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Molecular docking and network pharmacological analysis of *Scutellaria baicalensis* against renal cell carcinoma

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Abstract. – OBJECTIVE: This paper employs network pharmacology and molecular docking to analyze the active components, targets, and molecular mechanisms of *Scutellaria baicalensis* in treating renal cell carcinoma (RCC).

MATERIALS AND METHODS: The potential active target genes and components of *Scutellaria baicalensis* are obtained by searching the TCMSP database, and RCC targets are obtained using OMIM, Genecards, and Drugbank databases. The interaction of target proteins is analyzed thanks to STRING, and the component target disease network diagram is constructed through Cytoscape 3.8.2 software. Besides, KEGG, and GO enrichment analysis is performed using the Bioconductor bioinformatics R software package. AutoDock Vina 1.1.2, PyMol 2.5 and Maestro 12.9 software are used for molecular docking.

RESULTS: According to the results, *Scutellaria baicalensis*, which has 36 active ingredients, 500 drug targets, and 85 drug-disease common targets in the treatment of RCC, relies mainly on active ingredients, including wogonin, baicalein, acacetin, oroxylin A, moslosooflavone, salvigenin, and neobaicalein. In addition, the core components within *Scutellaria baicalensis* that contribute to the treatment of renal cancer are *TP53, CCND1, STAT3, CASP3, JUN, VEGFA, AKT1*, and *EGFR*; while the main molecular mechanisms that helps relieve RCC include *PI3K-Akt, Ras, MAPK, p53, VEGF*, and *JAK-STAT* signaling pathway. Molecular docking suggested that wogonin had a good binding affinity with core proteins *CASP3*, *CCND1*, *JUN*, *STAT3*, *TP53*, and *VEGFA*.

CONCLUSIONS: This study confirms that *Scutellaria baicalensis* can treat RCC in a multi-component, multi-target, and multi-way manner.

Key Words:
Scutellaria baicalensis, Renal cell carcinoma, Network pharmacology, Molecular mechanism, target, Signaling pathway.

Introduction

Renal cell carcinoma (RCC) is a rare but deadly urological malignancy, with incidence rates on the rise globally. Studies suggest[1-4] that 70-80% of RCC are clear cell RCC (ccRCC), presenting higher tumor recurrence and metastasis rates than other RCC subtypes. Based on the Cancer Statistics Report, it is claimed that there are about 140,000 deaths worldwide annually[1,5,6]. Although early-stage RCC can be controlled with surgery or radiofrequency ablation, up to one-third of patients still develop fatal distant metastasis[5-7]. Moreover, the major clinical methods, covering chemotherapy, immunotherapy and targeted drugs, perform obvious side effects and even incur unfavorable overall prognosis[6-8]. As a result, the exploration of safe and efficient therapeutic drugs that benefit the prognosis is taken as a priority.

Scutellaria baicalensis (also known as hollow grass), is a member of the *Lamiaceae* family. Modern pharmacological studies[9,10] prove that its main active components are flavonoids, glycosides, and mushroom compounds, which feature antioxidant, anti-inflammatory, antibacterial, and tumor growth inhibitory effects and relieve multiple diseases. When it comes to tumor diseases, such active components function by controlling the proliferation of tumor cells, inducing their apoptosis, and undermining their metastasis and angiogenesis, which indicates their prospect and value in anti-tumor application[11-13]. However, the active components, molecular targets, and action mechanisms of *Scutellaria baicalensis* against RCC are rarely reported. Network pharmacology refers to a systematic approach based on the interaction of medicinal materials, components, targets, and diseases, the latter packages information, and employs computational methods such as bioinfor-

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matics and network analysis to reveal drug targets and possible mechanisms[14,15]. This paper aims to elaborate on the biological process of *Scutellaria baicalensis* against RCC using network pharmacology and reveal its therapeutic mechanism from the perspective of targets and signaling pathways, thus providing insight into further experimental research and clinical application.

Materials and Methods

Active Ingredients of Scutellaria baicalensis and Target Screening

TCMSP lists the ingredients of *Scutellaria baicalensis*. The screening of such ingredients is usually completed with oral bioavailability (OB) ≥ 30% and drug-likeness (DL) ≥ 0.18 in previous literature16,17. In addition, the Canonical SMILES expression of Scutellaria baicalensis in the PubChe database is adopted in the Swiss Target Prediction database for target prediction. Then, the active components and 500 targets are imported into Cytoscape software to draw a "component-target" network, and the top 10 components and targets by degree value are obtained thanks to the Network Analyzer (California, USA) plug-in.

