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Yuting Bai

Department of Clinical Laboratory,
Affiliated to Hospital of North Sichuan Medical College,
Nanchong, 637000, China
Email: byt67899@163.com

Yulei Xie

Department of Rehabilitation Medicine,
Affiliated to Hospital of North Sichuan Medical College,
Nanchong, 637000, China
Email: 70730564@qq.com

Xiaowu Zhong

Department of Laboratory Medicine,
North Sichuan Medical College,
Nanchong, 637000, China
Email: zxw_strive@163.com

Can Luo, Qing Wu and Xin Chen*

Department of Rehabilitation Medicine,
Affiliated to Hospital of North Sichuan Medical College,
Nanchong, 637000, China
Email: 841354776@qq.com
Email: cbkf2017@163.com
Email: 488874309@qq.com
*Corresponding author

Abstract: This work focused on conducting pharmacological network analysis for identifying the mechanism of components of Artemisia annua herba (AAH) and corresponding target proteins related to cancer. We acquired chemical constituents of AAH based on traditional Chinese medicine systems pharmacology database (TCMSP), and obtained disease-related target-protein genes based on the comparative toxicogenomics database (CTD). A total of 18 AAH main active components such as Quercetin, Luteolin, Kaempferol, Isorhamnetin, etc., contained and 194 potential targets for cancer-related target proteins were identified. It mainly mediated pathways such as cancer, AGE-RAGE, IL-17, and TNF in the treatment of cancer, digestive system diseases, cardiovascular diseases, etc., by regulating 14 core targets such as TP53, RELA, RB1, NFKBIA, and MYC. Additionally, Cytoscape and

STRING were applied in establishing the protein interaction networks. The present study established the new concept and method to develop and apply AAH by preliminary revealing the substance the basis and multi-dimensional pharmacological action mechanism of AAH, as well as reflecting its multi-component-multi-target-multi-way action features.

Keywords: network pharmacology; mechanism; Artemisia annua herba; AAH; disease.

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Biographical notes: Yuting Bai completed her undergraduate studies in Medical Laboratory Science at Chengdu University of Traditional Chinese Medicine in 2005. She further enhanced her expertise by graduating from the Department of Laboratory Medicine at North Sichuan Medical College in 2022, where she specialised in Clinical Laboratory Diagnostics. Currently, she holds a prestigious position in the Department of Laboratory Medicine at the Affiliated Hospital of North Sichuan Medical College, located in Nanchong, Sichuan Province. Her professional endeavours predominantly revolve around clinical work, teaching, and research in the realms of microbiology and oncology. She has a keen research interest in the clinical foundational study of the tumour microenvironment. Her impressive academic portfolio includes leading or contributing to five provincial-level projects and authoring five papers in SCI-indexed journals.

Yulei Xie graduated with a Bachelor's degree in Clinical Medicine from North Sichuan Medical College in 2017, and completed his Master's degree in Rehabilitation Medicine and Physiotherapy at North Sichuan Medical College in 2022. He is currently pursuing his Doctoral degree in Rehabilitation Medicine and Physiotherapy at Capital Medical University. He has led and participated in one department-level and four university-level research projects. He has published ten SCI papers and two Chinese core journal papers as the first or corresponding author. He has worked in rehabilitation medicine for five years, specialising in neuromodulation treatments (transcranial magnetic stimulation, vagus nerve stimulation, spinal nerve stimulation) for diseases such as stroke and spinal cord injury.

Xiaowu Zhong is doctoral student, associate researcher, postgraduate tutor, and is now a member of the Special Committee of Laboratory Medicine of Sichuan Society of Rehabilitation Medicine, and mainly engaged in clinical, teaching and scientific research in the field of molecular biology. At present, he is mainly engaged in clinical, teaching and scientific research in the field of molecular biology testing, and his main research direction is the clinical basic research of tumours and autoimmune diseases, with rich experience in the implementation of topics, and has presided over/researched more than 20 national scientific research projects of the National Natural Science Foundation of China, the National Key R&D Program, the National Health and Family Planning Commission's public welfare industry scientific research projects and other provincial and departmental scientific research projects.

Can Luo completed her undergraduate degree at North Sichuan Medical College in 2018 and her graduate degree in Clinical Laboratory Diagnostics in 2022 from the same institution. Her postgraduate research focused on molecular biology and oncology. Currently, she works in the Microbiology

Laboratory at the Sichuan Provincial Center for Disease Control and Prevention, researching viral diarrhoea pathogens. She has contributed significantly to the scientific community, participating in a major provincial project and authoring two papers published in the Scientific Citation Index (SCI), highlighting her expertise in infectious diseases.

Qing Wu is the Deputy Chief Physician, an Associate Professor, Master Supervisor and the Director of Rehabilitation Medicine. He is currently a member of the Cerebrovascular Diseases Special Committee of the Chinese Rehabilitation Medical Association and the standing Committee of the physical Medicine and Rehabilitation Special Committee of Sichuan Medical Association. He has published more than 30 academic papers in academic journals at and above the provincial level. He is engaged in orthopaedics and rehabilitation medicine clinical, teaching, scientific research for more than 30 years, good at limb, joint disease diagnosis, treatment and rehabilitation.

Xin Chen graduated from the North Sichuan Medical College in 2022, majoring in rehabilitation therapy technology. His research interests include rehabilitation medicine, oncology and bioinformatics.

1 Introduction

Artemisia annua herba (AAH) is a plant belonging to the family Compositae and possesses a bitter, pungent, and slightly cold taste. It enters the liver and gallbladder meridian, and exerts heat-clearing and detoxification effects, cooling blood and steaming, relieving summer heat, and preventing malaria (Commission, 2015). Recently, several effective chemical constituents of AAH, such as sesquiterpenes, flavonoids, coumarins, and volatile oils and their derivatives, have been analysed and processed by modern Chinese medicine research methods. A combination of modern pharmacological experiments and pharmacodynamics proved that AAH has diverse pharmacological activities, including anti-malaria, anti-tumour, antibacterial, insecticidal, anti-inflammatory, and immunomodulatory properties.

