Mechanism of Action of a Chinese Herbal Compound Containing Quercetin, Luteolin, and Kaempferol in the Treatment of Vitiligo Based on Network Pharmacology and Experimental Verification

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1.Introduction

Vitiligo is an acquired, chronic depigmenting disorder of the skin. It results from the selective destruction of melanocytes [1]. Approximately 0.5%–1% of the global population is affected by vitiligo. Vitiligo prevalence is not associated with sex or ethnicity [1–3]. Vitiligo is considered to be a multifactorial disease. In addition to genetic and environmental factors, other factors (autoimmune, neural, and oxidative stress) have been suggested to have an effect on vitiligo [4].

Management of vitiligo includes the topical use of glucocorticoids, calcineurin inhibitors, and phototherapy. A small number of patients who meet the indications can also choose surgical transplantation of pigments or decolorization
Evidence-Based Complementary and Alternative Medicine

2 Evidence-Based Complementary and Alternative Medicine

active compounds with thresholds of OB
distribution, metabolism, and excretion, we used oral bio-
base (TCMSP; http://tcmspw.com/tcmsp.php/) [13], as were
Traditional Chinese Medicine System Pharmacology Data-
Te compounds Chaihu, Chishao, Xiangfu,
2.1.Identification of the Active Compounds in BST and Related

Studies have shown that TCM formulations have great
potential in vitiligo treatment [7, 8].
Baishi tablets (BSTs) consist primarily of Chaihu
(bupleurum), Chishao (red peony), Zhixiangfu (rhizome
cyperi), Baishao (white peony), and Zhishi (citrus aur-
antium). BST can replenish qi, promote stagnation, aid blood
circulation and detoxification, and dispel wind. The
dermatology department of our institution has used BST to treat
vitiligo for many years, and excellent outcomes have been
achieved. Our research group conducted a clinical ran-
donized trial in 2015, and the Vitiligo Disease Activity
(VIDA) score of the patients treated with BST was signifi-
cantly reduced [9]. Nevertheless, the components of TCM
formulations have a wide range of functions and complex
active ingredients, and the targets and mechanisms of their
regulation have not been fully studied.

Network pharmacology is a promising method that
combines pharmacology and computer science to construct
and visualize the interaction network of multiple genes,
targets, and signaling pathways. It is highly suitable for
researching drugs with complex ingredients (e.g., TCM
formulations) and is a cost-effective method of drug de-
velopment [10–12].

Herein, we applied network pharmacology to identify the
active ingredients and examine the core targets and signaling
pathways of BST for vitiligo treatment. We also undertook
molecular docking studies to ascertain how BST binds to its
predicted targets. Subsequently, we conducted a series of
in vitro experiments on immortalized human melanocytes.
The flowchart of our study is shown in Figure 1.

2. Materials and Methods

2.1. Identification of the Active Compounds in BST and Related
Target Genes. The compounds Chaihu, Chishao, Xiangfu,
Baishao, and Zhishi were searched and obtained from the
Traditional Chinese Medicine System Pharmacology Data-
base (TCMSP; http://tcmspw.com/tcmsp.php/) [13], as were
their related gene targets and other biological information.
Specifically, to evaluate the characteristics of absorption,
distribution, metabolism, and excretion, we used oral bio-
availability (OB) and drug likeness (DL) to filter candidate
active compounds with thresholds of \( \text{OB} \geq 30\% \) and
\( \text{DL} \geq 0.18 \) [14]. Moreover, the targets of the active com-
 pounds were transformed into gene symbols via the UniProt
database (http://www.uniprot.org/) by limiting the species to
Homo sapiens for further analyses [15].

2.2. Identifying the Target Genes Related to Vitiligo. Vitiligo-
related targets were extracted by screening the
Online Mendelian Inheritance in Man (OMIM; https://
omim.org/) [16], Genecards (http://www.genecards.org/)
[17], PharmGKB (http://www.pharmgkb.org/) [18], Thera-
peutic Target Database (TTD; http://db.idrblab.net/TTD/) [19]
and DrugBank (http://www.drugbank.ca/) [20] databases
using the keyword “vitiligo.” After removing duplicates, a
vitiligo-related gene set was established by combining the
search results.

2.3. Establishment of a Compound–Target–Vitiligo Network
and Functional Analyses. Having prepared two sets of target
lists for the gene targets of compounds and vitiligo-related
targets, screening for drug–disease crossover was carried
out. A Venn diagram was generated with R (R Institute for
Statistical Computing, Vienna, Austria) using the Venn
Diagram package to show the intersection sets. A
compound–target–disease network diagram was established
using Cytoscape 3.8.0 (https://cytoscape.org/) to show the
relationship among vitiligo, BST, and the related gene
targets [21].