Target Screening of Scutellaria baicalensis and RCC

The disease targets are collected using OMIM, Genecards, and Drugbank databases with keywords including renal cancer, renal carcinoma, kidney cancer, renal cell carcinoma, kidney tumor, and renal clear cell carcinoma. The Venn diagram of *Scutellaria baicalensis*-renal cancer common target is also drawn employing the Venny 2.1 online (available at: http://www.liuxiaoyuyuan.cn/) software mapping tool platform.

Analysis of Core Components of Scutellaria baicalensis in the Treatment of RCC and Construction of Scutellaria baicalensis-Component-Target-RCC Network

The 36 active components of *Scutellaria baicalensis* and 85 common targets of *Scutellaria baicalensis* and RCC were imported into Cytoscape 3.8.2 software to construct a "drug-ingredient-target-disease" network diagram. Topological analysis was performed on the network graph using Network Analyzer, and the main active components and therapeutic targets of *Scutellaria baicalensis* were ranked for analysis.

Scutellaria Baicalensis-Renal Cancer Common Target PPI Network Construction and Core Target Analysis

The 85 common targets of *Scutellaria baicalensis* and RCC are typed into the STRING database for a PPI network of protein interactions. PPI network is later imported into Cytoscap 3.8.2 (California, USA), a topological analysis is performed on the Network Analyzer, the top 20 genes are taken as core targets, and a bar graph is created using R 4.0.5 (The R Foundation for Statistical Computing, Vienna, Austria).

GO and KEGG Functional Enrichment Analysis of Core Biological Targets

The GO and KEGG functional enrichment analysis of key target genes is conducted with p-value < 0.05 and Q-value < 0.05 through Bioconductor bioinformatics software R 4.0.5 (The R Foundation for Statistical Computing, Vienna, Austria) package based on R software, whose top results are presented in bar graphs.

Construction of Active Ingredient-Target-Pathway Network of Scutellaria baicalensis

The top 20 pathways and related component targets in the *KEGG* enrichment analysis that are later input into Cytoscape 3.8.2 software, combined with the components, targets, and signaling pathways, contribute to the creation of a "component-target-pathway" network map.

Molecular Docking Analysis

AutoDock Vina 1.1.2 software (The Molecular Graphic Laboratory, The Scripps Research Institute, La Jolla, CA, USA) is used for molecular docking. Before docking, PyMol 2.5 (Pennsylvania, USA) is used to process all receptor proteins. When docking, the global search detail is set to 20, and the other parameters are set by default. The docking conformation with the highest score is considered as the combining conformation. Finally, PyMol 2.5 and Maestro 12.9 (Pennsylvania, USA) are used to analyze the docking results visually.

Results

Screening of Active Components of Scutellaria baicalensis and Target Prediction

Table I reveals that the active ingredients of *Scutellaria baicalensis* are screened with OB ≥ 30% and

Table I. Screening of active components from *Scutellaria baicalensis*.

