, including 2687 for biological processes (BP), 75 for cellular component (CC), and 171 for molecular function (MF). The results of GO enrichment analysis showed that the common targets of SLBZP in treating BA and AC mainly involved response to oxidative stress, response to molecular of bacterial origin, membrane region, membrane microdomain, signaling receptor activator activity, receptor ligand activity, and other biological functions (Figure 3). 182 significant pathways were obtained by KEGG pathway enrichment analysis, mainly involving PI3K-Akt signaling pathway, proteoglycans in cancer, MAPK signaling pathway, IL-17 signaling pathway, TNF signaling pathway, apoptosis, Th17 cell differentiation, and other pathways related to inflammation, cancer, apoptosis, and immunity (Figure 4).

3.5. Construction and Analysis of Active Compound-Key Target Network. The 149 common targets obtained above were screened by “cytoHubba”, a plug-in of Cytoscape software, and then the 20 key targets with the highest degree value were obtained (Figure 5). These 20 key targets and their corresponding active compounds were imported into Cytoscape software for network construction and visualization (Figure 6). There were 131 active compounds related to key targets (Table 3). In the active compound-key target network, the degree of the network topology analysis carried out by “Network Analysis” reflects the connectivity of nodes that respectively represent active compounds and key targets. A higher degree value indicates more associations between nodes, which explains the significances of active compounds and key targets. The results of network topology analysis showed that the 5 active compounds most connected to the key targets were quercetin, luteolin, beta-carotene, kaempferol, and naringenin, and the top 6 key targets of connectivity were prostaglandin G/H synthase 2 (PTGS2), caspase-3 (CASP3), RAC-alpha serine/threonine-protein kinase (AKTI), transcription factor AP-1 (JUN), cellular tumor antigen p53 (TP53), and vascular endothelial growth factor A (VEGFA), which indicated that the above compounds and targets were critical and had important implications in SLBZP for treating BA and AC.

3.6. Molecular Docking Results. Based on the above analysis results, the 5 important active compounds (quercetin, luteolin, beta-carotene, kaempferol, and naringenin) and the key targets were docked by AutoDockVina software. The docking results are shown in Table 4 and Figure 7. The smaller the binding free energy value, the lower the energy required for binding, which is more conducive to the binding of ligand and protein. Among them, the docking results of MMP9 with luteolin, quercetin, and kaempferol, ALB with luteolin, and PTGS2 with luteolin were the best, as shown in Figure 8. For example, luteolin formed conventional hydrogen bonds with MMP9 protein structure 6ESM amino acid residues A chain TYR245, LEU243, GLN227, LEU188, ALA189, formed π-σ interactions with amino acid residues A chain TYR248 and LEU188, formed π-π stacked interactions with amino acid residue A chain HIS226, and formed π-alkyl interactions with amino acid residues A chain VAL223 and LEU188. These forces reduced the binding energy and increased the affinity, which played an auxiliary role in the binding of compound ligand molecules to the residues of target protein structures.

3.7. Construction and Analysis of Key Target-miRNA Network. 94 miRNAs were predicted from 6 key targets by the miRTarBase database. Cytoscape software was used to

![Figure 2: Targets matching among SLBZP, BA, and AC.](image-url)
| No. | Target | Symbol | UniProt ID | No. | Target | Symbol | UniProt ID |
|-----|--------|--------|------------|-----|--------|--------|------------|
| 1   | 72 kDa type IV collagenase | MMP2 | P08253 | 76  | Prostaglandin E2 receptor EP3 subtype | PTGER3 | P43115 |
| 2   | Xanthine dehydrogenase/oxidase | XDH | P47989 | 77  | Urokinase-type plasminogen activator | PLAU | P00749 |
| 3   | Heat shock protein beta-1 | HSPB1 | P04792 | 78  | Phosphatidylinositol-3,4,5-trisphosphate 3-phosphatase and dual-specificity protein phosphatase | PTEN | P60484 |
| 4   | Nitric oxide synthase, inducible Hepatocyte growth factor receptor | NOS2 | P35228 | 79  | Sodium-dependent serotonin transporter | SLC6A4 | P31645 |
| 5   | UDP-glucuronosyltransferase 1-1 | UGT1A1 | P22309 | 80  | Arachidonate 5-lipoxygenase | ALOX5 | P09917 |
| 6   | Protein kinase C beta type | PRKCB | P05771 | 81  | Gap junction alpha-1 protein | GJA1 | P17302 |
| 7   | Collagen alpha-1(I) chain Bacuvolrial IAP repeat-containing protein 5 | COL1A1 | P02451 | 82  | Claudin-4 | CLDN4 | O14493 |
| 8   | Apoptosis regulator Bcl-2 | BIRC5 | O15392 | 83  | Dipeptidyl peptidase IV | DPP4 | P27487 |
| 9   | Alpha-2A adrenergic receptor | ADRA2A | P08913 | 84  | Serine/threonine-protein kinase | CASP8 | Q14790 |
| 10  | Cytochrome P450 1A1 | CYP1A1 | P04798 | 85  | Peroxisome proliferator activated receptor gamma | PPARG | P37231 |
| 11  | 5-Hydroxytryptamine receptor 3A | HTR3A | P46098 | 86  | C-X-C motif chemokine 11 | CXCL11 | O14625 |
| 12  | Mitogen-activated protein kinase | MAPK10 | P53779 | 87  | Interleukin-8 | CXCL8 | P10145 |
| 13  | Prostaglandin E synthase | PTGES | P01684 | 88  | E-selectin | SELE | P16581 |
| 14  | C-reactive protein | CRP | P02474 | 89  | Thrombomodulin | THBD | P07204 |
| 15  | Glutathione S-transferase P | GSTP1 | P09211 | 90  | Glucocorticoid receptor | NR3C1 | P04150 |
| 16  | Aryl hydrocarbon receptor | AHR | P35869 | 91  | Serine/threonine-protein kinase | MTOR | P42345 |
| 17  | Nuclear factor erythroid 2-related factor 2 | NFE2L2 | Q16236 | 92  | Mitogen-activated protein kinase 14 | MAPK14 | Q16539 |
| 18  | Tumor necrosis factor | TNF | P01375 | 93  | RAF proto-oncogene serine/threonine-protein kinase | RAF1 | P04049 |
| 19  | Interleukin-1 alpha | IL1A | P01583 | 94  | Cytosolic phospholipase A2 | PLA2G4A | P47712 |
| 20  | Pro-epidermal growth factor receptor Interleukin-1 alpha | ABCC2 | Q92887 | 95  | Myeloperoxidase | MPO | P05164 |
| 21  | Canalicular multispecific organic anion transporter 1 | GPR1 | Q16236 | 96  | Alpha-1B adrenergic receptor | ADRA1B | P35368 |
| 22  | Caspase-1 | CASP1 | P29466 | 97  | Inhibitor of nuclear factor kappa-B kinase subunit alpha | CHUK | O15111 |
| 23  | Osteopontin | SPP1 | P10451 | 98  | Signal transducer and activator of transcription 3 | STAT3 | P40763 |
| 24  | Thrombin | F2 | P00734 | 99  | Antileukoproteinase | SLPI | P03973 |
| 25  | Prostaglandin G/H synthase 2 | PTGS2 | P35354 | 100 | Cathepsin D | CTSD | P07339 |
| 26  | Nictinatin beta-1 | CTNNB1 | P35222 | 101 | Sterol O-acyltransferase 1 | SOAT1 | P35610 |
| 27  | G1/S-specific cyclin-D1 | CCND1 | P24385 | 102 | Acetylcholinesterase | ACHE | P22303 |
| 28  | Estrogen receptor | ESR1 | P03372 | 103 | Induced myeloid leukemia cell differentiation protein McI-1 | MCL1 | Q07820 |
| 29  | Vascular endothelial growth factor A | VEGFA | P15692 | 104 | C-C motif chemokine 2 | CCL2 | P13500 |
| 30  | Transforming growth factor beta-1 | TGFBI | P01137 | 105 | Interleukin-6 | IL6 | P05231 |
| 31  | Myc proto-oncogene protein | MYC | P01106 | 106 | Caspase-3 | CASP3 | P42574 |
| 32  | Cyclin-A2 | CCNA2 | P20248 | 107 | Heat shock protein HSP 90-alpha | HSPA9A1 | P68890 |
| 33  | Glycogen synthase kinase-3 beta | GSK3B | P49841 | 108 | Poly [ADP-ribose] polymerase | PARP1 | P09874 |
| 34  | Intersitial collagenase | MMP1 | P03956 | 109 | Tumor necrosis factor ligand superfamily member 6 | FASLG | P48023 |
| 35  | Signal transducer and activator of transcription 1-alpha/beta | STAT1 | P42224 | 110 | Maltase-glucoamylase, intestinal | MGAM | O43451 |
| 36  | Peroxisome proliferator activated receptor delta | PPARD | Q03181 | 111 | Vascular endothelial growth factor receptor 2 | KDR | P35968 |
| 37  | 3-Hydroxy-3-methylglutaryl-coenzyme a reductase | HMGCR | P04035 | 112 | Fos-related antigen 2 | FOSL2 | P15408 |
construct a key target-miRNA network (Figure 9), among which hsa-miR-16-5p, hsa-miR-101-3p, hsa-miR-143-3p, hsa-miR-199a-5p, hsa-miR-30d-3p, hsa-miR-30c-5p, hsa-miR-30e-5p, hsa-miR-302d-3p, hsa-miR-203a-3p, hsa-miR-200b-3p, hsa-miR-125a-5p, hsa-miR-15a-5p, hsa-miR-504-5p, and hsa-miR-150-5p all targeted multiple key targets.

