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Research Article

Based on network pharmacology and molecular docking techniques, the mechanism of action of Siraitia grosvenorii in the treatment of acute respiratory distress syndrome was explored

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Abstract

Objective: To use network pharmacology methods to deeply explore the mechanism of action of Momordica grosvenori on acute respiratory distress syndrome [1] (ARDS), aiming to provide scientific basis and theoretical support for the application of Momordica grosvenori in ARDS treatment. **Methods:** The effective components of Momordica grosvenori were preliminarily screened with the help of the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP), and its main active components and their corresponding targets were determined by PubChem and SwissTargetPrediction methods. Subsequently, disease targets related to ARDS were identified by querying the GeneCards, DisGeNET and OMIM databases. Next, the targets of Momordica grosvenori and ARDS were cross-analyzed to identify the key targets shared by Momordica grosvenori on ARDS. Subsequently, the interaction information between target proteins was collected using the STRING database, and then a protein interaction (PPI) network diagram was created using the Cytoscape tool to display these relationships. Next, the common genes screened were enriched by gene ontology (GO) function and Kyoto Encyclopedia of Genes and Genomes (KEGG) signaling pathway analysis. Microbiology software was used to generate bubble plots for enrichment analysis to visualize the functions of these genes and the degree of enrichment in their signaling pathways. Finally, molecular docking was used to explore the connection between key targets in ARDS and the main active ingredients of Momordica grosvenori. **Results:** Five active ingredients of Momordica grosvenori were ultimately screened for intersection with 81 ARDS-related targets. Calculations revealed 51 BPs, 53 CCs, 100 MFs, and 122 KEGG Pathways. Furthermore, molecular docking was performed between the active ingredients of Momordica grosvenori and the core targets, providing new insights for future validation experiments exploring its ARDS targets and mechanisms.

Keywords: Momordica grosvenori, ARDS, network pharmacology, molecular docking

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ARDS[1] is a serious disease caused by a variety of pulmonary factors[2] (such as pneumonia, aspiration, etc.) and non-pulmonary factors[2] (such as sepsis, acute pancreatitis, trauma, etc.). ARDS may lead to severe hypoxemia, decreased lung compliance[4], increased arteriovenous shunt[5] and increased physiological dead space[6], ultimately causing non-cardiogenic pulmonary edema, posing a great threat to life. According to global surveys and studies, the proportion of ARDS among total ICU inpatients is 10.4%, and the mortality rates of mild, moderate and severe ARDS are 34.9%, 40.3% and 46.1% respectively. Through in-depth interpretation of these data, we found that the mortality rate of ARDS is directly related to its mortality rate[3]. However, there is currently no specific treatment plan for ARDS using Chinese herbal medicine at home and abroad. Momordica grosvenori is a mature fruit of the Cucurbitaceae plant, which has the characteristics of being both a medicine and a food. It is mainly distributed in Guangxi. It tastes sweet and has a cool nature and is often used in traditional Chinese medicine. The pulp, roots, stems and leaves of Momordica grosvenori contain a large number of bioactive substances, which can play a variety of medical and pharmacological roles, such as balancing immunity, lowering blood sugar, resisting oxidation, maintaining liver health and fighting cancer [7]. In addition, Momordica grosvenori can also regulate the immune system [8]. Currently, the relevant mechanism of using Momordica grosvenori in the treatment of ARDS has not been reported. Network pharmacology [9] and molecular docking technology were used to explore the role of Momordica grosvenori in the treatment of ARDS. Using specific software for analysis, a "component-target-pathway" network system was constructed, thereby comprehensively and systematically predicting and identifying the target, providing a new path for the application of drug ingredients in the treatment of diseases [10, 11].

1. Materials and Methods

1.1 Screening and Retrieval of Active Components in Momordica grosvenori

The Traditional Chinese Medicine Systems Pharmacology Analysis Platform (TCMSP) was used to retrieve the relevant chemical component information of Momordica grosvenori by accessing TCMSP (http://ibts.hkbu.edu.hk/LSP/tcmsp.php) [12].