Mol ID	Molecule Name	OB (%)	DL
MOL001689	Acacetin	34.97	0.24
MOL000173	Wogonin	30.68	0.23
MOL000228	Alpinetin	55.23	0.2
MOL002714	baicalein	33.52	0.21
MOL002908	5,8,2'-Trihydroxy-7-methoxyflavone	37.01	0.27
MOL002909	5,7,2,5-tetrahydroxy-8,6-dimethoxyflavone	33.82	0.45
MOL002910	Carthamidin	41.15	0.24
MOL002911	2,6,2',4'-tetrahydroxy-6'-methoxychaleone	69.04	0.22
MOL002913	Dihydrobaicalin_qt	40.04	0.21
MOL002914	Eriodyctiol (flavanone)	41.35	0.24
MOL002915	Salvigenin	49.07	0.33
MOL002917	5,2',6'-Trihydroxy-7,8-dimethoxyflavone	45.05	0.33
MOL002925	5,7,2',6'-Tetrahydroxyflavone	37.01	0.24
MOL002926	Dihydrooroxylin A	38.72	0.23
MOL002927	Skullcapflavone II	69.51	0.44
MOL002928	Oroxylin a	41.37	0.23
MOL002932	Panicolin	76.26	0.29
MOL002933	5,7,4'-Trihydroxy-8-methoxyflavone	36.56	0.27
MOL002934	NEOBAICALEIN	104.34	0.44
MOL002937	DIHYDROOROXYLIN	66.06	0.23
MOL000358	Beta-sitosterol	36.91	0.75
MOL000359	Sitosterol	36.91	0.75
MOL000525	Norwogonin	39.4	0.21
MOL000552	5,2'-Dihydroxy-6,7,8-trimethoxyflavone	31.71	0.35
MOL000073	Ent-Epicatechin	48.96	0.24
MOL000449	Stigmasterol	43.83	0.76
MOL001458	Coptisine	30.67	0.86
MOL001490	Bis[(2S)-2-ethylhexyl] benzene-1,2-dicarboxylate	43.59	0.35
MOL001506	Supraene	33.55	0.42
MOL002879	Diop	43.59	0.39
MOL002897	Epiberberine	43.09	0.78
MOL008206	Moslosooflavone	44.09	0.25
MOL010415	11,13-Eicosadienoic acid, methyl ester	39.28	0.23
MOL012245	5,7,4'-trihydroxy-6-methoxyflavanone	36.63	0.27
MOL012246	5,7,4'-trihydroxy-8-methoxyflavanone	74.24	0.26
MOL012266	Rivularin	37.94	0.37

DL ≥ 0.18, and 36 active components are observed. The 500 drug targets that are screened thanks to the Swiss Target Prediction database and TCMSP database are duplicated. Figure 1 and Table II list the main active components, covering wogonin, baicalein, acacetin, oroxylin A, and moslosooflavone, as well as the main targets, including *PTGS2*, *ESR2*, *PTGS1*, *CYP19A1*, and *ADORA1.*

Screening of Core Active Components and Targets of Scutellaria baicalensis in the Treatment of RCC

Relevant literature is searched on OMIM, Genecards, and Drugbank databases, collecting and duplicating a total of 1,404 renal cancer targets. Figure 2A illustrates the 85 common drug-disease targets obtained by taking the intersection of 500 targets of *Scutellaria baicalensis* and RCC targets; Figure 2B and Table III list the main active components of *Scutellaria baicalensis* in the treatment of RCC, which are wogonin, baicalein, acacetin, oroxylin A, moslosooflavone, salvigenin, and neobaicalein. In addition, 85 drug-disease common targets are analyzed by PPI network (Figure 3A), protein interaction network (Figure 3B, the larger node leads to darker color, thus higher degree value), the PPI topology (Figure 3C), and clustering (Figure 3D), *TP53*, *CCND1*, *STAT3*, *CASP3*, *JUN*, *VEGFA*, *AKT1*, and *EGFR* are observed to be the main targets.

GO Enrichment Analysis of Scutellaria baicalensis in the Treatment of RCC

The GO enrichment analysis confirms the enrichment of 85 intersecting genes in 2,000 bio-