Ancient medical books mention AAH as a commonly used compound ingredient in traditional Chinese medicine. Its medicinal use was first described in the ‘female hemorrhoid prescription’ in the silk book ‘52 sick prescriptions’ unearthed from Ma wang dui No. 3 Han Tomb. The Shen Nong Materia Medica Classic in the Eastern Han Dynasty termed it AAH and recorded its use in treating summer fever and externally treating scabies. The Elbow Reserve Emergency Prescription written by Ge Hong in the Eastern Jin Dynasty was the first medical book to describe the role of AHA in treating malaria ‘AAH holds, water is two litres, juice is taken, and it is taken’. Furthermore, all medical books written by the Song, Yuan, Ming, and Qing dynasties have described its role in treating malaria (Xiaobo et al., 2016). At present, researchers are mainly evaluating the toxicity and drug properties of AAH and the studies on its mechanism of action are still very limited.

Chinese medicines consist of multiple components, multiple targets, and diverse regulatory methods, thus containing huge information. Therefore, it is difficult to reflect the systemic nature of Chinese medicines using a single target and single component research approach in Western medicine (Westerhoff, 2015). With the recent development

of system biology, the 'drug-target-disease' interaction-based network analysis has emerged as an important approach for investigating potential drug action mechanism. The method provides guidance for modernising research on traditional Chinese medicine. Primary effective components of AAH and the signal pathways involved in the corresponding targets were predicted and examined in the present work. In addition, the primary active components-targets-pathways visual network was established, providing a reference for further research on the broad pharmacological effects of AAH.

2 Materials and methods

2.1 Effective component selection

All active components of AAH and the targets were retrieved based on Traditional Chinese Medicine System Pharmacology (TCMSP, http://lsp.nwu.edu.cn/temspsearch.php) database analysis platform with keyword 'AAH' (Ru et al., 2014). Oral bioavailability (OB) ≥ 30% and compound drug-like property (DL) ≥ 0.18 were selected as the thresholds for selection, and a combination of literature mining and finishing were used for identifying effective component of AAH according to compound contents within individual drugs, research heat, and other criteria.

2.2 Effective component – target network establishment

Targets of effective components of AAH were translated into corresponding genes with UniProt database (http://www.uniprot.org/uploadlists/), and all targets were humanised (Pundir et al., 2016). Next, the compounds and corresponding genes were imported to Cytoscape for drawing active component-target network map for AAH. Each node in the Cytoscape network diagram refers to genes, proteins, or compounds and node connections stand for relationships among the biomolecules. The data indicate connection number among nodes within this network graph. A large compound value indicates that the compound is related to multiple targets with a significant role in treating diseases.

2.3 Target-disease network establishment

TCMSP platform was used for identifying possible targets associated with candidate compounds of AAH. The targets associated with disease were identified based on CTD database (http://ctdbase.org/) according to the obtained targets (Davis et al., 2023), and subsequently input in Cytoscape for constructing a target-disease interaction action network diagram. Connections between nodes and nodes represent the target-disease relation. Numerous connections were related to a close relationship.

2.4 Target protein interaction

After network construction, we screened hub genes to identify the interaction of potential target proteins of AAH. The screened target proteins were used to construct a target protein-protein interaction (PPI) network model on the STRING platform (http://string-db.org/) (Szklarczyk et al., 2019). We set protein type as 'Homo sapiens', minimum interaction threshold as the 'highest confidence' (0.900), whereas the rest parameters as

defaults to obtain a target protein network diagram. In addition, the network diagram was topologically analysed, and the hub gene was selected by the CytoNCA plug-in of the Cytoscape software.

2.5 Gene ontology (GO) functional annotation and KEGG analysis

For clarifying biological effect of potential target protein and its function in signalling pathways, GO functional annotation and Kyoto Encyclopedia of Genes and Genomes (KEGG) analysis were performed on potential target protein with ClusterProfiler package in R software. In addition, visual processing was performed, and a signalling pathway map was drawn using the pathview package.

2.6 Prediction of three-level structure of core targets

The SWISS-MODEL was utilised to construct three-level structures of core targets, and the Ramachandran curve is drawn (Waterhouse et al., 2018). The interaction between AAH and core targets amino acids was studied by Discovery Studio (Duan et al., 2022).

3 Results

3.1 Selection of AAH effective components

There were altogether 126 known pharmaceutical components of AAH retrieved from the TCMSP database. Using OB $\geq$ 30% and DL $\geq$ 18%, 22 compounds, which included isorhamnetin, eupatin, tamarixetin and sitosterol were screened as candidate compounds (Table 1).

3.2 Active component-target interaction network analysis

Action targets of 22 candidate compounds were identified using the TCMSP platform, among which 194 targets were found in 18 compounds, and no corresponding targets were found in four compounds. Next, an AAH compound-target network was constructed, including 182 nodes and 371 edges, in which 18 cyan nodes represented the active components, 164 pink nodes stood for the targets, whereas 371 edges indicated interaction of active components with targets. As demonstrated by active component-target network diagram, quercetin, luteolin, kaempferol, isorhamnetin, stigmasterol, and other active components in AAH significantly contributed to its pharmacology (Figure 1).