1.2 Targets of the active ingredients of Momordica grosvenori

The simplified molecular linear input specification (SMILES) format of the active ingredients of Momordica grosvenori was found in the PubChen database (https://pubchem.ncbi.nlm.nih.gov/) and saved. For the active ingredients that could not be found in the PubChen database, the corresponding small molecule 3D structure model was found in TCMSP and converted into SMILES through the 3D model molecule (https://www.novopro.cn/tools/mol2smiles.html) website. The SMILES structure of the active ingredients of Momordica grosvenori was input into the SwissTargetPrediction database for analysis. The potential targets of these active ingredients can be obtained through the prediction function of this database. Finally, the set of all potential targets of the active ingredients of Momordica grosvenori was obtained.

1.3 ARDS Targets

ARDS disease-related targets were identified using the GeneCards (https://www.genecards.org/), OMIM (https://www.omim.org/), and Disgent

(https://www.disgenet.org/) databases. Genes with two or three duplicates were removed from these databases, retaining only one duplicate. These identified genes were then considered ARDS targets.

1.4 Intersection of Disease Genes and Component Targets

ARDS targets were intersected with the active ingredient targets of Monk Grosvenor Momordica grosvenori using the Venny database (https://bioinfogp.cnb.csic.es/tools/venny/index.html). Intersection targets were identified for further analysis.

1.5 Drug-ingredient-gene target network construction

Lo Han Guo (Sheng Han Guo), its anti-inflammatory active pharmaceutical ingredients, and the intersection of ARDS targets and Siraitia grosvenorii active ingredient targets were imported into Cytoscape 3.9.1 software. Based on betweenness correlation, a drug-ingredient-gene target network was constructed.

1.6 Target-protein interaction (PPI) network construction

First, the intersection of Siraitia grosvenorii's active ingredients and ARDS-related targets was imported into the String database, with "human" selected as the research target. Next, the results were exported in TSV format and imported into Cytoscape 3.9.1 software to construct a protein-protein interaction network. A plug-in was then used to calculate the network's topological parameters, including degree, betweenness, and closeness. Finally, key core proteins were identified based on these parameters.

1.7 Enrichment analysis of potential Siraitia grosvenorii target genes for ARDS

Enrichment refers to the process of classifying genes of interest based on genomic annotation information. After the genes are classified, it is easier to observe whether they have commonalities in function or composition. GO (Gene Ontology) is a database created by the Gene Ontology Consortium. Its purpose is to provide a unified description of the functions of genes and proteins in different species and to continuously update it according to the latest research progress. KEGG Pathway focuses on the storage of gene pathway information in different species. The active ingredients in Siraitia grosvenorii targeting common targets of ARDS were imported into the DAVID database [13] (https://david.ncifcrf.gov/) according to the official gene names, and then GO functional enrichment analysis and KEGG signaling pathway enrichment analysis were performed to explore the possible functions of these common targets.

1.8 Docking of Siraitia grosvenorii's active ingredients with core protein molecules

The core protein was substituted into the Uniprot database (https://www.uniprot.org/) and the Pdb database (https://www.rcsb.org/) to search for related core protein ligands. Visual analysis was performed in Pymol software to further understand the docking binding energy of the core protein and active ingredients.

2 Results

2.1 Screening of active ingredients of Siraitia grosvenorii

After searching for "Siraitia grosvenorii" in the TCMSP database, 182 related active ingredients were collected. Oral bioavailability (OB) and drug likeness (DL) were used as screening criteria, with OB set to be no less than 30% and DL set to be no less than 18% [14]. Finally, 11 candidate active ingredients were screened out. Through further functional analysis, 6 ingredients with anti-inflammatory effects were selected as the effective active ingredients of Siraitia grosvenorii. See Table 1.