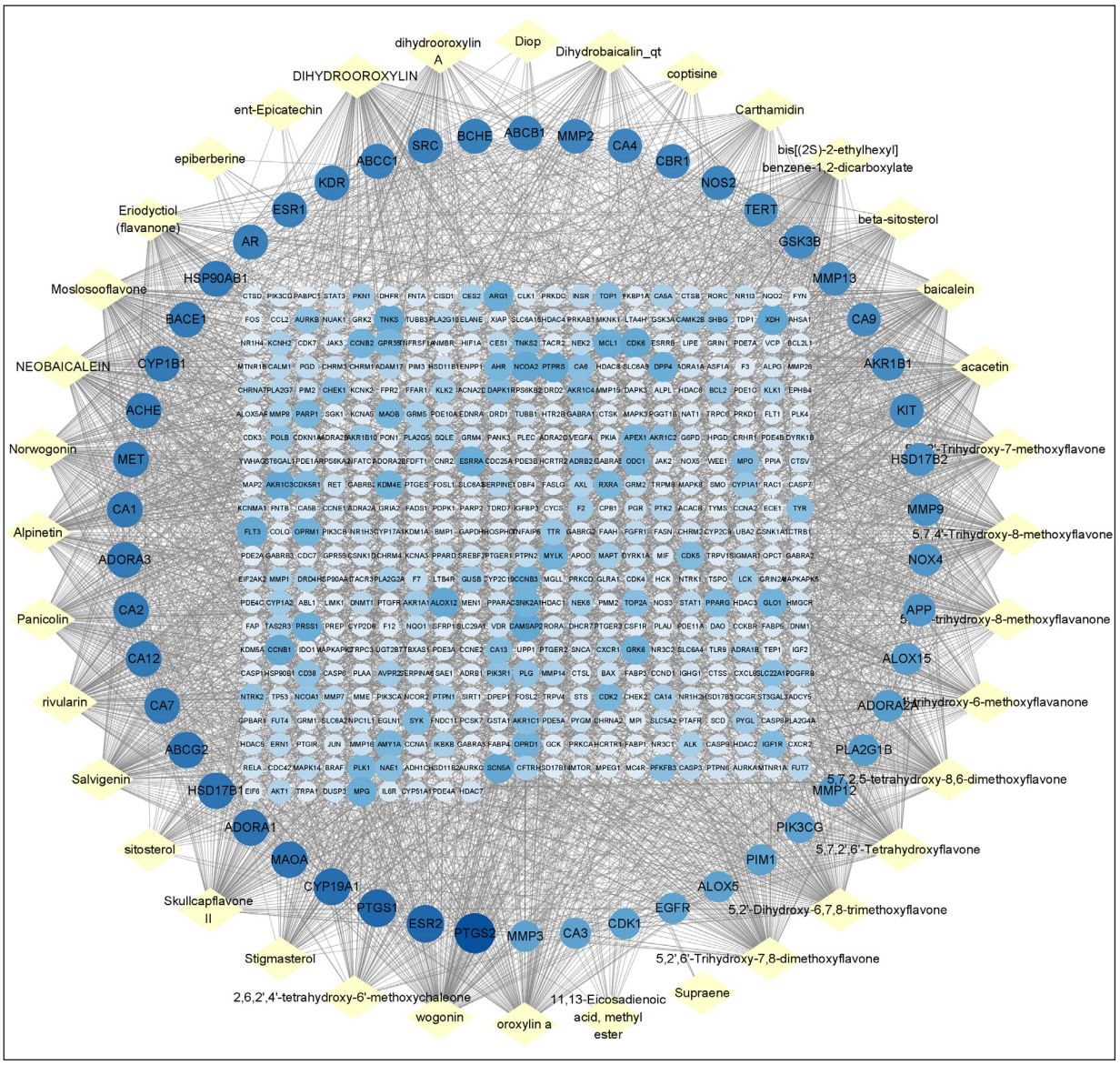

Figure 1. Network diagram of component targets of *Scutellaria baicalensis*. The diamonds represent the active ingredient of *Scutellaria baicalensis* and the circles represent the drug targets. The larger the diamond and the circle, the darker the color the higher the degree value of the active ingredient and target.

Table II. Major compositions and targets in *Scutellaria baicalensis* (top 10).

Composition	Degree value	Target	Degree value
Wogonin	138	PTGS2	32
Baicalein	130	ESR2	28
Acacetin	121	PTGS1	28
Oroxylin A	121	CYP19A1	27
Moslosooflavone	117	ADORA1	26
Salvigenin	116	HSD17B1	26
Neobaicalein	115	ABCG2	26
5,2'-Dihydroxy-6,7,8-trimethoxyflavone	114	MAOA	26
5,7,4'-Trihydroxy-8-methoxyflavone	114	CA7	25
Skullcapflavone II	114	CA12	25