4. Discussion

The theory of traditional Chinese medicine believes that the spleen is the foundation of acquired life and that the spleen is not harmonious and causes all kinds of diseases. Therefore, it has always paid attention to regulating the spleen to protect...
the five internal organs. The pathogenesis of spleen deficiency is involved in the occurrence and development of BA and AC. SLBZP, one of the classic Earth-cultivating and gold-generating prescriptions, can not only treat BA and AC with simultaneous treatment of different diseases but also protect the spleen to prevent and promote recovery. This study aimed to explore the action mechanism of SLBZP in treating BA and AC with simultaneous treatment of different diseases by using network pharmacology and molecular docking, so as to provide references for more in-depth experimental research and wider clinical applications.

GO annotation results showed that the biological functions involved in common targets were mainly response to oxidative stress, response to molecule of bacterial origin, membrane region, membrane microdomain, signaling receptor activator activity, receptor ligand activity, and so on. In addition, the main enrichment pathways of common targets were PI3K-Akt signaling pathway, proteoglycans in cancer, MAPK signaling pathway, IL-17 signaling pathway, TNF signaling pathway, apoptosis, Th17 cell differentiation, and other pathways related to inflammation, cancer, apoptosis, and immunity. Studies pointed out that, during the onset of asthma, both PI3K-Akt signaling pathway and MAPK signaling pathway were active [35, 36]. Many targets of the PI3K pathway play critical roles in the expression and activation of inflammatory mediators, inflammatory cell recruitment, immune cell function, airway remodeling, and corticosteroid insensitivity in chronic inflammatory airway disease [37]. There were evidences that selective PI3K inhibitors could reduce inflammation and some characteristics of diseases such as abnormal proliferation of airway smooth muscle cells (ASMC) in experimental animal models, which strongly supported that PI3K/Akt inhibitors might be a useful new therapy for asthma [37, 38]. In recent years, many studies confirmed that inhibiting PI3K–Akt signaling pathway and MAPK signaling pathway could effectively inhibit allergic airway inflammation, ASMC proliferation and migration, and phenotypic switching, so as to alleviate
Figure 4: KEGG pathway enrichment analysis of common targets.

Figure 5: PPI diagram of key targets.
airway remodeling and airway hyperresponsiveness (AHR) in asthma [39–42]. Additionally, upregulation of dual-specificity phosphatase-1 (DUSP1), a negative regulator in the MAPK signaling pathway, to healthy levels and down-regulation of inflammatory MAPKs at the gene and protein levels could reduce the prevalence of childhood asthma [43]. Proteoglycans enhanced deposition in the airway walls of asthmatics playing a role in airway remodeling, and the difference of deposition in the airways smooth muscle layer of moderate and severe asthmatic patients might affect the functional behavior of airway smooth muscle [44,45]. IL-17A in the IL-17 signaling pathway was positively correlated with neutrophil accumulation, mucus secretion, macrophage mobilization, and smooth muscle reactivity in various experimental airway models, as well as with disease severity, suggesting that specifically targeting IL-17A had the potential of clinical utility in patients with moderate and severe asthma and high reversibility [46]. Moreover, the reduction of skin inflammation and airway inflammation in the IL-17-induced mouse asthma model was related to the reduction of IL-17-mediated mRNA stability [47]. In TLR ligand-mediated allergic airway inflammation, TLR ligand induced TNF to send signals through airway epithelial cells to promote the development of Th2 in lymph nodes, and TNF was also indispensable in the allergen stimulation stage of neutrophilic and eosinophilic airway inflammation and AHR [48]. Activated TNF-TNFR2 signal transduction could inhibit the differentiation of Th2 and Th17 cells to alleviate allergic airway inflammation [49]. Bronchial cell apoptosis could be observed in some airway biopsies from asthmatic patients, especially those with serious diseases, possibly resulting in airway damage, and dysregulation of leukocyte, eosinophil, and neutrophil apoptosis could lead to asthmatic airway inflammation and was related to the pathogenesis of asthma [50]. Th17 cells, a potent and unique subset that modulated primary bronchial epithelial cell function, were related to the development and pathophysiology of asthma [51, 52]. A study found that asthma-associated IL4R variants promoted the transformation of regulatory T cells into TH17-like cells, thereby exacerbating airway inflammation [53]. It should be noted that because there have been relatively few studies related to allergic colitis all the time, there is almost no relevant research report on the relationship between the above signaling pathways and allergic colitis. However, it is worth mentioning that if further research is carried out on this basis in the future, it will be very innovative and instructive for clarifying the pathogenesis of allergic colitis and developing new drugs that can effectively target the disease. The above showed that SLBZP treated BA and AC with simultaneous treatment of different diseases by multiple functions and pathways, suggesting that further research in the future could be based on these biological functions and pathways, which had guiding significances.

The active compound-key target network of this study showed that the five active compounds of quercetin, luteolin, beta-carotene, kaempferol, and naringenin, and the 6 key targets of PTGS2, CASP3, AKT1, JUN, TP53, and VEGFA were particularly important. Moreover, the results of molecular docking also verified that these five active compounds had good binding characteristics with their corresponding important key targets, indicating that they played vital roles in SLBZP for treating BA and AC with simultaneous treatment of different diseases and had critical potential research values. Studies suggested that quercetin was known for its antioxidant activity in free radicals scavenging and antiallergic properties [54]. It is characterized by stimulating the immune system and antiviral activity, inhibiting histamine release, reducing proinflammatory cytokines, and producing leukotrienes [55]. It was reported to improve Th1/Th2 balance, inhibit the formation of antigen-specific IgE antibodies, and also be effective in inhibiting enzymes such as lipooxygenase, eosinophils, and peroxidase and inflammatory mediators [56]. All the mentioned mechanisms contribute to the anti-inflammatory and immunomodulatory properties of quercetin, which can be effectively used to treat advanced bronchial asthma, allergic rhinitis, and restrictive allergic reactions caused by peanuts [55]. Luteolin, having anti-inflammatory, antiallergic, and immune-enhancing functions, can reduce airway inflammation and allergies in asthma and has antiallergic effects in mouse models of allergic asthma and rhinitis, which has shown therapeutic effects in treating inflammatory diseases, allergies, bronchial asthma, and
Table 3: Active compounds related to key targets.