3.3 Target-disease interaction network analysis

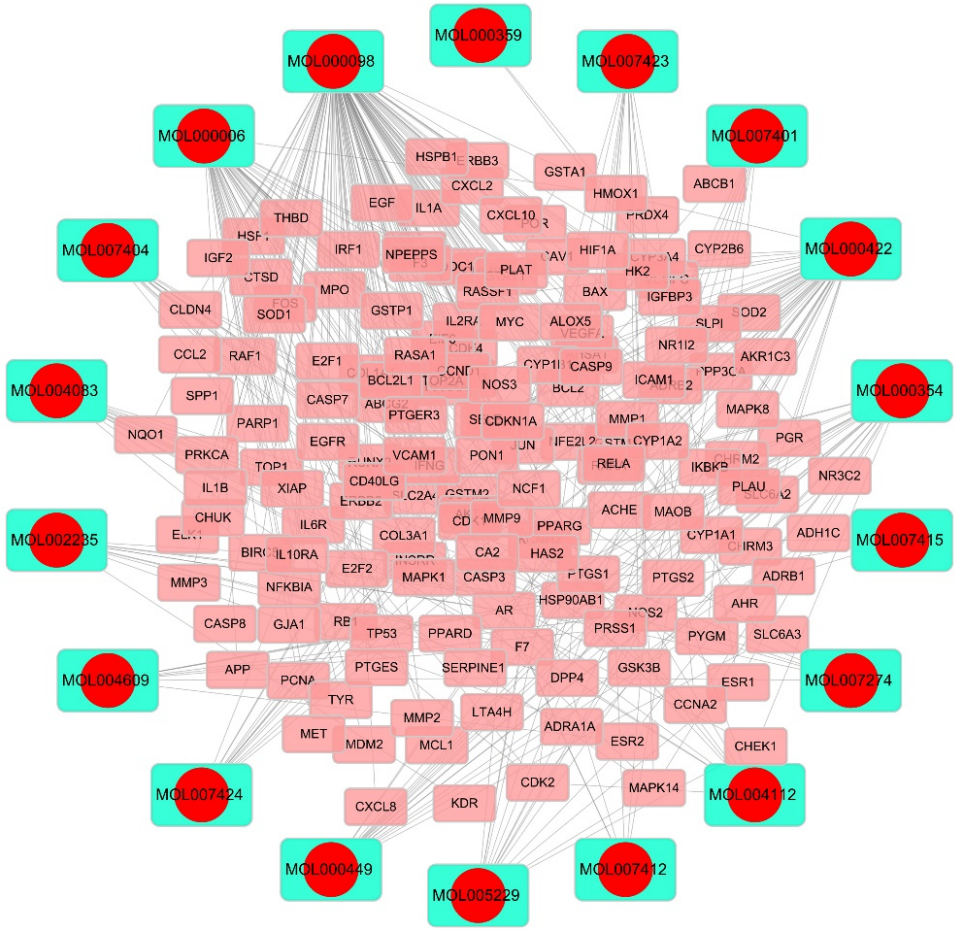
The target-disease interaction network diagram between potential targets and related diseases consisted of 210 nodes with 1,705 edges. Of these, 21 pink nodes represented different diseases, 189 blue nodes represented disease targets, and 1,705 edges represented the interaction relationship between disease targets and different diseases. Five of the 194 AAH targets did not have corresponding diseases in the target-disease network diagram, suggesting that there were still undiscovered pathways. To analyse

related diseases, 21 diseases related to AAH targets were depicted in the network diagram, including 141 cancer-related targets, 139 digestive system diseases, 120 cardiovascular diseases, 111 nervous system diseases, 107 urinary system diseases, 99 skin diseases, 96 immune system diseases, and 95 respiratory system diseases, indicating the substantial pharmacological function of AAH in treating several diseases. For target analysis, the degree value of superoxide dismutase (SOD)2 in the network diagram was the largest and related to 21 diseases, including male reproductive system diseases, skin diseases, respiratory diseases, nervous system diseases, tumours, and cardiovascular diseases (Figure 2). These results were consistent with those obtained from modern pharmacological experiments. The top ten diseases with high degrees were subsequently screened out, including tumours (141), digestive system disease (139), cardiovascular disease (120), nervous system disease (111), male reproductive system disease (107), skin disease (99), immune system disease (96), respiratory disease (95), metabolic disease (92), and endocrine system disease (86). Thus, AAH plays a significant therapeutic role in several diseases, which is consistent with its anti-inflammatory, anti-tumour, and immune regulation effects.

Table 1 TCMSP database and analysis platform for the main active chemical components of AAH

Mol ID	*Component*	*Molecular weight*	*Formula*	*OB (%)*	*DL (%)*
MOL002235	Eupatin	360.31	$C_{18}H_{16}O_8$	50.8	0.41
MOL000354	Isorhamnetin	316.26	$C_{16}H_{12}O_7$	49.6	0.31
MOL000359	Sitosterol	736.99	$C_{47}H_{60}O_7$	36.91	0.75
MOL004083	Tamarixetin	316.26	$C_{16}H_{12}O_7$	32.86	0.31
MOL004112	Patuletin	332.26	$C_{16}H_{12}O_8$	53.11	0.34
MOL000422	Kaempferol	286.24	$C_{15}H_{10}O_6$	41.88	0.24
MOL000449	Stigmasterol	412.70	$C_{29}H_{48}O$	43.83	0.76
MOL004609	Areapillin	360.32	$C_{18}H_{16}O8$	48.96	0.41
MOL005229	Artemetin	388.37	$C_{20}H_{20}O_8$	49.55	0.48
MOL000006	Luteolin	286.24	$C_{15}H_{10}O_6$	36.16	0.25
MOL007274	Skrofulein	314.29	$C_{17}H_{14}O_6$	30.35	0.3
MOL007389	Artemisitene	280.32	$C_{15}H_{20}O_5$	54.36	0.31
MOL007400	Vicenin-2_qt	594.52	$C_{27}H_{30}O_{15}$	45.84	0.21
MOL007401	Cirsiliol	330.29	$C_{17}H_{14}O_7$	43.46	0.34
MOL007404	Vitexin_qt	432.38	$C_{21}H_{20}O_{10}$	52.18	0.21
MOL007412	Dmqt	346.29	$C_{17}H_{14}O_8$	42.6	0.37
MOL007415	[(2S)-2-[[(2S)-2-(benzoylamino)-3-phenylpropanoyl]amino]-3-phenylpropyl] acetate	444.50	$C_{27}H_{28}N_2O_4$	58.02	0.52
MOL007423	6,8-di-c-glucosylapigenin_qt	594.52	$C_{27}H_{30}O_{15}$	59.85	0.21
MOL007424	Artemisinin	282.33	$C_{15}H_{22}O_5$	49.88	0.31
MOL007425	Dihydroartemisinin	284.35	$C_{15}H_{24}O_5$	50.75	0.3
MOL007426	Deoxyartemisinin	266.33	$C_{15}H_{22}O_4$	54.47	0.26
MOL000098	Quercetin	302.24	$C_{15}H_{10}O_7$	46.43	0.28

Figure 1 Component-target network diagram (see online version for colours)