Tab.1 SIX active ingredients of monk fruit

Molecule ID	Component Name	Chinese Name	OB (%)	DL
MOL001494	Mandenol	Mannitol	42.00	0.19
MOL001749	ZINC03860434	Di(2-ethylhexyl) phthalate	43.59	0.35
MOL002140	Perlolyrine	Chuanxiongzine	65.95	0.27
MOL000358	beta-sitosterol	β-Sitosterol	36.91	0.75
MOL000422	kaempferol	Kaempferol	41.88	0.24
MOL009295	Flazin	Flazin	94.28	0.39

2.2 Collection of Targets for Siraitia grosvenorii Active Ingredients

The SMILES numbers of candidate active ingredients were obtained from the PubChen database. For one active ingredient (Molecule ID: MOL001749), no corresponding SMILES molecular structure could be found. 3D structural models of related small molecules were found using TCMSP and converted into SMILES. The SMILES of six active ingredients were imported into the Swisstargetprediction database to identify Siraitia grosvenorii targets. With the exception of one active ingredient (Molecule ID: MOL002140), no relevant target could be found in the Swisstargetprediction database. This active ingredient was removed, resulting in a total of 500 drug targets for five Siraitia grosvenorii active ingredients. Using a probability greater than 0.1 as the selection criterion, duplicate genes were removed, resulting in a total of 314 targets for Siraitia grosvenorii active ingredients.

2.3 Collection of ARDS Disease Targets and Intersection of Disease and Drug Component Targets

Using the keyword "Acute Respiratory Distress Syndrome (ARDS)" in the GeneCards database, 5,145 relevant disease targets were collected. Median chi-squared scores were calculated, retaining a total of 1,287 relevant disease targets. 640 relevant disease targets were collected from the OMIM database, and 147 relevant disease targets were collected from the Disgent database. Duplicates were removed from the disease targets obtained from these three databases, resulting in a total of 1,911 relevant disease targets. Using the Venny database, we combined 314 active ingredient targets from Monk Grosvenor Momordica fruit with the collected ARDS disease targets, resulting in a total of 81 common targets. Next, we used these 81 common targets to investigate the effects of Monk Grosvenor Momordica fruit's active ingredients on ARDS. (See Figure 1)

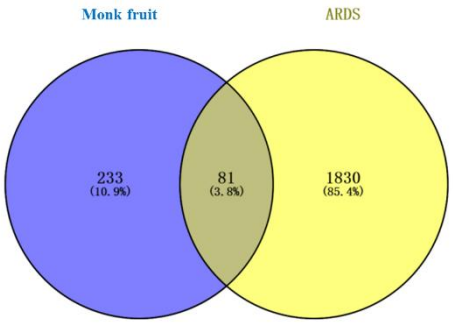


Figure 1 (color image in online version) shows a schematic diagram of the intersection of the targets of the active ingredients of Monk Grosvenor Momordica grosvenori and ARDS-related targets.

2.4 Construction of a Siraitia grosvenorii Active Ingredient-Target-Disease Network

Siraitia grosvenorii, its anti-inflammatory active ingredients, and their intersection genes were imported into Cytoscape 3.9.1 software (luo1 represents mandenol, luo2 represents ZINC03860434, luo3 represents beta-sitosterol, luo4 represents kaempferol, and luo5 represents flazin). Correlations were calculated based on betweenness (betweenness), with greater correlations indicating larger graph areas. Figure 2 shows that mandenol, kaempferol, and flazin have the strongest associations with the intersection targets of ARDS, indicating that these three active ingredients exert the greatest anti-inflammatory effects in ARDS.

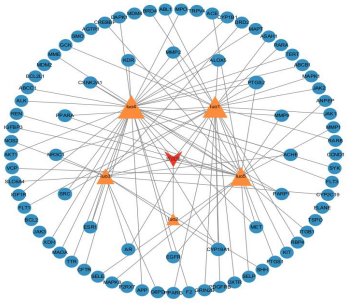


Figure 2 Construction of the Momordica grosvenori active ingredient-target-disease network

2.5 Target Protein Screening and Interaction Network Construction

The 81 intersecting targets were imported into the String database, the species selected was human, and the target protein interaction network was exported in .tsv format. This .tsv format was then imported into Cytoscape 3.9.1 software to construct a target protein interaction network consisting of 81 nodes and 833 edges. Using the software, three topological parameters were calculated: degree, betweenness, and closeness. Degree > 21.80246914, betweenness > 62.24691358, and closeness > 0.007153119 were screened. A total of 17 core targets with 116 edges were identified (see Table 2). In the network diagram, green circles represent target proteins, while gray dashed lines represent the interactions between targets. Additionally, yellow circles represent core targets (see Figure 3). Degree values were calculated, and the magnitude of the degree value corresponds to the importance of the node in the network and the size of the circle area. It can be seen that the targets in the core position are AKT1, EGFR, BCL2, ESR1, PTGS2, MMP9, SRC, and PPARG.