| Code | Molecule ID   | Molecule name | OB (%) | DL  | Degree | Herbs                     |
|------|---------------|---------------|--------|-----|--------|---------------------------|
| P172 | MOL000098     | Quercetin     | 46.43  | 0.28| 16     | Gancao, sharen, baibiandou|
| P184 | MOL000006     | Luteolin      | 36.16  | 0.25| 11     | Jiegeng                   |
| P84  | MOL002773     | Beta-carotene | 37.18  | 0.58| 7      | Baibiandou                |
| P187 | MOL000422     | Kaempferol    | 41.88  | 0.24| 6      | Renshen, gancao, baibiandou|
| P202 | MOL004328     | Naringenin    | 59.29  | 0.21| 5      | Gancao, yiyiren, jiegeng  |
| P20  | MOL000546     | Diosgenin     | 80.88  | 0.81| 4      | Shanyao                   |
| P89  | MOL005344     | Ginsenoside rh2| 36.32 | 0.56| 4      | Renshen                   |
| P171 | MOL009135     | Ellipticine   | 30.82  | 0.28| 3      | Fuling, sharen            |
| P191 | MOL001689     | Acacetin      | 34.97  | 0.24| 3      | Jiegeng                   |
| P114 | MOL001002     | Ellagic acid  | 43.06  | 0.43| 3      | Fuling, sharen            |
| P42  | MOL000358     | Beta-sitosterol| 36.91 | 0.75| 3      | Renshen, sharen           |
| P168 | MOL000497     | Licochalcone a | 40.79 | 0.29| 3      | Gancao                    |
| P201 | MOL000392     | Formononetin  | 69.67  | 0.21| 2      | Gancao, baibiandou        |
| P151 | MOL005321     | Frutinone A   | 65.90  | 0.34| 1      | Renshen                   |
| P94  | MOL003648     | Inermine      | 65.83  | 0.54| 1      | Renshen                   |
| P159 | MOL005356     | Girinimbín    | 61.22  | 0.31| 1      | Renshen                   |
| P10  | MOL000787     | Fumarine      | 59.26  | 0.83| 1      | Renshen                   |
| P88  | MOL005384     | Suchilactone  | 57.52  | 0.56| 1      | Renshen, baizhu           |
| P205 | MOL005320     | Archidionate  | 45.57  | 0.20| 1      | Renshen                   |
| P34  | MOL000449     | Stigmasterol  | 43.83  | 0.76| 1      | Shanyao                   |
| P206 | MOL005318     | Dianthrmine   | 40.45  | 0.20| 1      | Renshen                   |
| P68  | MOL004567     | Isoengelitin  | 34.65  | 0.70| 1      | Renshen                   |
| P173 | MOL004576     | Taxifolin     | 57.84  | 0.27| 1      | Renshen                   |
| P64  | MOL000493     | Campesterol   | 37.58  | 0.71| 1      | Renshen                   |
| P164 | MOL000022 14 | Acetyl-12-senecioyl-2E,8Z,10E-atractylentriol | 63.37 | 0.30| 1      | Baizhu                    |
| P196 | MOL000049 3b | acetoxyatractylone | 54.07 | 0.22| 1      | Baizhu                    |
| P198 | MOL000072 8b | ethoxy atractylonolide III | 35.95 | 0.21| 1      | Baizhu                    |
| P199 | MOL010586 Formononetin | 66.39 | 0.21| 1      | Baizhu                    |
| P53  | MOL009387 Didehydrotubersestonine | 51.91 | 0.74| 1      | Baizhu                    |
| P45  | MOL000296 Hederagenin | 36.91 | 0.75| 1      | Fuling                    |
| P59  | MOL009149 Cheilanthifoline | 46.51 | 0.72| 1      | Fuling                    |
| P154 | MOL011072 Quinicine | 75.44 | 0.33| 1      | Fuling, baikiandou         |
| P72  | MOL002311 Glycerr | 90.78 | 0.67| 1      | Gancao                    |
| P174 | MOL004990 7,2′,4′-trihydroxy-5-methoxy-3-arylcoumarin | 83.71 | 0.27| 1      | Gancao                    |
| P74  | MOL004904 Licopyranocoumarin | 80.36 | 0.65| 1      | Gancao                    |
| P56  | MOL004891 Shinpterocarpin | 80.30 | 0.73| 1      | Gancao                    |
| P82  | MOL005017 Phaseol | 78.77 | 0.58| 1      | Gancao                    |
| P211 | MOL004841 Licochalcone B | 76.76 | 0.19| 1      | Gancao                    |
| P95  | MOL004810 Glyasperin F | 75.84 | 0.54| 1      | Gancao                    |
| P96  | MOL001484 Inermine | 75.18 | 0.54| 1      | Gancao                    |
| P200 | MOL000500 Vestitol | 74.66 | 0.21| 1      | Gancao                    |
| P80  | MOL005007 Glyasperins M | 72.67 | 0.59| 1      | Gancao                    |
| P215 | MOL004941 (2R)-7-hydroxy-2-(4-hydroxyphenyl)chroman-4-one | 71.12 | 0.18| 1      | Gancao                    |
| P75  | MOL004959 1-Methoxyphaseololidin | 69.98 | 0.64| 1      | Gancao                    |
| P122 | MOL004863 3-(3,4-dihydroxyphenyl)-5,7-dihydroxy-8-(3-methylbut-2-enyl) chromone | 66.37 | 0.41| 1      | Gancao                    |
| P54  | MOL004903 Liquiritin | 65.69 | 0.74| 1      | Gancao                    |
| P112 | MOL004808 Glyasperin B | 65.22 | 0.44| 1      | Gancao                    |
| P152 | MOL004829 Glepidotin B | 64.46 | 0.34| 1      | Gancao                    |
| P106 | MOL004855 Licoricone | 63.58 | 0.47| 1      | Gancao                    |
| P212 | MOL004835 Glypallichalcone | 61.60 | 0.19| 1      | Gancao                    |
| P148 | MOL004907 Glyzaglabrin | 61.07 | 0.35| 1      | Gancao                    |
| P135 | MOL005000 Gancaonin G | 60.44 | 0.39| 1      | Gancao                    |
| P78  | MOL004824 (2S)-6-(2,4-dihydroxyphenyl)-2-(2-hydroxypropan-2-yl)-4-methoxy-2,3-dihydrofuro[3,2-g]chromen-7-one | 60.25 | 0.63| 1      | Gancao                    |
| Code | Molecule ID | Molecule name | OB (%) | DL | Degree | Herbs |
|------|-------------|---------------|--------|----|--------|-------|
| P115 | MOL004849   | 3-(2,4-dihydroxyphenyl)-8-(1,1-dimethylprop-2-enyl)-7-hydroxy-5-methoxy-coumarin | 59.62  | 0.43 | 1 | Gancao |
| P83  | MOL005003   | Licoagrocarpin | 58.81  | 0.58 | 1 | Gancao |
| P137 | MOL004838   | 8-(6-Hydroxy-2-benzo(furan)-2,2-dimethyl-5-chromenol | 58.44  | 0.38 | 1 | Gancao |
| P105 | MOL005012   | Licoagroisoflavone | 57.28  | 0.49 | 1 | Gancao |
| P3   | MOL005018   | Xamibooona | 54.85  | 0.87 | 1 | Gancao |
| P141 | MOL004993   | Dehydroglyasperins C | 53.82  | 0.37 | 1 | Gancao |
| P128 | MOL004908   | 8-Prenylated eriodictyol | 53.79  | 0.40 | 1 | Gancao |
| P107 | MOL004910   | Glabrin | 53.25  | 0.47 | 1 | Gancao |
| P161 | MOL004879   | Glycyrrhiza | 52.90  | 0.31 | 1 | Gancao |
| P108 | MOL004912   | Glycyrin | 52.61  | 0.47 | 1 | Gancao |
| P97  | MOL004885   | Licoisoflavanone | 52.47  | 0.54 | 1 | Gancao |
| P142 | MOL003656   | Lupinwiteone | 51.64  | 0.37 | 1 | Gancao |
| P129 | MOL004856   | Gankaoninic A | 51.08  | 0.40 | 1 | Gancao |
| P167 | MOL000239   | Jaranol | 50.83  | 0.29 | 1 | Gancao |
| P100 | MOL004820   | Kanzonols W | 50.48  | 0.52 | 1 | Gancao |
| P30  | MOL005001   | Gankaoninic H | 50.10  | 0.78 | 1 | Gancao |
| P165 | MOL005016   | Odoaratin | 49.95  | 0.30 | 1 | Gancao |
| P162 | MOL000354   | Isorhamnetin | 49.60  | 0.31 | 1 | Gancao, baibiandou |
| P157 | MOL004848   | Licochalcone G | 49.25  | 0.32 | 1 | Gancao |
| P153 | MOL002565   | Medicarpin | 49.22  | 0.34 | 1 | Gancao |
| P110 | MOL004857   | Gankaoninic B | 48.79  | 0.45 | 1 | Gancao |
| P91  | MOL004827   | Semilicoisoflavone B | 48.78  | 0.55 | 1 | Gancao |
| P188 | MOL000417   | Calycosin | 47.75  | 0.24 | 1 | Gancao |
| P155 | MOL004961   | Quercetin der. | 46.45  | 0.33 | 1 | Gancao |
| P163 | MOL004898   | (E)-3-[3,4-dihydroxy-5-(3-methylbut-2-enyl)phenyl]-1-(2,4-dihydroxyphenyl)prop-2-en-1-one | 46.27  | 0.31 | 1 | Gancao |
| P113 | MOL004911   | Glabrene | 46.27  | 0.44 | 1 | Gancao |
| P85  | MOL004974   | 3’-methoxyglabridin | 46.16  | 0.57 | 1 | Gancao |
| P130 | MOL004811   | Glyasperin C | 45.56  | 0.40 | 1 | Gancao |
| P118 | MOL004949   | Isolicoisoflavonol | 45.17  | 0.42 | 1 | Gancao |
| P149 | MOL004828   | Glepidotin A | 44.72  | 0.35 | 1 | Gancao |
| P123 | MOL004866   | 2’-(3,4-dihydroxyphenyl)-5,7-dihydroxy-6-(3-methylbut-2-enyl)chromone | 44.15  | 0.41 | 1 | Gancao |
| P86  | MOL004966   | 3’-hydroxy-4’-O-Methylglabridin | 43.71  | 0.57 | 1 | Gancao |
| P143 | MOL004915   | Eurycarnip A | 43.28  | 0.37 | 1 | Gancao |
| P207 | MOL003896   | 7-Methoxy-2-methyl isoflavone | 42.56  | 0.20 | 1 | Gancao |
| P119 | MOL004883   | Licoisoflavone | 41.61  | 0.42 | 1 | Gancao |
| P79  | MOL005008   | Glicyrhiza flavonol A | 41.28  | 0.60 | 1 | Gancao |
| P1   | MOL004924   | ( )-Medicarpin | 40.99  | 0.95 | 1 | Gancao |
| P156 | MOL004980   | Inflacoumarin A | 39.71  | 0.33 | 1 | Gancao |
| P150 | MOL004815   | (E)-1-(2,4-dihydroxyphenyl)-3-(2,2-dimethylchromen-6-yl)prop-2-en-1-one | 39.62  | 0.35 | 1 | Gancao |
| P124 | MOL004989   | 6-Prenylated eriodictyol | 39.22  | 0.41 | 1 | Gancao |
| P92  | MOL004844   | Licoisoflavone B | 38.93  | 0.55 | 1 | Gancao |
| P181 | MOL004991   | 7-Acetoxy-2-methylisoflavone | 38.92  | 0.26 | 1 | Gancao |
| P203 | MOL004957   | HMO | 38.37  | 0.21 | 1 | Gancao |
| P158 | MOL004945   | (2S)-7-hydroxy-2-(4-hydroxyphenyl)-8-(3-methylbut-2-enyl)chroman-4-one | 36.57  | 0.32 | 1 | Gancao |
| P101 | MOL004978   | 2’-[3(R)-8,8-dimethyl-3,4-dihydro-2h-pyran-6,5-f]chromen-3-yl]-5-methoxyphenol | 36.21  | 0.52 | 1 | Gancao |
| P125 | MOL004935   | Sigmodin-B | 34.88  | 0.41 | 1 | Gancao |
| P216 | MOL001792   | DFV | 32.76  | 0.18 | 1 | Gancao |
| P172 | MOL004988   | Kanzonol F | 32.47  | 0.89 | 1 | Gancao |
| P211 | MOL004833   | Phaseolinosilvan | 32.01  | 0.45 | 1 | Gancao |
| P120 | MOL004814   | Isotrifoliol | 31.94  | 0.42 | 1 | Gancao |
systemic damage caused by free radicals [57–59]. It was reported to block the activation of MAPK and NF-κB signaling pathways to protect ARPE-19 cells from the proliferation of IL-6, IL-8, sICAM-1, and MCP-1 stimulated by IL-1β, thereby alleviating the inflammatory response [60]. Kaempferol, having antioxidant, anti-inflammatory, anti-cancer, and antidiabetic effects, could effectively improve allergic and inflammatory airway diseases by interfering with NF-κB signal transduction, which may help alleviate the inflammatory response associated with Cox2 expression [61–63]. Naringenin, having immunomodulatory, anticancer, antimutation, anti-inflammatory, antioxidant, antiproliferative, antiarthritic, and anticarcinogenic effects, can be used for treating osteoporosis, cancer, cardiovascular disease, and rheumatoid arthritis, which exhibits lipid-lowering and insulin-like properties, can inhibit allergen-induced airway inflammation and airway responsiveness, and inhibit NF-κB activity in a mouse model of asthma [64–66]. The above results indicate that SLBZP can fully exert its therapeutic effect by the synergy of multiple compounds, multiple targets, and multiple pathways and provide more new clues for the development of traditional Chinese medicine monomers to treat BA and AC. In addition, the effects of beta-carotene in treating BA and AC are currently seldom studied and reported, which can be used as a direction for in-depth research in the future.