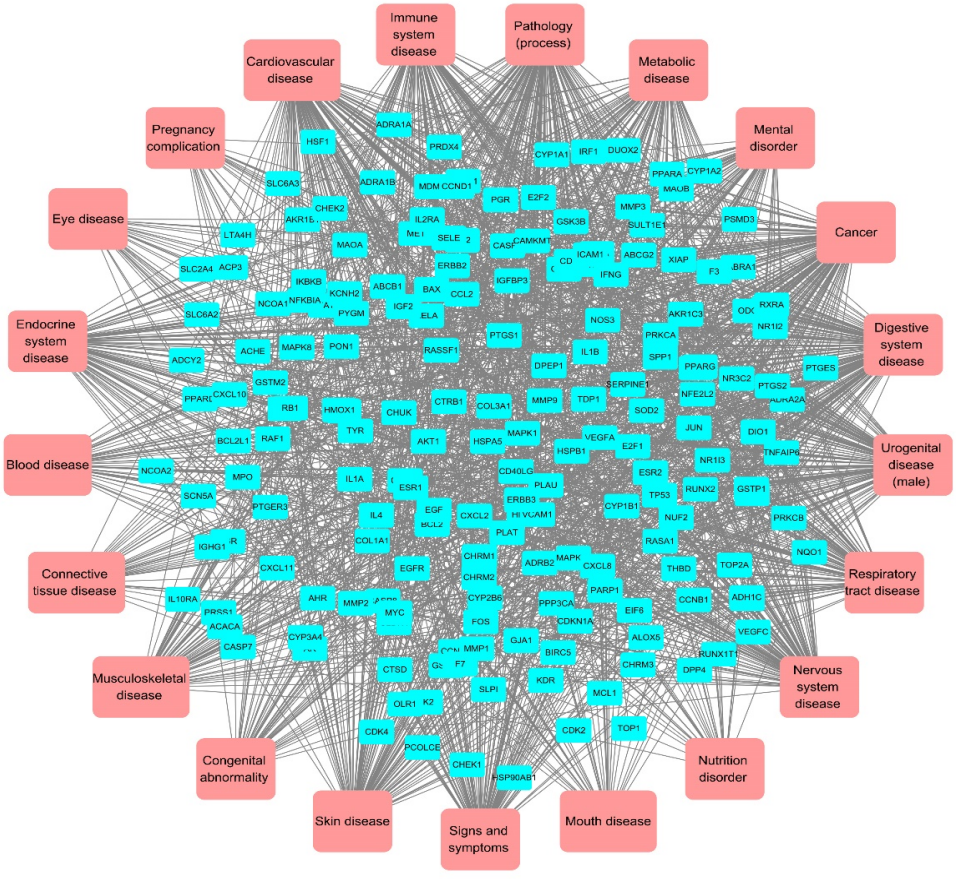


Notes: The large cyan rectangle in the outer circle represents the active ingredients of AAH, whereas the small pink rectangle in the inner circle represents the potential targets of AAH. The grey line indicates the relationship between the active components of AAH and potential targets. The network diagram contains 182 nodes and 371 edges.

3.4 Target protein interaction network establishment and hub gene selection

We input altogether 194 targets of AAH in STRING database, and defined the species as 'human' to construct the PPI map. Certain proteins with no relationship with each other were not reflected in the network diagram. Moreover, we input data in the Cytoscape software for constructing the PPI map. The topological analysis of our constructed PPI network was conducted with CytoNCA plug-in. The genes displayed BC > 12.26, CC > 0.54, DC > 9, EC > 0.12, LAC > 4, and NC > 4.95. Fourteen hub genes were screened namely, TP53, RELA, RB1, NFKBIA, MYC, MAPK14, MAPK1, JUN, HIF1A, FOS, ESR1, CDKN1A, CCND1, and AKT1, suggesting their significant role the pharmacological mechanism of AAH (Figure 3).

Figure 2 Target-disease interaction network diagram (see online version for colours)



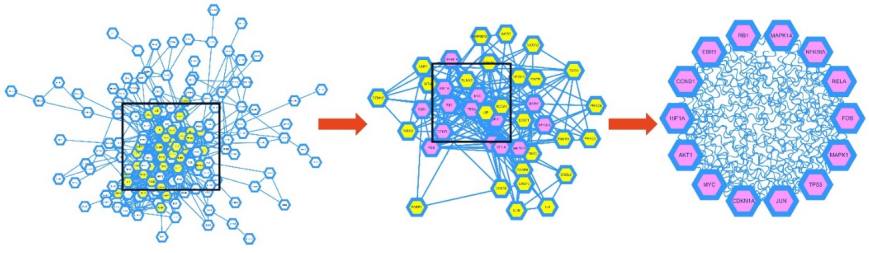
Notes: The large pink rectangles in the outer circle represent 21 diseases, and the small blue rectangles in the inner circle represent potential targets of AAH. The grey line represents the relationship of the disease to the potential target. The network diagram contains 210 nodes and 1,705 edges.

3.5 GO analysis of 194 therapeutic targets of AAH

GO annotation of 194 target genes of AAH was conducted using the R software based on DAVID database upon the threshold of $p < 0.05$. The GO annotations were divided as three types: biological processes (BP), cellular components (CC), as well as molecular functions (MF). We then used these annotations for defining and describing the functions of a single gene. A total of 15 most significant entries were chosen for mapping using the R software. As shown in Figure 4, Y-axis stands for BP, CC, and MF entry names, whereas X-axis indicates GeneRatio in each entry, with box colour representing p-value. BP with a high concentration of target genes in AAH were largely cell response to drugs, cell response to chemical stress, cell response to lipopolysaccharide, cell response to metal ions, and cell response to reactive oxygen species. The highly enriched cell components were largely concentrated in the membrane raft, membrane microdomain, total enzyme complex, protein kinase complex, and lumen. Simultaneously, the

pharmacological effect of AAH was intricately related to the MF of DNA-binding transcription factors, ligand-activated transcription factor activity, RNA polymerase II specificity, peroxidase inactivity, and ubiquitin-protein ligase binding.