TabIe 2 Key targets and topological Properties of Siraitia grosvenorii in the treatment of ARDS

Targets	Betweenness	Closeness	Degree
ABCB1	82.84850413	0.00729927	25
MMP2	67.09491303	0.008064516	37
CCND1	88.63454402	0.008403361	42
NR3C1	67.01142108	0.007633588	29
EGFR	653.8811199	0.00990099	59
PTGS2	293.4580783	0.008928571	48
MMP9	170.4451643	0.008928571	48
SRC	178.4796213	0.00877193	46
BCL2L1	66.83006109	0.007874016	33
BCL2	410.0268523	0.009803922	58
ESR1	342.7657068	0.009259259	52
AKT1	610.7163165	0.010416667	64
APP	75.78092754	0.007575758	29
SYK	117.3763942	0.007246377	23
ACE	106.6929896	0.007633588	30
PPARG	265.1487264	0.008695652	45
JAK2	72.5970591	0.0078125	32

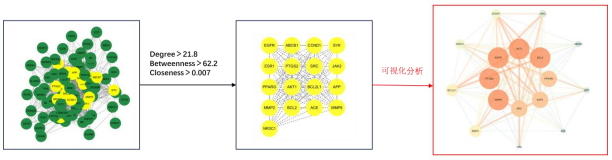


Figure 3 Visual analysis of the intersection targets between the active ingredients of Momordica grosvenori and ARDS - core targets - core targets

2.5 Enrichment Analysis: GO Function and KEGG Signaling Pathway

81 shared targets were imported into the DAVID database and subjected to GO analysis, encompassing three key aspects: biological process (BP), cellular component (CC), and molecular function (MF) to complete gene annotation. Calculations revealed enrichment of 51 BPs, 53 CCs, 100 MFs, and 122 KEGG pathways. The top 10 enriched BPs, CCs, and MFs, and the top 20 enriched KEGG pathways, were selected for analysis. See Figures 4-5 for detailed

results. The horizontal axis represents pathway enrichment; a higher value indicates a more significant pathway in the study data. The vertical axis displays disease-related functions and pathways. The size of the bubble represents the number of enriched genes; larger bubble size indicates a greater number of genes. The color of the bubble is proportional to the negative logarithm of the significance P value: redder bubbles indicate higher statistical significance (i.e., lower P values); greener bubbles indicate lower statistical significance (i.e., higher P values). According to the analysis results, the main biological processes involved in the study include: protein phosphorylation, positive regulation of kinase activity, transmembrane receptor protein tyrosine kinase signaling pathways, and positive regulation of MAPK cascade reactions. In terms of cellular components, the main ones involved are the plasma membrane and receptor complex. In terms of molecular biological functions, the main functions include transmembrane receptor protein tyrosine kinase activity and RNA polymerase II transcription factor activity, which involve DNA binding to specific sequences activated by ligands. In the KEGG pathway enrichment analysis, the top 20 major signaling pathways include: cancer pathways, EGFR tyrosine kinase inhibitor resistance, endocrine resistance, PI3K-Akt signaling pathway, Ras signaling pathway, Rap1 signaling pathway, prolactin signaling pathway, AGE-RAGE signaling pathway in diabetic complications, as well as lipids and atherosclerosis.