PTGS2, as the most critical target in the network, is one of the key factors of cell response to inflammation and has long been considered to play a key role in the pathogenesis of respiratory inflammation, including asthma [67, 68]. In addition to its anti-inflammatory effect, it can also exert anti-inflammatory/bronchial protection functions in the airway and can be expressed quickly and powerfully in response to various proinflammatory cytokines and mediators [68]. Caspase-3 is necessary for the development of various tissues, playing an important role in neurogenesis, synaptic activity, neuron growth cone guidance, and glial development. It was reported to mediate many nonapoptotic functions in cells and cell death in the process of apoptosis, participate in T and B cell homeostasis in a way that did not depend on apoptosis, and protect compressed organs from cell death [69]. AKT1 ablation promoted the polarization of macrophage M1, which could affect the severity of inflammatory diseases, such as inflammatory bowel disease, and was related to the regulation of innate immunity and inflammation [70]. JUN, the activation of which is caused by the imbalance of pulmonary oxidation and antioxidation in asthma, is an important therapeutic target for allergic airway inflammation and a key transcription factor for the anti-inflammatory activity of dexamethasone and may be an important molecular mechanism of steroids in asthma and other chronic inflammatory lung diseases [71, 72]. As an important mediator of oncogenic β-catenin signaling in the intestine, JUN is not only involved in inflammatory response and tumorigenesis but is also related to the inflammatory response in mice with LPS-induced macrophages and DSS-