Figure 3 PPI core network screening flowchart, (a) a total of 194 potential therapeutic targets of AAH. Yellow represents key targets from the primary topological analysis, (b) key targets obtained from first-order topological analysis. Purple represents core key genes acquired by secondary topological molecules, (c) fourteen core key targets (see online version for colours)



(a) (b) (c)

3.6 KEGG analysis on 194 targets of AAH

KEGG signalling pathways were enriched in 194 target genes of AAH upon $p < 0.05$. Those ten most significant signalling pathways were chosen for mapping using the R software. According to Figure 5, Y-axis stands for pathway name, whereas X-axis indicates gene number associated with the pathway, with box colour representing p-value size. Those 194 targets of AAH were largely involved in cancer, AGE-RAGE, IL-17, and TNF signalling pathways. Of them, the cancer pathway with the highest concentration of targets contained 72 genes and 13 hub genes. In addition, six hub genes were associated with AGE-RAGE pathway, six related to IL-17 pathway, while seven associated with TNF pathway. In addition, pathview package of the R software was utilised for drawing tumour signalling pathway map in the follow-up study; genes marked in red were the potential genes of AAH playing pharmacological effects (Figure 6). These results suggest that active components of AAH exerted anti-tumour effects by influencing certain potential genes.

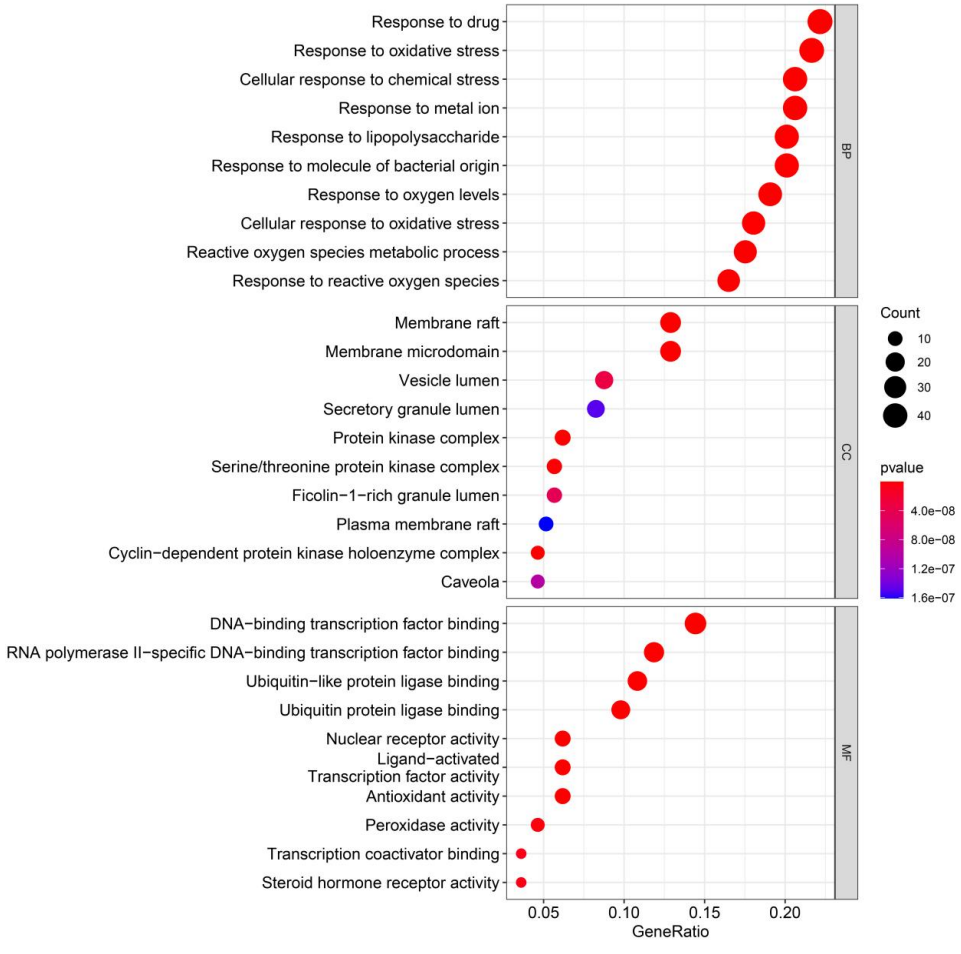
3.7 Molecular docking of AAH with TP53, RB1 and RELA

The three core targets of CytoNCA screening are TP53, RB1 and RELA. By searching the sequences of three proteins in the PBD, the tertiary structure of the three proteins are established by SWISS-MODEL [Figure 7(a)]. Meanwhile, according to Ramachandran diagram of Figure 7(b), the three proteins had an increased protein residue proportion within the desirable region.

We utilised the discovery studio for determining interaction of AAH with amino acids in TP53, RB1 and RELA. Amino acids interacting with AAH in TP53 include SER A:269, PRO A:128, TYR A:126, PHE A:113, ASN A:268, THR A:102 and so on. The

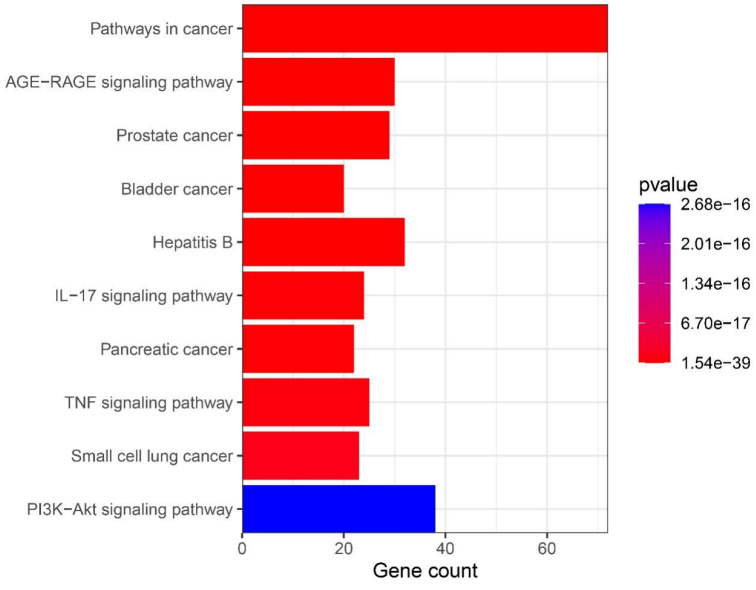
interactions between TP53 and AAH are van der waals, unfavourable acceptor-acceptor, conventional hydrogen bond, pi-alkyl, and pi-donor hydrogen bond [Figure 8(a)]. The amino acids that interact with AAH in RB1 include VAL A:193, VAL A:190, SER A:187, SER A:230, LEU A:234 and so on. The interactions between RB1 and AAH are van der waals, carbon hydrogen bond, conventional hydrogen bond, pi-alkyl, and pi-sigma [Figure 8(b)]. The amino acids that interact with AAH in RELA include ILE A:46, ASP A:126, LYS A:122, SER A:45 and so on. The interactions between RELA and AAH are conventional hydrogen bond, van der waals, pi-donor hydrogen bond, pi-cation, pi-alkyl, and pi-sigma [Figure 8(c)].