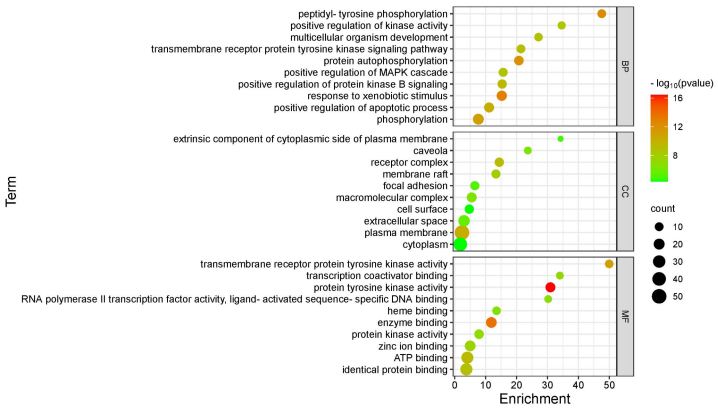


Figure 4: Histograms of GO functional enrichment results of key targets of monk fruit in treatment of ARDS

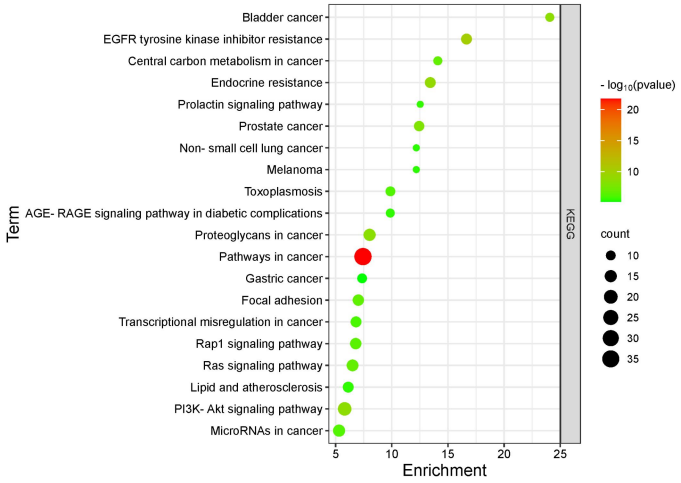


Figure 5: Distribution charts representing the enrichment outcomes for crucial pathways associated with monk fruit's impact on addressing Acute Respiratory Distress Syndrome (ARDS) within the KEGG database.

2.6 Molecular Docking

Molecular docking analysis was performed on the five main active ingredients in Siraitia grosvenorii (mandenol, ZINC03860434, beta-sitosterol, kaempferol, and flazin) and eight core proteins located at key positions identified through the PPI network (AKT1, EGFR, BCL2, ESR1, PTGS2, MMP9, SRC, and PPARG). First, the Uniprot database (https://www.uniprot.org/) and the PDB database (https://www.rcsb.org/) were searched for target structures related to the core proteins (see Table 3). Next, the TCMSP

database was used to query the mol structures of the active ingredients. Finally, the ligand and protein files required for molecular docking were prepared using AutoDockTools and pymol software. Finally, the affinity (kcal/mol) value was calculated by molecularly pairing the target structure with the active element structure, representing the strength of their connection. The lower the affinity, the greater the stability of the ligand-receptor connection. By using Pymol for visualization, the pairing results can be seen in Table 4 and Figure 5. It is generally believed that a connection capacity value lower than -4.25 kcal/mol indicates a certain degree of binding activity between the two, lower than -5.0 kcal/mol indicates good binding activity, and lower than -7.0 kcal/mol indicates high binding activity. [15] Through binding energy analysis, it can be seen that the two active ingredients, beta-sitosterol and kaempferol, have good molecular docking binding energy with the eight core proteins.