| Code | Molecule ID | Molecule name | OB (%) | DL | Degree | Herbs       |
|------|-------------|---------------|--------|----|--------|-------------|
| P60  | MOL004805   | (2S)-2-[(4-hydroxy-3-(3-methylbut-2-etyl)phenyl]-8,8-dimethyl-2,3-dihydroprano [2,3-f]chromen-4-one | 31.79  | 0.72 | 1      | Gancao     |
| P126 | MOL004864   | 5,7-Dihyroxy-3-(4-methoxyphenyl)-8-(3-methylbut-2-etyl) | 30.49  | 0.41 | 1      | Gancao     |
| P87  | MOL004806   | Euchrenone    | 30.29  | 0.57 | 1      | Gancao     |
| P210 | MOL000230   | Pinocembrin   | 57.56  | 0.20 | 1      | Gancao     |
| P189 | MOL005573   | Genkwanin     | 37.13  | 0.24 | 1      | Gancao     |
| P176 | MOL005575   | Gentiacaulein | 72.82  | 0.27 | 1      | Gancao     |
| P147 | MOL003673   | Wighteone     | 42.80  | 0.36 | 1      | Gancao     |
| P177 | MOL001735   | Hispidulin    | 30.97  | 0.27 | 1      | Gancao     |
| P183 | MOL003617   | Isogosferol   | 30.07  | 0.25 | 1      | Gancao     |
| P76  | MOL004071   | Tetrahidropalmatine | 73.94  | 0.64 | 1      | Gancao     |
| P169 | MOL007206   | Armpavine     | 69.31  | 0.29 | 1      | Lianzi     |
| P144 | MOL009172   | Pronuiferine  | 32.75  | 0.37 | 1      | Lianzi     |
| P131 | MOL007213   | Nuciferine    | 34.43  | 0.40 | 1      | Lianzi     |
| P31  | MOL001323   | Sitosterol alpha1 | 43.28  | 0.78 | 1      | Yiyiren    |
| P213 | MOL001494   | Mandenol      | 42.00  | 0.19 | 1      | Yiyiren    |
| P6   | MOL001474   | Sanguinarine  | 37.81  | 0.86 | 1      | Sharen     |
| P138 | MOL006980   | Papaverine    | 64.04  | 0.38 | 1      | Sharen     |
| P190 | MOL000492   | (+)-Catechin  | 54.83  | 0.24 | 1      | Sharen, baibiandou |
| P178 | MOL004580   | cis-dihydroquercetin | 66.44  | 0.27 | 1      | Jiegeng    |
| P9   | MOL008752   | Dihydroverticillatine | 42.69  | 0.84 | 1      | Jiegeng    |
| P179 | MOL001736   | (-)-Taxifolin | 60.51  | 0.27 | 1      | Shanyao    |
| P136 | MOL005430   | Hancinone C   | 59.05  | 0.39 | 1      | Shanyao    |
| P139 | MOL003322   | Kadsurenone   | 54.72  | 0.38 | 1      | Shanyao    |
| P33  | MOL005465   | AIDS180907    | 45.33  | 0.77 | 1      | Shanyao    |
| P180 | MOL005267   | Elymoclavine  | 72.87  | 0.27 | 1      | Shanyao    |
| P214 | MOL004058   | Deltoside     | 33.19  | 0.19 | 1      | Shanyao    |
induced colitis [73, 74]. TP53, as a tumor suppressor protein, can produce anti-inflammatory reactions in the lungs and has a potential therapeutic effect in pneumonia, whose dysfunction is associated with acute lung injury, acute respiratory distress syndrome, chronic obstructive pulmonary disease, pulmonary fibrosis, bronchial asthma, pulmonary hypertension, pneumonia and tuberculosis, and so on [75]. It often mutates in human cancers. After the mutations, it prolongs the activation of NF-κB and promotes chronic inflammation and inflammation-related colorectal cancer,

*Table 4: Docking results of target proteins and active compounds.*

| Target proteins | PDB ID | Compounds | Binding energy (kcal/mol) | Target proteins | PDB ID | Compounds | Binding energy (kcal/mol) |
|-----------------|--------|-----------|---------------------------|-----------------|--------|-----------|---------------------------|
| IL6             | 1ALU   | Quercetin | −7.2                      | AKT1           | 1UNQ   | Quercetin | −6.2                      |
|                 |        | Luteolin  | −7.2                      |                 |        | Luteolin  | −6.3                      |
|                 |        | Beta-carotene | −7.6                  |                 |        | Beta-carotene | −6.9                  |
|                 |        | Kaempferol | −6.8                      |                 |        | Kaempferol | −6.0                      |
|                 |        | Naringenin | −6.9                      |                 |        | Naringenin | −7.0                      |
| ALB             | 6YG9   | Quercetin | −9.8                      | TP53           | 5MHC   | Quercetin | −7.4                      |
|                 |        | Luteolin  | −10.1                     |                 |        | Luteolin  | −7.9                      |
|                 |        | Beta-carotene | −8.2                  |                 |        | Beta-carotene | −9.1                  |
|                 |        | Kaempferol | −8.8                      |                 |        | Kaempferol | −7.6                      |
|                 |        | Naringenin | −8.2                      |                 |        | Naringenin | −7.2                      |
| VEGFA           | 1MKK   | Quercetin | −7.4                      | TNF            | 5UUI   | Quercetin | −6.9                      |
|                 |        | Luteolin  | −7.8                      |                 |        | Luteolin  | −7.0                      |
|                 |        | Beta-carotene | −7.6                  |                 |        | Beta-carotene | −7.3                  |
|                 |        | Kaempferol | −7.3                      |                 |        | Kaempferol | −6.9                      |
|                 |        | Naringenin | −7.5                      |                 |        | Naringenin | −6.4                      |
| MAPK3           | 4QTB   | Quercetin | −9.3                      | CASP3          | 2DKO   | Quercetin | −7.0                      |
|                 |        | Luteolin  | −9.5                      |                 |        | Luteolin  | −6.9                      |
|                 |        | Beta-carotene | −9.0                  |                 |        | Beta-carotene | −6.2                  |
|                 |        | Kaempferol | −9.3                      |                 |        | Kaempferol | −6.7                      |
|                 |        | Naringenin | −7.9                      |                 |        | Naringenin | −6.5                      |
| JUN             | 6Y3V   | Quercetin | −6.5                      | PTGS2          | 5F19   | Quercetin | −9.7                      |
|                 |        | Luteolin  | −6.5                      |                 |        | Luteolin  | −10.0                     |
|                 |        | Beta-carotene | −7.3                  |                 |        | Beta-carotene | −8.7                  |
|                 |        | Kaempferol | −6.3                      |                 |        | Kaempferol | −9.3                      |
|                 |        | Naringenin | −6.5                      |                 |        | Naringenin | −8.2                      |
| STAT3           | 6NJS   | Quercetin | −8.2                      | MAPK8          | 2XRW   | Quercetin | −8.2                      |
|                 |        | Luteolin  | −8.0                      |                 |        | Luteolin  | −8.6                      |
|                 |        | Beta-carotene | −7.0                  |                 |        | Beta-carotene | −9.7                  |
|                 |        | Kaempferol | −7.9                      |                 |        | Kaempferol | −8.6                      |
|                 |        | Naringenin | −7.2                      |                 |        | Naringenin | −6.4                      |
| MMP9            | 6ESM   | Quercetin | −10.7                     | CXCL8          | 4XDX   | Quercetin | −7.5                      |
|                 |        | Luteolin  | −10.9                     |                 |        | Luteolin  | −7.7                      |
|                 |        | Beta-carotene | −8.8                  |                 |        | Beta-carotene | −9.2                  |
|                 |        | Kaempferol | −10.3                     |                 |        | Kaempferol | −7.6                      |
|                 |        | Naringenin | −8.7                      |                 |        | Naringenin | −6.7                      |
| EGFR            | 5HG8   | Quercetin | −8.3                      | MAPK1          | 6SLG   | Quercetin | −8.1                      |
|                 |        | Luteolin  | −8.6                      |                 |        | Luteolin  | −8.3                      |
|                 |        | Beta-carotene | −9.2                  |                 |        | Beta-carotene | −8.4                  |
|                 |        | Kaempferol | −8.5                      |                 |        | Kaempferol | −8.1                      |
|                 |        | Naringenin | −7.9                      |                 |        | Naringenin | −7.5                      |
| EGF             | 1JL9   | Quercetin | −6.6                      | MYC            | 6G6K   | Quercetin | −7.2                      |
|                 |        | Luteolin  | −6.8                      |                 |        | Luteolin  | −7.9                      |
|                 |        | Beta-carotene | −6.8                  |                 |        | Beta-carotene | −7.8                  |
|                 |        | Kaempferol | −6.8                      |                 |        | Kaempferol | −7.6                      |
|                 |        | Naringenin | −5.9                      |                 |        | Naringenin | −7.4                      |
| IL1B            | 5R8Q   | Quercetin | −7.1                      | FOS            | 1A02   | Quercetin | −8.3                      |
|                 |        | Luteolin  | −7.8                      |                 |        | Luteolin  | −9.3                      |
|                 |        | Beta-carotene | −7.8                  |                 |        | Beta-carotene | −8.8                  |
|                 |        | Kaempferol | −7.0                      |                 |        | Kaempferol | −8.1                      |
|                 |        | Naringenin | −6.9                      |                 |        | Naringenin | −9.3                      |
which is also related to the occurrence and development of inflammatory bowel disease [76–78]. VEGFA plays a fundamental role in the physiological and pathophysiological forms of angiogenesis. During airway growth, the balance regulation of angiogenic growth factor and vascular inhibitory protein enables the lung to obtain rich blood supply [79]. However, during chronic inflammation, VEGF stimulates angiogenesis and edema and induces Th2 and eosinophilic inflammation, mucous metaplasia, subepithelial fibrosis, myocyte proliferation, and dendritic cell activation, which is a sign of asthma exacerbation and can be used as a target for treating lung diseases and inflammatory bowel diseases [79–82]. The above studies indicate that these six key targets deserve attention in the study of the molecular mechanism of SLBZP for treating BA and AC with simultaneous treatment of different diseases and can be used as potential research objects.