Figure 4 GO analysis of potential therapeutic targets of AAH (see online version for colours)



Note: The X-axis indicates the GeneRatio in each item, whereas the Y-axis indicates the BP, CC, and MF involving the target gene and the colour indicates the *p*-value.

Figure 5 KEGG pathway enrichment analysis of potential therapeutic targets of AAH (see online version for colours)

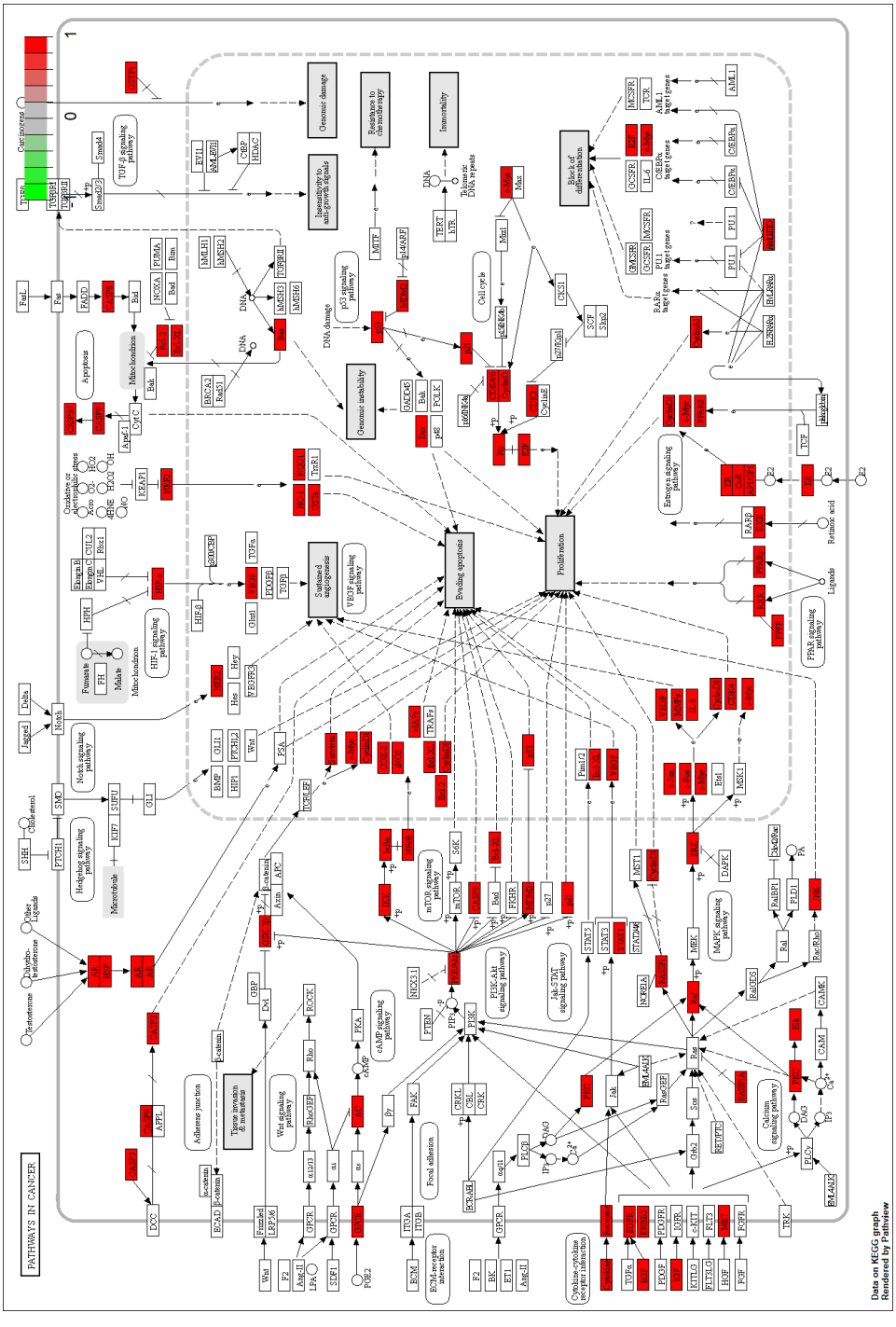


Note: The X-axis represents the number of genes enriched in each pathway, whereas the Y-axis represents the name of the pathways, and the colour represents the *p*-value.

4 Discussion

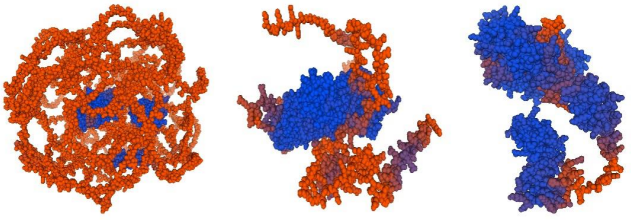
AAH is rich in chemical components. It has been widely used as the first-choice drug for treating cerebral malaria and falciparum malaria with high efficiency and low toxicity, thereby attracting worldwide attention. The application and the mechanism of action of AAH are highly comprehensive. Although most of the current efficacy studies are in vitro experiments, their clinical application prospects are undoubtedly considerable. Thanks to the continuous development and innovation of science and technology, more and more studies have been conducted for investigating pharmacological mechanisms of AAH, such as anti-malaria, anti-tumour, anti-inflammation, immunomodulatory, bactericidal, and insecticidal properties. The network pharmacology analysis conformed to the traditional Chinese medicine concept. Network pharmacology helps to easily explain material basis of AAH and its action mechanism. Altogether 126 chemical components of AAH were retrieved, and 22 compounds were selected as the main active components of AAH, most of which were in line with Lipinski's five rules (Lipinski et al., 2001). The active ingredient-target network diagram demonstrated that interactions in AAH involved multiple components and multiple targets, largely through quercetin, luteolin, kaempferol, and other active ingredients.