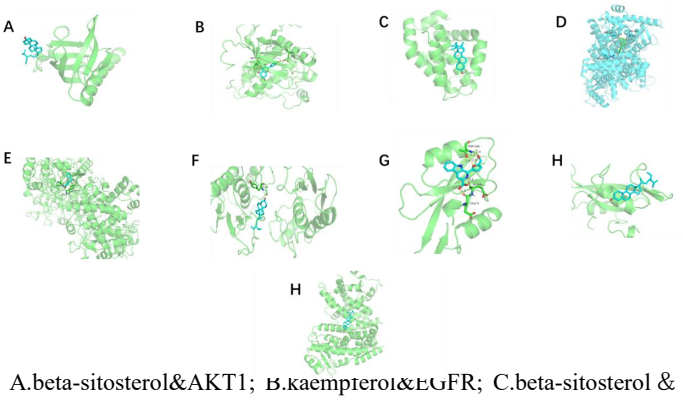
Table 3: Protein Identification

Number	Protein name	Pdbid
1	AKT1	1UNQ
2	EGFR	2ITN
3	BCL2	8HOG
4	ESR1	7RS8
5	PTGS2	5F19
6	MMP9	4H1Q
7	SRC	1O43
8	AKT1	1UNQ

Table 4 Binding energy of active ingredients to target sites

Docking binding energy: (kcal/mol)

Ligand/ protein	Mandenol	ZINC03 860434	beta-sitosterol	kaempferol	Flazin
AKT1	-2.7	-4.4	-6.3	-5.9	-5.3
EGFR	-3.7	-5.4	-7.6	-8.1	-6.0
BCL2	-2.1	-5.6	-7.6	-6.9	-7.1
ESR1	-3.9	-6.0	-7.4	-8.4	-7.2
PTGS2	-5.7	-7.4	-8.3	-8.7	-8.4
MMP9	-3.5	-7.1	-9.8	-9.5	-8.4
SRC	-2.3	-3.7	-6.8	-6.0	-6.8
PPARG	-4.1	-5.9	-8.0	-6.9	-6.8



A.beta-sitosterol&AKT1; B.kaempferol&EGFR; C.beta-sitosterol & BCL2; D.kaempferol&ESR1; E.kaempferol&PTGS2; F.beta-sitosterol&MMP9;
G.beta-sitosterol&SRC; H.Flazin&SRC; I.beta-sitosterol&PPARG;

Fig.6: Diagram of interfhce between actiVe ingredient and core target

3 Discussion

Acute respiratory distress syndrome (ARDS) is essentially a lung inflammatory response, which is mainly caused indirectly by a variety of inflammatory cells and the inflammatory mediators and cytokines they release [16]. The two main core elements, inflammatory cells and inflammatory mediators, play a key role. Chen Yumei et al. [17] found that Siraitia grosvenorii alcohol may alleviate lung injury in rats caused by severe acute pancreatitis by inhibiting cell pyroptosis, and its mechanism of action may be related to regulating the TREM-1/NLRP3 signaling pathway. Liu Bohao et al. [18] proposed that Siraitia grosvenorii alcohol may inhibit NLRP3-mediated cell pyroptosis by promoting the phosphorylation of AMPK, thereby alleviating LPS-induced acute lung injury. Therefore, on this basis, we screened the effective active ingredients and ARDS disease targets of Siraitia grosvenorii through network pharmacology and other methods, and searched for the action targets and core networks of related drugs and diseases. Through GO and

KEGG enrichment analysis, we identified the effective functions of the targets and related action pathways. We observed the docking binding energy between the active ingredients and the core targets during molecular docking, and revealed the pharmacological mechanism of Siraitia grosvenorii on ARDS, providing a theoretical basis and direction for subsequent clinical trials. In the network diagram construction, it can be seen that the three components of Mandenol, Kaempferol, and Flazin have the greatest connection with the intersection target of ARDS, indicating that these three active ingredients play the greatest role in ARDS. In the molecular docking, β-sitosterol and kaempferol scored the most, indicating that the two have the greatest direct or indirect effect on ARDS. Further inquiries show that β-sitosterol is an important component of the cell membrane, has a good free radical scavenging effect, and also has the effect of chemically preventing diseases such as hyperlipidemia, arteriosclerosis and inflammation [19]. Kaempferol also has the ability to inhibit the expression of related inflammatory factors and has a strong anti-inflammatory effect. [20-22]