The key target-miRNA network shows that hsa-miR-16-5p, hsa-miR-101-3p, hsa-miR-143-3p, hsa-miR-199a-5p, hsa-miR-30d-5p, hsa-miR-30c-5p, hsa-miR-30e-5p, hsa-miR-302d-3p, hsa-miR-203a-3p, hsa-miR-200b-3p, hsa-miR-125a-5p, hsa-miR-15a-5p, and hsa-miR-199a-5p all target and regulate multiple key targets, which may have important upstream regulatory effects and are of great significance for the occurrence, development, and treatment of BA and AC. Studies suggested that baseline airway secretion signatures of hsa-miR-302d-3p and hsa-miR-612 were detected during rhinovirus (RV) infection that was the most common cause of asthma exacerbation and the most important early risk factor for asthma development after childhood in children, which was helpful to develop novel strategies for treating and monitoring respiratory conditions in all age groups [83]. The low tissue level of hsa-miR-200b-3p is related to the cytopathic inflammation caused by human cytomegalovirus infection [84]. Hsa-miR-15a-5p may play an important role in reducing retinal leukopenia by inhibiting inflammatory cell signals, which can be used as a potential target for the inhibition of inflammatory mediators in diabetic retinopathy [85]. In addition to these miRNAs that could target and regulate multiple key targets, hsa-miR-146a-5p, as one of the predicted miRNAs, was upregulated in asthmatic patients to inhibit the expression level of PDE7A, which might be involved in mediating the pathogenesis of asthma [86]. Upregulation of Hsa_circ_0005519 could inhibit the expression of has-let-7a-5p in CD4 T cells of asthmatic patients and promote the production of IL-13 and IL-6, thereby exacerbating asthma [87]. Combining hsa-miR-155-5p and has-miR-532-5p could predict changes in asthma budesonide (ICS) treatment response over time [88]. In allergic settings, the expressions of hsa-miR-139-5p and has-miR-542-3p significantly decreased, resulting in increasing expression of pro-inflammatory and antiviral response genes, which might be important during asthma exacerbations [89]. Hsa-miR-19b-3p decreased in the plasma of BA patients, and the ROC curve showed that it could be used as a biomarker for the diagnosis of BA [90]. Hsa-miR-20a-5p, one of the dysregulated miRNAs in asthmatic patients, targeted and inhibited the expression of HDAC4, suppressed the expressions of TNF-α, IL-1β, and IFN-γ, and promoted the production of IL-10, thereby reducing allergic inflammation [91]. Downregulation of hsa-miR-145-5p that increased airway smooth muscle cell proliferation was a risk factor for an early decline (ED) pattern of lung function growth in asthmatic children with chronic obstructive pulmonary disease (COPD) [92]. Once again, it is
particularly noted that, at present, there are basically no relevant research reports on these predicted miRNAs related to AC, and there are also very few research reports on these predicted miRNAs related to BA, which means that this study not only provides new insights for in-depth understanding of the pathogenesis of BA and AC and formulating corresponding new treatment strategies but also provides a practical basis for future validation studies. In general, there are few reports on the above-mentioned miRNAs that have great research potentials.

Figure 8: 3D and 2D diagrams of molecular docking. (a) MMP9 (6ESM) and luteolin. (b) MMP9 (6ESM) and quercetin. (c) MMP9 (6ESM) and kaempferol. (d) ALB (6YG9) and luteolin. (e) PTGS2 (5F19) and luteolin.
5. Conclusions

In conclusion, network pharmacology and molecular docking technology demonstrated that SLBZP in treating BA and AC with simultaneous treatment of different diseases was a complex process involving multiple compounds, multiple targets, and multiple pathways. It may involve important active compounds and key targets represented by quercetin, luteolin, beta-carotene, kaempferol, naringenin, PTGS2, CASP3, AKT1, JUN, TP53, and VEGFA, may be related to inflammation, cancer, apoptosis, and immune-related pathways, and may involve the targeted regulation of multiple upstream miRNAs. These can provide references for future clinical and experimental studies.

Data Availability

The data used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Liying Zeng collected and analyzed all the data and is the major writer of the paper. Shaodan Sun, Piwen Chen, and Qina Ye helped in writing the paper and contributed to the analysis of these data. Xiaoling Lin, Hongjun Wan, and Yawan Cai revised the paper. Liying Zeng and Xiaogang Chen designed the study. Xiaogang Chen also revised the paper. All the authors have read and approved the manuscript.

Acknowledgments

This study was supported by grants from the National Natural Science Foundation of China (No. 81674021), the Natural Science Foundation of Guangdong Province (No. 2017A030313788), and National Famous Old Chinese Medicine Expert Li Yirui’s Inheritance Studio Construction Project (Chinese Medicine Ren Jiao Han (No.[2018]134)).