Figure 6 Pathways in cancer networks adapted from KEGG (ID: hsa05200) (see online version for colours)

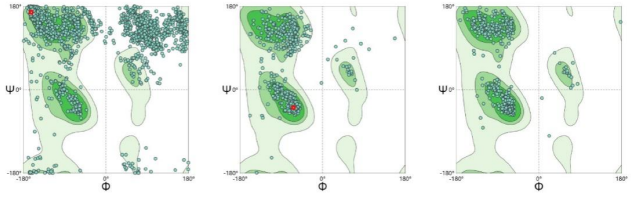


Note: The red rectangle is the major target of AAH in cancer pathways.

Figure 7 Analysis of the TP53, RB1, and RELA protein structures, (a) 3D visualisation of the structures of TP53, RB1 and RELA, (b) Ramachandran plots of TP53, RB1 and RELA (see online version for colours)

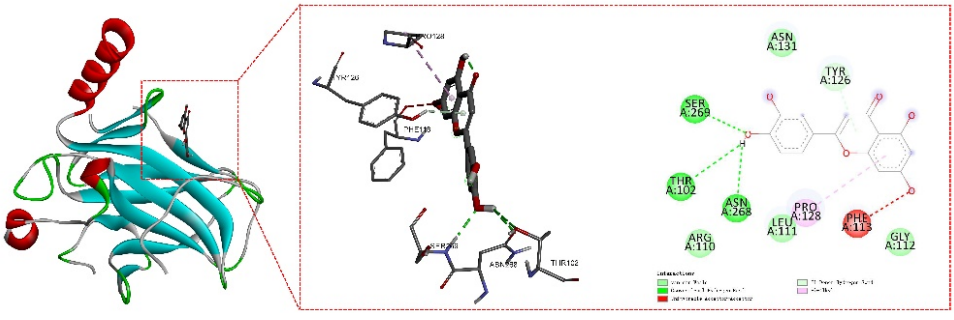


(a)

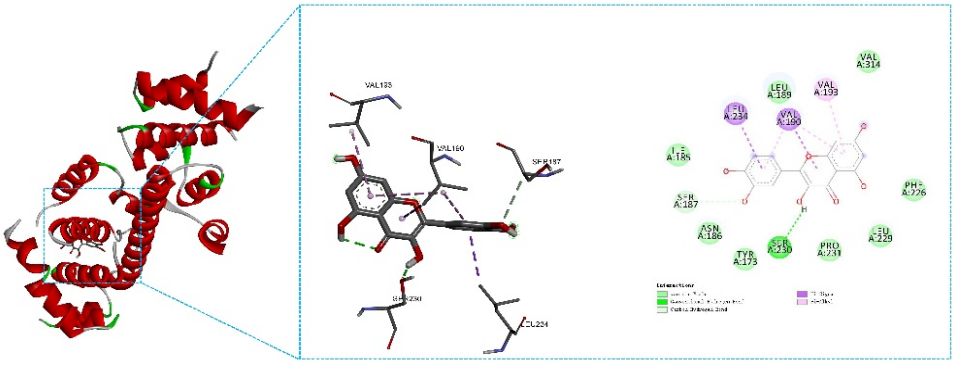


(b)

Figure 8 Molecular docking results of AAH and its core targets, (a) molecular docking results of Luteolin and TP53, (b) molecular docking results of Quercetin and RB1, (c) molecular docking results of Kaempferol and RELA (see online version for colours)

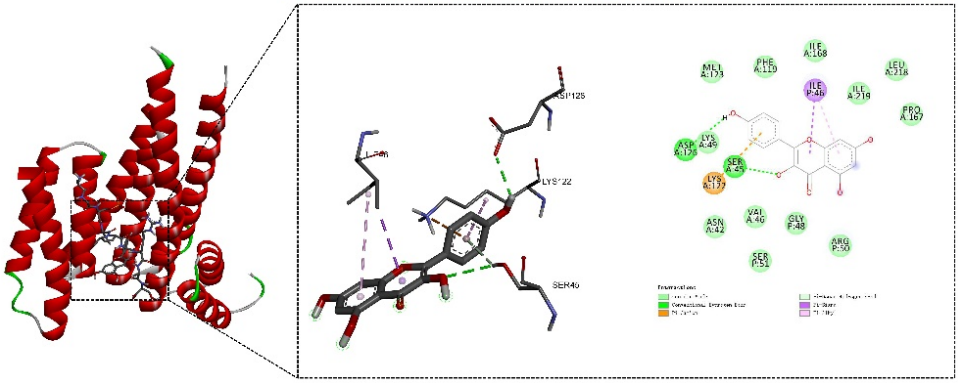


(a)



(b)

Figure 8 Molecular docking results of AAH and its core targets, (a) molecular docking results of Luteolin and TP53, (b) molecular docking results of Quercetin and RB1, (c) molecular docking results of Kaempferol and RELA (continued) (see online version for colours)



(c)