3.1 Protein interaction network analysis

In the protein interaction network analysis, it can be seen that the core proteins are AKT1, EGFR, BCL2, ESR1, PTGS2, MMP9, SRC, and PPARG. It is predicted that these proteins are jointly involved in regulating the treatment of ARDS. AKT1 (serine and threonine kinase AKT), also known as protein kinase B (PKB), is activated by insulin and various growth and survival factors and plays a key role in regulating cell growth, division, and inhibiting cell apoptosis [23]. The loss of Akt1 does not affect leukocyte function in vitro. Bone marrow transplantation experiments have shown that host Akt1 regulates the migration of leukocytes into inflamed tissues, mainly by regulating vascular permeability, causing edema and leukocyte extravasation [24]. EGFR mainly induces TACE or TACE-like metalloproteinase expression through the TLR family signaling pathway, which promotes the cleavage and release of TGF-α. TGF-α then binds to EGFR as a ligand, and EGFR dimerizes and phosphorylates to activate downstream signaling pathways such as MAPK and PI3-K, ultimately regulating the transcription of cytokines and exerting anti-inflammatory effects [25]. Bcl-2 alleviates inflammatory responses by reducing the activation of the NLRP1 inflammasome [26]. ESR1 is a member of the NR3 subfamily of the nuclear hormone receptor family and is involved in the proliferation, differentiation and homeostasis of target cells [27]. PTGS2 is an important inflammatory regulator that regulates and transmits inflammatory responses by synthesizing inflammatory mediators such as prostaglandins, promoting the release of inflammatory factors such as TNF-α, IL-1β, and IL-6 [28]. Matrix metalloproteinase 9 (MMP-9) is an enzyme that decomposes the extracellular matrix, has a positive feedback effect on a variety of proinflammatory factors, and plays a key regulatory role in the inflammatory process [29]. SRC kinase (SRC) is a tyrosine protein kinase responsible for regulating cell metabolism, survival and proliferation. Numerous studies have shown that it plays multiple functions in macrophage-mediated innate immunity, including phagocytosis, the production of inflammatory cytokines and mediators, and the promotion of cell migration [30]. PPARG can inhibit the activation of pro-inflammatory signaling pathways in M1 macrophages, while promoting the expression of anti-inflammatory signals in M2 macrophages [31].

3.2 Enrichment Analysis

In the top 20 signaling pathways in the KEGG pathway

enrichment analysis, it was found that endocrine resistance, PI3K-Akt signaling pathway, Ras signaling pathway, Rap1 signaling pathway, AGE-RAGE signaling pathway, and lipid metabolism and atherosclerosis pathways were also involved in the mechanism of Siraitia grosvenorii in treating ARDS, involving lipid metabolism, inflammatory response, and cancer. Therefore, we can infer that the active ingredients of Siraitia grosvenorii may alleviate the pathological process of ARDS through the above pathways. More and more studies have shown that chronic inflammation plays an important role in the pathological process of insulin resistance. The molecular mechanism of inflammation-induced insulin resistance (IR) has become the focus of extensive research. IR weakens the ability of insulin to regulate blood sugar levels, mainly affecting the liver, skeletal muscle, and adipose tissue. Most obese or type 2 diabetic patients have IR, the root cause of which is the defect of insulin receptor post-signaling pathway in target cells [32]. This also suggests that in the process of ARDS formation, inflammatory release may be involved in the process of lipid metabolism and endocrine resistance to a certain extent. Recent studies have shown that the PI3K/AKT/mTOR signaling pathway and related regulatory factors (including mitochondria, pro-apoptotic proteins, glycogen synthase kinase 3 and NF-κB) play an important role in the formation and progression of acute lung injury. These factors not only play a role in early inflammatory response and pulmonary edema, but also play a key role in subsequent tissue repair, airway remodeling and the formation of emphysema [33]. The Ras-Mitogen activated protein kinase pathway (Ras-MAPK Pathway) plays a key role in important stages of the cell life cycle such as growth, development, survival and migration. In the context of inflammatory response, inflammatory-related cells improve their functional efficiency by enhancing their aggregation properties. The rap1 signaling pathway plays a regulatory role in this. It manages the associated aggregation molecules inside the cell, thereby affecting the aggregation and activity of inflammatory-related cells. The Rap1 signaling pathway can regulate intracellular information transmission molecules, thereby playing a role in the formation and release of inflammatory factors. cAMP can intervene in the progression of ARDS through the Epac/Rap1 signaling pathway, and the Epac/Rap1 signaling pathway is a potential target for the prevention and treatment of ARDS [34]. The advanced glycation end product-receptor (AGE-RAGE) signaling pathway refers to the signal transduction pathway in which protein glycation products (AGEs) caused by hyperglycemia bind to their receptors (RAGE), thereby triggering a series of reactions. It has a key impact on the occurrence and progression of diabetic complications. AGEs are a class of compounds formed by the interaction of sugars with biological macromolecules such as proteins or nucleic acids, and they increase abnormally in a hyperglycemic environment. This type of chemical component has the ability to interact with RAGE and trigger multiple information transmission pathways, such as NF-κB, MAPK and PI3K-AKT-mTOR, further causing inflammation, oxidative stress, vascular endothelial cell dysfunction, cell death and other adverse effects [35, 36]. The above signaling pathways can affect the generation and development of inflammation in a direct or indirect way, which suggests that ARDS may exert its effects by inhibiting multiple inflammation-related signaling pathways. This provides us with a new perspective that inhibiting multiple inflammatory pathways may be an effective ARDS treatment strategy.