Subsequently, analyses of functional enrichment and
enrichment of signaling pathways were undertaken using the
gene ontology (GO; http://geneontology.org/) and Kyoto
genome.jp/kegg/) databases, respectively. The “clusterpro-
file” and “bioconductor” packages within R were employed
to assess the biological process (BP), cellular component
(CC), molecular function (MF), and key signaling pathways.
Significantly enriched terms were identified, and \( p < 0.05 \)
and \( q < 0.05 \) indicated a strong association with related BPs
[22, 23].

2.4. Protein–Protein Interaction (PPI) Networks and Critical
Subnetworks. The Search Tool for the retrieval of interacting
genes/proteins (STRING) (http://string-db.org/) database
[24] was used to identify the biological interactions among
the potential gene targets. Intersecting PPIs were obtained
through the intersecting gene sets of BST and vitiligo. After
importing the results of PPIs into Cytoscape, a diagram of
critical subnetworks was established, and core genes were
investigated using the CytoNca plugin [25]. Eligible genes
were selected if each score was higher than the median value
of betweenness, closeness, degree, the eigenvector, the local
average connectivity-based method, and network scores.
After displaying this analytical process twice, the final results
of the core genes were utilized to establish a critical
subnetwork.

2.5. Molecular Docking. Compounds with the top-three
highest numbers of related critical genes and their com-
mon core genes were selected for molecular docking. After
downloading the two-dimensional (2D) molecular
structure of ligands from the PubChem database (https://
pubchem.ncbi.nlm.nih.gov/) [26], the 3D structure with
the minimum energy was calculated and exported via
ChemBio 3D (http://www.adeptscience.co.uk/products/lab/chembio3d/). Moreover, the 3D structure of the receptor proteins encoded by the core genes was searched in the UniProt database and downloaded from the Research Collaboratory for Structural Bioinformatics Protein Database (https://www.rcsb.org/) [27]. After preparing the files for the 3D structure, the receptor proteins were dehydrated, and ligands were removed using PyMOL (https://pymol.org/2/). AutoDock (https://autodock.scripps.edu/) was utilized to modify the receptor protein as well as carry out the hydrogenation and charging calculations of proteins [28]. Subsequently, the parameters of the docking site of the receptor protein were set to include the sites of the active pocket. Molecular docking between compounds and receptors was investigated via Vina within AutoDock [29].

2.6. Cells and Cell Culture. An immortalized human melanocyte cell line (PIG1) was purchased from the American Type Cell Collection (Manassas, VT, USA). PIG1 cells were cultured in Dulbecco’s modified Eagle’s medium (Gibco, Grand Island, NY, USA) supplemented with 10% fetal bovine serum (Gibco). PIG1 cells were cultured in a 37°C incubator in an atmosphere of 5% CO₂.

2.7. Apoptosis Measurement. PIG1 cells were cultured in 60 mm petri dishes after treatment with 50 μmol/L QU, LU, or KA for 24 h. Then, H₂O₂ (final concentration: 1 mmol/L) was added to each well, and incubation was undertaken for an additional 2 h. Simultaneously, we set up simple compound-treatment groups and a control group (without any treatment). After the previous treatment, we digested PIG1 cells with EDTA-free trypsin, collected them in tubes, washed them twice with phosphate-buffered saline (PBS), and resuspended them in PBS. According to the protocol, PIG1 cells were stained with an Annexin V-FITC Apoptosis Detection Kit (Liankebio, Hangzhou, China) and detected by flow cytometry. FlowJo (http://www.flowjo.com/) was used to measure the percentage of apoptotic cells.

2.8. Measurement of Levels of Intracellular Reactive Oxygen Species (ROS). QU, LU, and KA were purchased from Aladdin (purity ≥98.5%; Shanghai, China). QU, LU, and KA were dissolved in dimethyl sulfoxide (DMSO; Millipore Sigma–Aldrich, Burlington, Massachusetts MA, USA) for further use. PIG1 cells were cultured in six-well plates after being treated with different concentrations (25 or 50 μmol/L) of QU, LU, and KA for 24 h. H₂O₂ was added (final concentration: 1 mmol/L) to each well and incubated for an additional 2 h. After the corresponding treatment, we washed cells twice with serum-free medium. According to product instructions, cells were stained with dichlorodihydrofluorescein diacetate using a reactive oxygen species kit (Shanghai Biyuntian Biotechnology, Shanghai, China) and photographed under an inverted fluorescence microscope (Olympus, Tokyo, Japan).