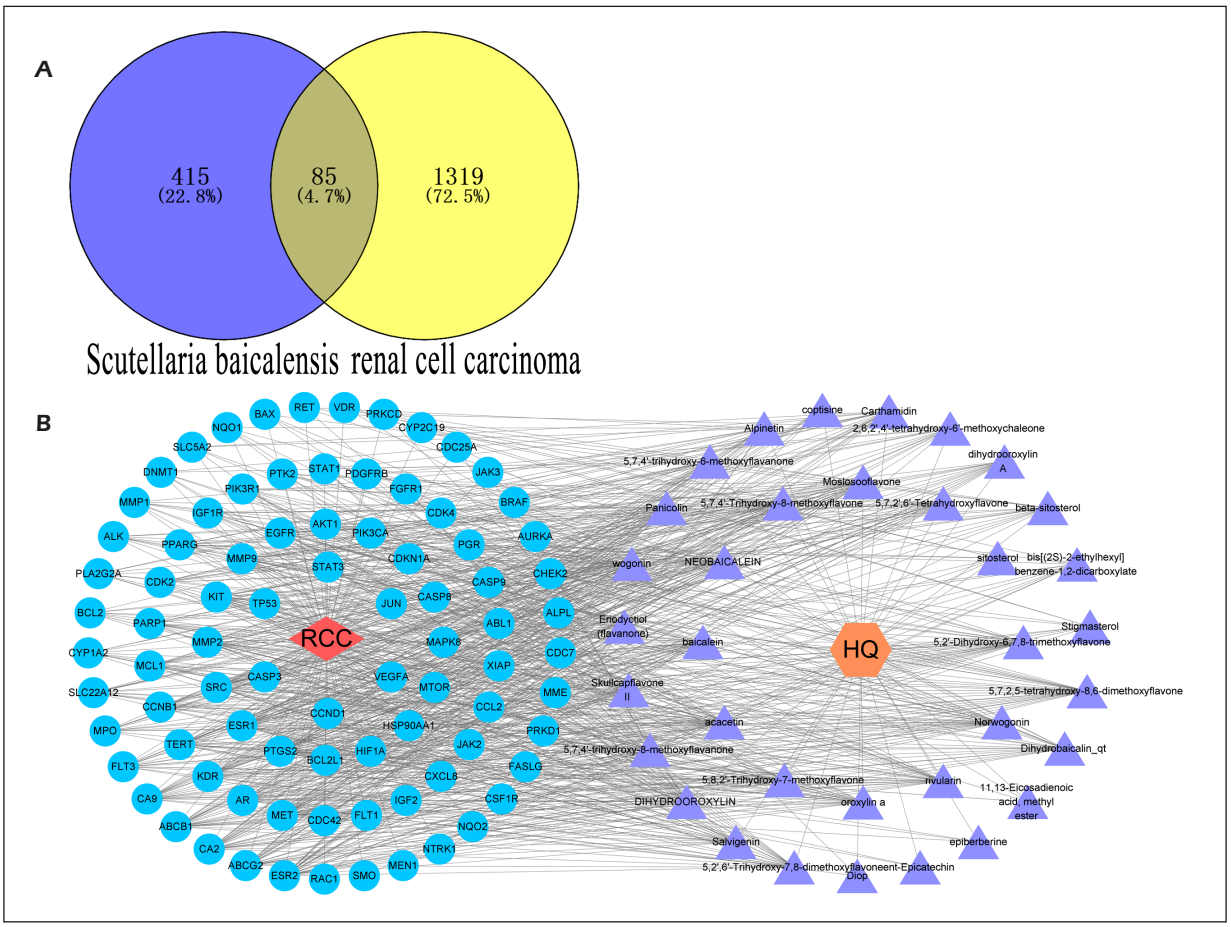

Figure 2. Network analysis of common targets in *Scutellaria baicalensis* and renal cancer; (**A**), represents Venn diagram analysis of common targets of *Scutellaria baicalensis* and renal cancer, and (**B**) a network graph analysis of the interaction between active components of *Scutellaria baicalensis* and a common target in renal cancer.

logical process pathways, 42 in the expression process of cellular components, and 115 in the process of molecular function. Figure 4 shows the top 20 ranked by combined score in a bar graph. The major enrichment biological processes are as follows: protein autophosphorylation, epithelial cell proliferation, neuron death, regulation of neuron death, peptidyl-tyrosine phosphorylation, cellular response to chemical stress, peptidyl-tyrosine modification, etc., while the main molecular functions include protein tyrosine kinase activity, transmembrane receptor protein tyrosine kinase activity, transmembrane receptor protein kinase activity, protein phosphatase binding, ubiquitin-like protein ligase binding, nuclear receptor activity, etc. Meanwhile, the main cell components cover membrane raft, membrane microdomain, membrane region, organelle outer membrane, outer membrane, etc.

KEGG Target Pathway Annotation Analysis and Drug-Target-Pathway Map Analysis

The KEGG analysis reveals the enrichment of 85 intersecting genes in 148 KEGG pathways (**Supplementary Data 1**). Figure 5 shows the first 20 based on *p*-value through a bar graph. Meanwhile, the top 20 pathways and related component targets obtained are input into Cytoscape software for a network diagram of "component-target-pathway" interaction (Figure 6). Figure 5 and **Supplementary Data 1** list the pathways with abundant enriched genes, covering tumor-related pathways, *PI3K-Akt*, *Ras*, *MAPK*, *p53*, *VEGF*, and *JAK-STAT* signaling pathways.