3.3 Molecular docking

During the molecular docking process, it was observed that β-sitosterol and kaempferol had the highest scores with 8 key proteins, and the docking binding energy fluctuated below -5.3 kcal/mol, showing good binding activity. β-sitosterol is a tetracyclic triterpenoid compound with multiple physiological functions such as lowering blood lipids, anti-oxidation, anti-inflammation and anti-apoptosis [37, 38]. The study of Zhou's team [39] showed that β-sitosterol can block the RIG-I and IFN/STAT signaling pathways, thereby alleviating acute lung injury caused by influenza A virus. In addition, inhibiting NF-κB signaling has a reasonable effect on alleviating lung injury. At present, a large amount of evidence shows that β-sitosterol has the ability to block NF-κB activation [40]. Kaempferol has anti-inflammatory and antioxidant pharmacological activities and antibacterial, anti-tumor and antitussive and expectorant effects [22]. Wang Zhengye's team [41] studied the effect of kaempferol on the airway inflammatory response of rats with chronic obstructive pulmonary disease and found that kaempferol may inhibit the TLR4/NF-KB signaling pathway, reduce the occurrence and development of inflammation, and reverse the oxidative stress response to produce a protective effect on the lung function of COPD rats. Liu Caihong's team [42] studied the ability of kaempferol to reduce the inflammatory response of mice with chronic obstructive pulmonary disease model and believed that it has a certain therapeutic effect on COPD in mice, which may be related to its anti-inflammatory, antioxidant and inhibition of NF-κB signaling pathway. Li Yan's team [43] found that kaempferol can effectively reduce the inflammatory response and oxidative stress damage of acute lung injury in mice caused by H9N2 swine influenza A virus by inhibiting the activity of the NF-κB signaling pathway. This result shows that kaempferol may be an effective strategy for alleviating the severity of acute lung injury caused by influenza virus. In summary, we discovered five active components in Momordica grosvenori (Shengguo) with anti-inflammatory effects. These components overlap with disease targets, resulting in a total of 81 targets identified. These targets primarily involve multiple signaling pathways, including endocrine resistance, the PI3K-Akt signaling pathway, the Ras signaling pathway, the Rap1 signaling pathway, the AGE-RAGE signaling pathway, lipid metabolism, and atherosclerosis. Further molecular docking revealed that β-sitosterol and kaempferol exhibited the strongest docking energies with key targets. This study provides an in-depth analysis of the complex mechanism of action of Momordica grosvenori (Shengguo) in the treatment of ARDS, revealing that its therapeutic effects are exerted through multiple components, multiple targets, and multiple pathways. This discovery not only helps to better understand the specific role of Momordica grosvenori in the treatment of ARDS but also provides new perspectives and insights for the clinical application of Traditional Chinese Medicine (TCM) and the modernization of TCM.

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None

Conflict of Interests

None

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