References

[1] A. Papi, C. Brightling, S. E. Pedersen, and H. K. Reddel, “Asthma,” The Lancet, vol. 391, no. 10122, pp. 783–800, 2018.
[2] M. W. Pijnenburg and L. Fleming, “Advances in understanding and reducing the burden of severe asthma in children,” The Lancet Respiratory Medicine, vol. 8, no. 10, pp. 1032–1044, 2020.
[3] M.-C. Yu, C.-L. Tsai, Y.-J. Yang et al., “Allergic colitis in infants related to cow’s milk: clinical characteristics, pathologic changes, and immunologic findings,” Pediatrics & Neonatology, vol. 54, no. 1, pp. 49–55, 2013.
[4] M. E. Baldassarre, A. Cappiello, N. Laforgia, and J. Vanderhoof, “Allergic colitis in monozygotic preterm twins,” Immunopharmacology and Immunotoxicology, vol. 35, no. 1, pp. 198–201, 2013.
[5] J. M. E. Fell, “Neonatal inflammatory intestinal diseases: necrotising enterocolitis and allergic colitis,” Early Human Development, vol. 81, no. 1, pp. 117–122, 2005.
[6] D. E. Campbell, R. J. Boyle, C. A. Thornton, and S. L. Prescott, “Mechanisms of allergic disease - environmental and genetic determinants for the development of allergy,” Clinical and Experimental Allergy: Journal of the British Society for Allergy and Clinical Immunology, vol. 45, no. 5, pp. 844–858, 2015.
[7] G. F. Parisi, A. Licari, and M. Papale, “Antihistamines: ABC for the pediatricians,” Pediatric allergy and immunology:
Evidence-Based Complementary and Alternative Medicine

official publication of the European Society of Pediatric Allergy and Immunology, vol. 31, no. S24, pp. 34–36, 2020.

[8] P. Kuna, D. Jurkiewicz, M. M. Czarnecka-Operacz et al., “The role and choice criteria of antihistamines in allergy management - expert opinion,” Advances in Dermatology and Allergology, vol. 33, no. 6, pp. 397–410, 2016.

[9] D. Silva, I. Ansotegui, and M. Moraís-Almeida, “Off-label prescribing for allergic diseases in children,” The World Allergy Organization journal, vol. 7, no. 1, p. 4, 2014.

[10] X.-M. Li, “Traditional Chinese herbal remedies for asthma and food allergy,” The Journal of Allergy and Clinical Immunology, vol. 120, no. 1, pp. 25–31, 2007.

[11] X.-M. Li and K. Szivastava, “Traditional Chinese medicine for the therapy of allergic disorders,” Current Opinion in Otolaryngology & Head and Neck Surgery, vol. 14, no. 3, pp. 191–196, 2006.

[12] P. B. D. Bureau and J. Liu, Prescriptions of Peaceful Beneficent Dispensary, People’s Health Publishing House, Beijing, 2017.

[13] Y. Bai, J. Wang, L. Chi, Y. Ba, and W. Wang, “Modern recognition of the role and choice criteria of antihistamines in allergy management - expert opinion,” Allergy, vol. 71, no. 4, pp. 486–491, 2016.

[14] J. Ru, P. Li, J. Wang et al., “TCMSP: a database of systems management - expert opinion,” OMICS: A Journal of Integrative Biology, vol. 16, no. 5, pp. 284–287, 2012.

[15] D. Otasek, J. H. Morris, J. Bouças, A. R. Pico, and B. Demchak, “Cytoscape Automation: empowering workflow-based network analysis,” Genome Biology, vol. 20, no. 1, p. 185, 2019.

[16] H.-Y. Xu, Y.-Q. Zhang, Z.-M. Liu et al., “ETCM: an encyclopedia of traditional Chinese medicine,” Nucleic Acids Research, vol. 47, no. D1, pp. D976–D982, 2019.

[17] H. Yuan, Q. Ma, H. Cui et al., “How can synergism of traditional medicines benefit from network pharmacology?” Molecules, vol. 22, no. 7, p. 1135, 2017.

[18] Z. Liu, F. Guo, Y. Wang et al., “BATMAN-TCM: a Bioinformatics analysis tool for molecular mechANism of traditional Chinese medicine,” Scientific Reports, vol. 6, no. 1, p. 21146, 2016.

[19] T. E. Klein, “PharmGKB: a worldwide resource for pharmacogenomic information,” Wiley interdisciplinary reviews. Systems biology and medicine, vol. 10, no. 4, Article ID e1417, 2018.

[20] J. S. Amberger, C. A. Bocchini, F. Schiettecatte, A. F. Scott, and A. Hamosh, “OMIM.org: online Mendelian Inheritance in Man (OMIM), an online catalog of human genes and genetic disorders,” Nucleic Acids Research, vol. 43, no. D1, pp. D789–D794, 2015, Database issue.

[21] G. R. Brown, V. Hem, K. S. Katz et al., “Gene: a gene-centered information resource at NCBI,” Nucleic Acids Research, vol. 43, no. D1, pp. D36–D42, 2015, Database issue.

[22] S. Kühler, M. Gargano, N. Matentzoglu et al., “The Human Phenotype Ontology in 2021,” Nucleic Acids Research, vol. 49, no. D1, pp. D1207–D1217, 2021.

[23] Y. Wu, F. Zhang, K. Yang et al., “Cross-talk of signaling pathways in the pathogenesis of allergic asthma and cataract,” Protein and Peptide Letters, vol. 27, no. 9, pp. 810–822, 2020.

[24] W. Liu, Q. Liang, S. Balzar, S. Wenzel, M. Gorska, and R. Alam, “Cell-specific activation profile of extracellular signal-regulated kinase 1/2, Jun N-terminal kinase, and p38 mitogen-activated protein kinases in asthmatic airways,” The Journal of Allergy and Clinical Immunology, vol. 121, no. 4, pp. 893–902, 2008.

[25] Y. Rose, J. M. Duarte, R. Lowe et al., “RCSB protein data bank: architectural advances towards integrated searching and efficient access to macromolecular structure data from the PDB archive,” Journal of Molecular Biology, vol. 433, no. 11, Article ID 166704, 2021.

[26] J. M. Barbarino, M. Whirl-Carrillo, R. B. Altman, and T. E. Klein, “PharmGKB: a worldwide resource for pharmacogenomic information,” Wiley interdisciplinary reviews. Systems biology and medicine, vol. 10, no. 4, Article ID e1417, 2018.
signalling pathway in asthma,” *Journal of Cellular and Molecular Medicine*, vol. 24, no. 23, pp. 13739–13750, 2020.

[42] C. Pelaia, A. Vatrella, C. Crimi, L. Gallelli, R. Terracciano, and G. Pelaia, “Clinical relevance of understanding mitogen-activated protein kinases involved in asthma,” *Expert Review of Respiratory Medicine*, vol. 14, no. 5, pp. 501–510, 2020.

[43] J. Theodorou, E. Nowak, and A. Böck, “Mitogen-activated protein kinase signaling in childhood asthma development and environment-mediated protection,” *Pediatric Allergy & Immunology: Official Publication of the European Society of Pediatric Allergy and Immunology*, vol. 33, no. 1, p. e13657, 2022.

[44] J. Huang, R. Olivenstein, R. Taha, Q. Hamid, and M. Ludwig, “Enhanced proteoglycan deposition in the airway wall of atopic asthmatics,” *American Journal of Respiratory and Critical Care Medicine*, vol. 160, no. 2, pp. 725–729, 1999.

[45] L. Pini, Q. Hamid, J. Shannon et al., “Enhanced proteoglycan deposition in the airways of moderate and severe asthmatics,” *European Respiratory Journal*, vol. 29, no. 1, pp. 71–77, 2007.

[46] T. Herjan, L. Hong, J. Bubenik et al., “IL-17-receptor-associated adaptor Act1 directly stabilizes mRNAs to mediate IL-17 inflammatory signaling,” *Nature Immunology*, vol. 19, no. 4, pp. 354–365, 2018.

[47] A. Linden and B. Dahlen, “Interleukin-17 cytokine signalling in patients with asthma,” *European Respiratory Journal*, vol. 44, no. 5, pp. 1319–1331, 2014.

[48] M. Sauler, I. S. Bazan, and P. J. Lee, “Cell death in the lung: the apoptosis-necroptosis Axis,” *Annual Review of Physiology*, vol. 81, no. 1, pp. 375–402, 2019.

[49] J. Louten, K. Boniface, and R. de Waal Malefyt, “Development and function of TH17 cells in health and disease,” *The Journal of Allergy and Clinical Immunology*, vol. 123, no. 5, pp. 1004–1011, 2009.