2.9. Statistical Analyses. The data are the mean ± SD. Statistical analyses were carried out using Prism 7.0 (GraphPad, San Diego, CA, USA) or SPSS 22.0 (IBM, Armonk, NY, USA). The Student’s t- test or one-way analysis of variance was used for multiple group comparisons. The experiments...
were repeated at least three times. \( p < 0.05 \) was considered significant.

### 3. Results

#### 3.1. Active Compounds and Potential Targets.

Using the criteria of \( DL \geq 0.18 \) and \( OB \geq 30\% \), 55 main and efficacious compounds of the five herbs were retrieved and selected (Supplementary Table 1). Subsequently, the compound-related targets were annotated into a gene-symbol set using the UniProt database. After removing duplicates, a set of 1205 vitiligo-related targets (Supplementary Table 2A) were established by extraction from the OMIM, GeneCards, PharmGkb, TTD, and DrugBank databases (Figure 2(a), Supplementary Table 2B). Moreover, an intersection of the compound targets and vitiligo-related genes, which contained 71 target proteins (Supplementary Table 2C), was obtained (Figure 2(b)).

#### 3.2. Network Analysis of Targets.

A compound–disease–target interaction network (Figure 3) was visualized using the Cytoscape to reflect the relationship among the compounds in BST, vitiligo, and their intersecting genes. The number of possible efficacious compounds of BST related to vitiligo treatment was 43. The top five active ingredients influencing the most genes were QU (50 genes), LU (25 genes), KA (24 genes), isorhamnetin (15 genes), and baicalein (15 genes). The top five related gene proteins in the intersecting genes were POLG (15 genes), CALM1 (20 genes), DPP4 (18 genes), F2 (18 genes), and PRSS1 (16 genes).

#### 3.3. Enrichment Analyses.

Analyses of functional enrichment using the GO database revealed the underlying BPs, CCs, and MFs of the 71 target genes. Using \( p < 0.05 \) and \( q < 0.05 \) as criteria, 2112 significantly enriched GO terms were obtained: 1975 BPs, 26 CCs, and 111 MFs. The top 10 terms is shown in Figure 4(a).

The top 10 BPs were responses to metal ions; nutrient levels; lipopolysaccharide; molecules of “bacterial origin,” “radiation,” “oxidative stress,” “aging,” “antibiotics,” “drugs,” and “reactive to oxygen species.”

The top 10 CCs were “cyclin-dependent protein kinase holoenzyme complex,” “membrane raft,” “membrane microdomain,” “membrane region,” “caveola,” “serine/threonine-protein kinase complex,” “transcription factor complex,” “nuclear chromatin,” “mitochondrial outer membrane,” and “plasma membrane raft.”

The top 10 MFs were “cytokine activity,” “cytokine receptor binding,” “receptor ligand activity,” “phosphatase binding,” “transcription cofactor binding,” “RNA polymerase II basal transcription factor binding,” “gene binding,” “protein phosphatase binding,” “tetrapyrrole binding,” and “transcription coactivator binding.”

Using \( p < 0.05 \) and \( q < 0.05 \) as criteria, analyses of signaling-pathway enrichment using the KEGG database were performed. We found that 165 potential signaling pathways were enriched (Supplementary Table 3), and the top 30 signaling pathways are shown in Figure 4(b). Bubble plots demonstrated that these gene targets affected signaling pathways related to the “biological process of oxidative stress such as lipid and atherosclerosis,” “AGE-RAGE signaling pathway in diabetic complications,” “fluid shear stress,” and “atherosclerosis.”
3.4. PPI Diagram and Core Subnetwork. Seventy-one overlapping genes associated with vitiligo and BST were inputted into the STRING database, and a PPI network diagram was established after selecting Homo sapiens. The PPI network contained 71 nodes and 821 edges (Figure 5(a), Supplementary Table 4). After importing the results from the PPI network into Cytoscape and using the CytoNCA plugin, these related genes were identified twice to establish a core-gene subnetwork. The median values of betweenness, closeness, degree, eigenvector, local average connectivity-based method, and network scores in the calculations were 17.06899034, 0.584745763, 22.5, 0.109364353, 15.794871795, and 18.691161565, respectively, in the first identification and 5.78362403, 0.8170634925, 22.5, 0.180951178, 18.09090909, and 20.229612495, respectively, in the second identification. A further core subnetwork containing 13 nodes and 77 edges was obtained. These 13 core gene targets were HMOX1, CXCL8, CCL2, IL6, MAPK8, CASP3, PTGS2, AKT1, IL1B, MYC, TP53, IFNG, and IL2 (Figure 5(b)). The results from the analyses of functional enrichment and enrichment of signaling pathways using the GO and KEGG databases, respectively, revealed that the core genes were involved in the "cellular response to oxidative stress" and had critical roles in signaling pathways. Detailed information on these compounds is summarized in Supplementary Table 5.