Quercetin, an effective flavonoid antioxidant, is contained in 188 kinds of Chinese herbs, such as Sophora flavescent, forsythias, and ginkgo. It is known to protect the heart, resist ulcer, virus, inflammation, infection, allergy and regulate the immune responses (Na et al., 2018). Moreover, numerous studies have reported the anti-tumour effect of quercetin. According to Ezzati et al. (2020), quercetin caused human breast cancer cell apoptosis through anti-mitochondrial pathways and activating Caspase pathway. Similarly, Pang et al. (2019) reported that quercetin reduced the mortality rate among patients with rectal cancer by targeting SLCO1B1 to inhibit cell growth and induce tumour cell apoptosis. Luteolin is a natural flavonoid widely found in vegetables, Chinese herbs, fruits, and other plants. It has anti-inflammatory, anti-allergic, reductive uric acid, antibacterial, antiviral, and other effects, and is largely used in clinical cough, expectorants, and as an anti-inflammatory compound. Luteolin has been reported to display wide anticancer activities through suppressing proliferation, enhancing apoptosis, decreasing metastasis and sensitising drug resistance (Du et al., 2015; Lin et al., 2008). Kaempferol and its glycoylated derivatives are known to protect the heart, and resist inflammation, diabetes, tumour and oxidation (Chen and Chen, 2013). It exhibits multiple anti-tumour effects, including inhibiting cancer cell growth and invasion, promoting apoptosis while hindering angiogenesis (Imran et al., 2019). The above studies indicated that AAH has several pharmacological effects through the active ingredients mentioned above.

The AAH-disease interaction network analysis revealed that 141 genes, 139 genes, and 121 genes were related to tumours, digestive system diseases, and cardiovascular diseases, respectively. Genes inducing apoptosis and regulating inflammation were closely related to them. For example, VEGFA, AHR, BCL2, PON1, etc., can inhibit cancer cell proliferation, induce apoptosis through controlling mitochondrial membrane permeability, and reduce inflammation by preventing the activation of inflammatory bodies (Mohammadi et al., 2020; Ye et al., 2018; Hanahan and Weinberg, 2011; Yuan et al., 2021). In addition, the analysis of potential disease genes of AAH demonstrated the SOD2 gene to be enriched in 21 diseases, indicating the intricate association of SOD2 with the treatment of these diseases. SOD is an antioxidant enzyme to protect the cells

from damage caused by reactive oxygen species. Among the three known isoenzymes of SODs in mammals, SOD2 is present in human mitochondria. The expression of SOD2 affects the balance between oxidation and antioxidation in the body, and it has been implicated disease genesis and progression, like tumour (Alateyah et al., 2022; Cyr et al., 2013; Ashtekar et al., 2018).

Interaction analysis on active proteins of AAH revealed the involvement of target proteins of AAH in an interlaced network relationship, thus not acting alone. Based on the network topology analyses on 194 shared targets, TP53, RB1, and RELA were the potential core targets of AAH. Therefore, we analysed the mode of interaction between effective components of AAH and amino acid residues in TP53, RB1, and RELA, which indicated that active components of AAH interacted with the core targets mainly through van der waals forces, ionic interactions, conventional hydrogen bonds, and other molecular forces. Collectively, we found that TP53, RB1, and RELA can combine stably with the components of AAH through different types of molecular interactions. TP53 gene is responsible for encoding the tumour suppressor proteins that possess transcription activity, as well as the oligomerisation and DNA binding domains. It has been recognised as the tumour suppressor inducing cell cycle arrest, apoptosis, and aging. The mutation of the TP53 gene is related to several human tumours (Marcel et al., 2010; Yin et al., 2002). RB1 is a tumour suppressor gene first discovered during the research on human retinoblastoma. It can modulate the levels of genes related to cell proliferation and differentiation by combining with transcription factors to maintain the balance of cell growth and development via cell cycle, cell aging, and cell apoptosis (Gong et al., 2019). Similarly, RELA belongs to the NF-κB family, whose post-translational modification is known to modulate NF-κB transcriptional activity and consequently control important processes like inflammation, immune response, tumour metabolism, and disease genesis and progression (Lu and Yarbrough, 2015).

The GO analysis of 194 potential therapeutic targets of AAH demonstrated that the BP in which AAH was involved were largely cell response to drugs, cell response to chemical stress, cell response to lipopolysaccharide, cell response to metal ions, and cell response to reactive oxygen species. They primarily act on CC such as membrane rafts, membrane domains, whole enzyme complex, protein kinase complex, and vesicle cavities. The KEGG signalling pathway enrichment analysis demonstrated that AAH exerted the activities against inflammation, analgesia, and cancer primarily through the cancer pathway, AGE-RAGE, IL-17, and TNF pathways. Abnormal AGE-RAGE pathway has been related to the pathogenesis of diabetic nephropathy. AGEs are metabolites in the high-sugar environment, also called ‘glycotoxins’. RAGE belongs to the low-affinity pattern recognition receptor family, which contributes to both innate and adaptive immunity (Vlassara and Striker, 2013). The toxic effects of AGEs involve the destruction of kidney cells and tissues. In addition, they can combine with RAGE to form the AGE-RAGE signalling pathway and activate the downstream signalling pathways, including p38MAPK, PI3K/Akt and NF-κB, and they are jointly associated with apoptosis, inflammation, and oxidative stress in diabetic nephropathy (Manigrasso et al., 2014). IL-17 is an early promoter of the inflammatory response induced by T cells. It binds to IL-17R on the cell surface to induce different cell types to secrete inflammatory factors like TNF-a, IL-1, IL-6, and other chemokines, and promote inflammation (Yu et al., 2020). Besides, IL-17 binding to receptor activates related downstream signalling pathways and participates in the development of inflammation, autoimmune diseases, and tumours (Huang et al., 2016). According to our results, a majority of potential therapeutic

targets of AAH were associated with these above two signalling pathways, suggesting its role in the treatment of diabetic nephropathy and autoimmune diseases via these two pathways. However, no relevant literature is available on the same, warranting follow-up research related to its action mechanism to offer guidance for developing novel indications of AAH.

5 Conclusions

The material basis and pharmacological mechanism of action of AAH were analysed using network pharmacology. The results conformed to the multi-component, multi-target, and diverse regulation modes of Chinese medicines. The predicted therapeutic targets related to those known pharmacological effects, indicating that our target prediction results were accurate. However, existing literature has mostly focused on the anti-tumour mechanism of AAH, while little research is conducted to examine its analgesic and anti-inflammatory properties. In the future, research in these areas is warranted for providing new ideas for developing and applying AAH.

Data availability

Data utilised in the present work can be obtained from the corresponding author.

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