[50] S. Burgler, N. Ouaked, C. Bassin et al., “Differentiation and functional analysis of human TH17 cells,” *The Journal of Allergy and Clinical Immunology*, vol. 123, no. 3, pp. 588–595, 2009.

[51] A. H. Massoud, L.-M. Charbonnier, D. Lopez, M. Pellegrini, W. Phipatanakul, and T. A. Chatila, “An asthma-associated IL4R variant exacerbates airway inflammation by promoting conversion of regulatory T cells to TH17-like cells,” *Nature Medicine*, vol. 22, no. 9, pp. 1013–1022, 2016.

[52] S.-C. Cheng, W.-C. Huang, J.-H. S Pang, Y.-H. Wu, and C.-Y. Cheng, “Quercetin inhibits the production of IL-1β-induced inflammatory cytokines and chemokines in ARPE-19 cells via the MAPK and NF-kB signaling pathways,” *International Journal of Molecular Sciences*, vol. 20, no. 12, p. 2957, 2019.

[53] J. Mlcek, T. Jurikova, S. Skrovankova, and J. Sochor, “Quercetin and its anti-allergic immune response,” *Molecules*, vol. 21, no. 5, p. 623, 2016.

[54] J.-j. Park, C.-M. Lee, I. D. Jung et al., “Quercetin regulates Th1/Th2 balance in a murine model of asthma,” *International Immunopharmacology*, vol. 9, no. 3, pp. 261–267, 2009.

[55] J. Mlcek, T. Jurikova, S. Skrovankova, and J. Sochor, “Quercetin regulates Th2/Th1 balance in a murine model of asthma,” *International Immunopharmacology*, vol. 9, no. 3, pp. 261–267, 2009.
regulation of AP-1 transcription factor in human lung epithelial cells," *Gene*, vol. 645, pp. 85–94, 2018.

[72] C. Nguyen, J.-L. Teo, A. Matsuda et al., "Chemogenomic identification of Ref-1/AP-1 as a therapeutic target for asthma," *Proceedings of the National Academy of Sciences*, vol. 100, no. 3, pp. 1169–1173, 2003.

[73] P. Hasselblatt, L. Gresh, H. Kudo, J. Guinea-Viniegra, and E. F. Wagner, "The role of the transcription factor AP-1 in colitis-associated and beta-catenin-dependent intestinal tumorigenesis in mice, " *Oncogene*, vol. 27, no. 47, pp. 6102–6109, 2008.

[74] T. Kim, J. Shin, K. Chung, Y. Lee, N. Baek, and K. Lee, "Anti-inflammatory mechanisms of koreanaside A, a lignan isolated from the flower of forsythia koreana, against LPS-induced macrophage activation and DSS-induced colitis mice: the crucial role of AP-1, NF-κB, and JAK/STAT signaling," *Cells*, vol. 8, no. 10, p. 1163, 2019.

[75] M. A. Uddin and N. Barabutis, "P53 in the impaired lungs," *DNA Repair*, vol. 95, Article ID 102952, 2020.

[76] D. Tran, S. M. Go, S.-M. Park, E.-M. Jung, and E.-B. Jeung, "Loss of Nckx3 exacerbates experimental DSS-induced colitis in mice through p53/NF-κB pathway," *International Journal of Molecular Sciences*, vol. 22, no. 5, p. 2645, 2021.

[77] S. M. Go, S.-M. Park, E.-M. Jung, and E.-B. Jeung, "Loss of Nckx3 exacerbates experimental DSS-induced colitis in mice through p53/NF-κB pathway," *International Journal of Molecular Sciences*, vol. 22, no. 5, p. 2645, 2021.

[78] J. Zhang, M. Xu, W. Zhou et al., "Deficiency in the anti-apoptotic protein DJ-1 promotes intestinal epithelial cell apoptosis and aggravates inflammatory bowel disease via p53," *Journal of Biological Chemistry*, vol. 295, no. 13, pp. 4237–4251, 2020.

[79] J.-H. Kim, "Serum vascular endothelial growth factor as a marker of asthma exacerbation," *Korean Journal of Internal Medicine*, vol. 32, no. 2, pp. 258–260, 2017.

[80] A. P. Laddha and Y. A. Kulkarni, "VEGF and FGF-2: promising targets for the treatment of respiratory disorders," *Respiratory Medicine*, vol. 156, pp. 33–46, 2019.

[81] J. L. Knod, K. Crawford, M. Dusing, M. H. Collins, A. Chernoguz, and J. S. Frischer, "Angiogenesis and vascular endothelial growth factor-A expression associated with inflammation in pediatric crohn's disease," *Journal of Gastrointestinal Surgery*, vol. 20, no. 3, pp. 624–630, 2016.

[82] R. B. Mateescu, A. E. Bastian, L. Nichita et al., "Vascular endothelial growth factor - key mediator of angiogenesis and promising therapeutic target in ulcerative colitis," *Romanian journal of morphology and embryology = Revue roumaine de morphologie et embryologie*, vol. 58, no. 4, pp. 1339–1345, 2017.

[83] M. J. Gutierrez, J. L. Gomez, G. F. Perez et al., "Airway secretory microRNAome changes during rhinovirus infection in early childhood," *PLoS One*, vol. 11, no. 9, Article ID e0162244, 2016.

[84] K. H. Lee, B. J. Lim, V. H. Ferreira et al., "Expression of human miR-200b-3p and -200c-3p in cytomegalovirus-infected tissues," *Bioscience Reports*, vol. 38, no. 6, Article ID R20180961, 2018.

[85] E.-A. Ye, L. Liu, Y. Jiang et al., "miR-15a/16 reduces retinal leukostasis through decreased pro-inflammatory signaling," *Journal of Neuroinflammation*, vol. 13, no. 1, p. 305, 2016.

[86] M.-J. Tsai, Y.-C. Tsai, W.-A. Chang et al., "Deducing MicroRNA-mediated changes common in bronchial epithelial cells of asthma and chronic obstructive pulmonary disease-A next-generation sequencing-guided bioinformatic approach," *International Journal of Molecular Sciences*, vol. 20, no. 3, p. 553, 2019.

[87] Z. Huang, Y. Cao, M. Zhou et al., "Hsa_circ_0005519 increases IL-13/IL-6 by regulating hsa-let-7a-5p in CD4+ T cells to affect asthma," *Clinical and Experimental Allergy: Journal of the British Society for Allergy and Clinical Immunology*, vol. 49, no. 8, pp. 1116–1127, 2019.

[88] J. Li, R. Ranganiban, A. T. Kho et al., "Circulating MicroRNAs and treatment response in childhood asthma," *American Journal of Respiratory and Critical Care Medicine*, vol. 202, no. 1, pp. 65–72, 2020.

[89] C. Herbert, M. Sebesf, Q.-X. Zeng, B. G. Oliver, P. S. Foster, and R. K. Kumar, "Using multiple online databases to help identify microRNAs regulating the airway epithelial cell response to a virus-like stimulus," *Respirology*, vol. 20, no. 8, pp. 1206–1212, 2015.

[90] R. Bersimbaev, A. Aripova, O. Bulgakova, A. Kussainova, A. Akparova, and A. Izzotti, "The plasma levels of hsa-miR-19b-3p, hsa-miR-125b-5p, and hsa-miR-320c-3p in patients with asthma, COPD and asthma-COPD overlap syndrome (ACOS)," *MicroRNA*, vol. 10, no. 2, pp. 130–138, 2021.

[91] Y. Lu, Z. Li, B. Xie, Y. Song, X. Ye, and P. Liu, "hsa-miR-20a-5p attenuates allergic inflammation in HMC-1 cells by targeting HDAC4," *Molecular Immunology*, vol. 107, pp. 84–90, 2019.

[92] A. Tiwari, J. Li, A. T. Kho et al., "COPD-associated miR-145-5p is downregulated in early-decline FEV1 trajectories in childhood asthma," *The Journal of Allergy and Clinical Immunology*, vol. 147, no. 6, pp. 2181–2190, 2021.