3.5. Molecular Docking. Referring to the results of the core gene network, we selected the top-three compounds (QU, LU, and KA) that influenced most vitiligo-related genes as ligands. Then, we conducted molecular docking on these core genes. According to our previous analyses, QU influenced 12 core genes (PTGS2, AKT1, IL6, CASP3, TP53, HMOX1, MYC, IL1B, CCL2, CXCL8, IL2, and IFNG), LU affected eight core genes (PTGS2, AKT1, IL6, CASP3, TP53, HMOX1, IL2, and IFNG) and KA regulated five core genes (PTGS2, AKT1, CASP3, MAPK8, and HMOX1). Subsequently, an additional calculation was made to simulate the molecular docking of three compounds with four common protein receptors: PTGS2 (protein database (PDB) code: 5KIR), AKT1 (PDB code: 6HHG), CASP3 (PDB code: 3PD0) and HMOX1 (PDB code: 1N45). The results of molecular docking and affinity values are listed in Figure 6. A greater absolute value for the docking affinity indicates a stronger binding ability between the active site of a protein receptor and a compound. The docking results indicated that QU, LU, and KA could enter and bind the active pocket of the four core target proteins, could form hydrogen bonds with amino acid residues, and exhibited high binding affinity.

3.6. Experimental Validation

3.6.1. QU, LU, And KA Reduced H2O2-Induced PIG1 Apoptosis. We wished to verify the prediction results of the previous compound–disease–target interaction network. We screened out the three compounds with the most extensive targets for vitiligo for experimental verification: QU, LU, and KA. The role of QU, LU, and KA in melanocytes
response to metal ion
response to nutrient levels
response to lipopolysaccharide
response to molecule of bacterial origin
response to radiation
response to oxidative stress
aging
response to antibiotic
cellular response to drug
response to reactive oxygen species
membrane raft
membrane microdomain
membrane region
transcription factor complex
nuclear chromatin
mitochondrial outer membrane
cyclin–dependent protein kinase holoenzyme complex
caveola
serine/threonine protein kinase complex
plasma membrane raft
receptor ligand activity
cytokine activity
cytokine receptor binding
phosphatase binding
heme binding
protein phosphatase binding
tetrapyrrole binding
transcription cofactor binding
RNA polymerase II basal transcription factor binding
transcription coactivator binding

Figure 4: Continued.
under oxidative stress was explored by treating PIG1 cells with H$_2$O$_2$ to mimic the environment of cellular oxidative stress. We used flow cytometry to measure H$_2$O$_2$-induced apoptosis in PIG1 cells. H$_2$O$_2$ induced apoptosis, but pretreatment with QU, LU, or KA significantly reduced apoptosis. PIG1 cells treated with QU, LU, or KA alone did not induce significant apoptosis. There was a significant difference in the percent apoptosis between the pure H$_2$O$_2$-treated group and compound-pretreated groups ($p < 0.05$ and $p < 0.01$) (Figure 7).

3.6.2. QU, LU, And KA Scavenged H$_2$O$_2$-Induced Intracellular ROS in PIG1 Cells. First, PIG1 cells in the treatment groups were pretreated with different concentrations (25 or 50 μmol/L) of QU, LU, or KA. Subsequently, PIG1 cells were treated with H$_2$O$_2$ to simulate the environment of cellular oxidative stress, and we measured ROS production by fluorescence staining. Compared with PIG1 cells in the pure H$_2$O$_2$ environment, ROS levels in PIG1 cells decreased in all three groups that were pretreated with 25 or 50 μmol/L of compounds. ROS levels decreased in the same treatment group with increasing concentrations of the compound, respectively (Figure 8). These results suggested that QU, LU, and KA could reduce ROS in melanocytes and protect melanocytes from oxidative stress to a certain extent.

4. Discussion
Vitiligo is caused by melanocyte destruction. Vitiligo pathogenesis could be due to heredity, autoimmunity, neurochemical factors, or oxidative stress [1, 2]. Oxidative
Figure 5: Continued.
Figure 5: Protein-protein interaction network for BST in the treatment of vitiligo and core targets. (a) Protein-protein interactions among the 71 genes. Network nodes represent proteins, and edges represent protein-protein associations. (b) Core gene subnetwork of 71 overlapping genes.

Figure 6: Virtual molecular docking results.
Figure 7: QU, LU, and KA attenuate H₂O₂-induced apoptosis in PIG1 cells. The cells were pretreated with QU, LU, and KA 50 μmol/L for 24 h; then, the cells were treated with H₂O₂ (final concentrations: 1.0 mmol/L) for 2 h. In addition, we set up QU, LU, KA-treated (50 μmol/mL), pure-H₂O₂-treated (1.0 mmol/L), and control groups.

Figure 8: QU, LU, and KA scavenge H₂O₂-induced intracellular ROS in PIG1 cells. The cells were pretreated with QU, LU, and KA at different concentrations (25 and 50 μmol/L) for 24 h and then treated with H₂O₂ (final concentrations: 1.0 mmol/L) for 2 h; we set up QU, LU, and KA-treated (25, 50 μmol/mL), pure-H₂O₂-treated (1.0 mmol/L), and control groups.
stress may be the initial event leading to vitiligo development [30]. Melanocytes from patients with vitiligo are inherently defective and susceptible to oxidative stress [31]. ROS generation occurs during melanin synthesis by melanocytes. The stress status of melanocytes can also lead to an excessive accumulation of ROS, which results in changes to the antioxidant system. The imbalance of oxidative and antioxidant systems in vitiligo patients increases the sensitivity of melanocytes to external oxidants, thereby resulting in premature aging and apoptosis [32, 33]. Excessive accumulation of ROS can also cause cellular DNA damage and lipid peroxidation, which affect cellular function [34, 35]. Therefore, reducing oxidative stress in melanocytes should be a rational strategy for vitiligo treatment.

BST has a satisfactory effect in the clinical treatment of vitiligo. However, due to the complex components of TCM formulations, a more accurate and systematic study of their possible targets and mechanisms is needed. We used network pharmacology to explore the mechanism of action of BST for vitiligo treatment. QU, LU, KA, baicalein, nobiletin, and isorhamnetin were screened out as the main active ingredients of BST. QU, LU, and KA had the most extensive targets in vitiligo, so we selected them for experimental verification.

QU is a polyphenolic flavonoid found widely in onions, cabbage, apples, and tea [36, 37]. In recent years, scholars have revealed that QU has powerful antioxidant effects. It has a preventive effect on osteoporosis, certain tumor types, and certain cardiovascular diseases. The antioxidant activity of QU occurs mainly through the direct induction of glutathione (GSH) synthesis in the body. GSH acts as a hydrogen donor for redox reactions in the body, while superoxide dismutase captures O2 molecules and transforms them into H2O2, thereby having an antioxidant effect [38]. In addition, the -OH group in QU can bind to the active sites of oxidative enzymes, such as acetylcholinesterase and butyrylcholinesterase, to inhibit their activity and elicited an antioxidant effect [39]. QU can also regulate the Nrf2, 5′ adenosine monophosphate-activated protein kinase, and mitogen-activated protein kinase signaling pathways [40, 41]. Studies have shown that QU increases the tyrosinase activity and synthesis of melanoma cells and normal melanocytes to promote melanogenesis [42]. QU has a weakening and protective effect on H2O2-induced endoplasmic reticulum stress in melanocytes [43]. Here, we demonstrated that a certain concentration of QU reduced the ROS level in human immortalized melanocytes induced by H2O2 and had a certain degree of protection against oxidative stress in melanocytes. Combined with the results of network pharmacology, we showed that QU had the most extensive binding targets in BST.

LU is a flavonoid found in vegetables and fruits and is used in Chinese herbal medicines [44, 45]. TCM formulations containing LU have been employed to treat high blood pressure, inflammation, and cancer [44]. LU can inhibit the release of interleukin (IL)8, a critical proinflammatory chemokine in vitiligo and may have the potential to treat vitiligo [46].

KA is a natural flavonoid found in tea, fruits, and vegetables. Lee and colleagues found that KA could inhibit ultraviolet B-induced expression of cyclooxygenase-2 (COX-2) release in mouse skin epidermal (J66P) cells and attenuate ultraviolet B-induced COX-2 release and activator protein-1 transcriptional activity [47]. KA can also improve the skin fibrosis induced by bleomycin by reducing oxidative stress and inflammation [48]. Our experimental study revealed that a certain concentration range of KA could reduce ROS levels and protect melanocytes.

Hence, QU, LU, and KA are flavonoids that have anti-inflammatory and antioxidant effects. Therefore, we speculated that they could affect the oxidative stress of melanocytes. We conducted experiments to verify that under oxidative stress (mimicked by H2O2 use), melanocyte apoptosis and ROS production were reduced under pretreatment by QU, LU, or KA. Therefore, BST may have a specific protective role in the oxidative stress pathway of melanocytes.

In the PPI network analysis of BST, HMOX1, CXCL8, CCL2, IL6, MAPK8, CASP3, PTGS2, AKT1, IL1B, MYC, TP53, IFNG, and IL2 were screened out, all of which are core targets in the treatment of vitiligo. PTGS2 is also known as COX2, which plays an essential part in producing prostaglandin (PG)E2 and is made by epidermal keratinocytes in response to ultraviolet radiation [49, 50]. PGE2 is essential for the proliferation and melanogenesis of melanocytes, the loss of which can lead to vitiligo. In addition, studies have shown that the functional polymorphisms of COX2 affect the risk of vitiligo [51]. Heme oxygenase-1 (HMOX1) is the most highly induced antioxidant gene in H2O2-treated PIG1 cells. HMOX1 has been demonstrated to protect human melanocytes from oxidative damage via the E2-related factor 2 (Nrf2)-antioxidant response element (ARE) pathway [52]. AKT1 is a RAC-alpha serine/threonine protein kinase. The phosphorylation of AKT1 could promote the accumulation of β-catenin, thereby activating the microphthalmia-associated transcription factor and tyrosinase family, eventually leading to melanogenesis of melanocytes [53]. Overexpression of cellular tumor antigen P53 (TP53) could protect the pigmentation around hair follicles in vitiligo patients after ultraviolet-B treatment, change the migration ability of melanocytes, and improve pigmentation in vitiligo patients [54]. IL-6 is a vital immune factor involved in autoimmune inflammation in vitiligo. Its increased expression in serum and a skin lesion could trigger an immune response that targets and kills melanocytes and leads to vitiligo [1, 55]. These results suggest that QA, LU, and KA could protect melanocytes, promote melanogenesis, inhibit melanocyte death, and protect melanocytes from oxidative damage through various mechanisms.

Our study had three main limitations. First, experimentally validated targets were the predicted results of network pharmacology, but there were certain deviations compared with the actual targets. Second, we revealed that the main compounds QU, LU, and KA could protect melanocytes from oxidative stress; however, how they regulate targets and affect downstream signaling pathways to have a role in vitiligo treatment was not tested. Third, our study
was based on network pharmacology, so the compounds with the most targets were selected for experimental verification according to the results of network pharmacology, but their concentration in BST could not be determined.

5. Conclusions

Under the prediction obtained using network pharmacology, we clarified the active compounds in BST and their main targets in vitiligo treatment. Based on network pharmacology and in vivo experiments, QA, LU, and KA can be utilized to protect PIG1 cells. This phenomenon was achieved thanks to the inhibition of oxidative stress by reducing the intracellular level of ROS. This may explain the underlying mechanism of action of BST therapy and could provide a novel strategy for the treatment of vitiligo.

Data Availability

The datasets presented in this study are openly available from TCMSp, GeneCardS, OMIM, TTD, PharmGkb, and DrugBank belong to public databases. The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors’ Contributions

Ziqian Xu and Yihui Xie contributed equally to this work. WS and JH conceived and designed the study. ZX and YX provided equal contributions to research design, data analysis, and article writing. JS revised the manuscript. All persons designated as the authors have participated sufficiently in the work to take public responsibility for the content of the manuscript. All the authors ensure that they all gave substantial contributions.

Supplementary Materials

Supplementary Table 1. Compounds and related targets genes of Baishi Tablet. Supplementary Table 2A. Summarized vitiligo-related genes. Supplementary Table 2B. Vitiligo-related genes from five database respectively. Supplementary Table 2C. The interacting genes between vitiligo and Baishi tablet. Supplementary 3. Go enrichment analysis results. Supplementary 4. Protein-protein interaction network results. Supplementary 5. Description about compound-vitiligo-target network. (Supplementary Materials)

References

Evidence-Based Complementary and Alternative Medicine

13


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