Molecular Docking Analysis

Network pharmacology suggests that wogonin is the most important active ingredient of *Scutellaria baicalensis*. Then, we made molec-

Table III. Core active components of *Scutellaria baicalensis* in the treatment of renal cell carcinoma.

Composition	Degree value
Wogonin	41
Acacetin	36
Baicalein	33
NEOBAICALEIN	32
5,7,4'-Trihydroxy-8-methoxyflavone	30
Moslosooflavone	28
5,2'-Dihydroxy-6,7,8-trimethoxyflavone	27
5,7,2,5-tetrahydroxy-8,6-dimethoxyflavone	27
5,7,2',6'-Tetrahydroxyflavone	27
Norwogonin	27
Oroxylin a	26
Rivularin	26
5,2',6'-Trihydroxy-7,8-dimethoxyflavone	25
DIHYDROOROXYLIN	25
Salvigenin	25
5,7,4'-trihydroxy-8-methoxyflavanone	24
Eriodyctiol (flavanone)	24
Skullcapflavone II	24
5,8,2'-Trihydroxy-7-methoxyflavone	23
Panicolin	23
5,7,4'-trihydroxy-6-methoxyflavanone	22
Alpinetin	21
Dihydrobaicalin_qt	21
Carthamidin	20
2,6,2',4'-tetrahydroxy-6'-methoxychaleone	16
dihydrooroxylin A	16
Beta-sitosterol	15
Bis[(2S)-2-ethylhexyl] benzene-1,2-dicarboxylate	11
Stigmasterol	9
Sitosterol	8
Coptisine	7
11,13-Eicosadienoic acid, methyl ester	5
Epiberberine	4
Diop	3
Ent-Epicatechin	3

ular docking between wogonin and core target molecules *TP53*, *CCND1*, *STAT3*, *CASP3*, *JUN*, and *VEGFA*. We found that wogonin can form hydrogen bonds with *ARG-207* in *CASP3* and hydrophobic interaction with *HIS-121* and *PHE-128* (Figure 7A). Wogonin forms a hydrogen bond with *ARG-235* and *PHE-232* of *CCND1* and hydrophobic interaction with *ARG-29* and *LEU-2861* (Figure 7B). In the interaction with *JUN* (Figure 7C), we found that wogonin can form a hydrogen bond with *GLU-275* and hydrophobic interaction with *LEU-280* and *ARG-279*. In the interaction with *STAT3* (Figure 7D), it can be found that wogonin forms a hydrogen bond with *MET-660* and hydrophobic interaction with *ALA-662*, *GLU-625*, and *VAL-667*. Wogonin can form hydrogen bonds with *GLY-224*, *MET-246*, *ASN-247*, *GLY-244*, and *TYR-163* of *TP53*, and hydrophobic interaction with *GLU-171*. Wogonin can form hydrogen bonds with *GLY-59* of *VEGFA* and hydrophobic interaction with *LEU-32*, *ILE-29*, and *THR-31*. In addition, the binding affinity score of wogonin with each protein is lower than -6 kcal/mol (Table IV), which indicates that wogonin has good binding affinity with *CASP3*, *CCND1*, *JUN*, *STAT3*, *TP53*, and *VEGFA*.

Discussion

RCC, which accounts for 2% of malignant tumors, causes the death of over 100,000 people every year[1,2]. Numerous patients still suffer from post-surgery recurrence or metastasis despite the prior treatment of kidney cancer in the infancy stage[1,2]. Moreover, while immunotherapy and targeted drugs have contributed significantly to the prognosis and survival of patients with renal cell carcinoma (RCC), their therapeutic effect is limited, and they often cause noticeable side effects. Therefore, there is a need to develop new drugs that are more effective and have fewer side effects, thereby improving both efficacy and life expectancy[3-8]. *Scutellaria baicalensis*, the dry root of the *Lamiaceae* plant, is used in traditional Chinese medicine, and its anti-inflammatory, antioxidant, and anti-tumor effects have been proved by modern research[9-13]. Despite the essential role of its bioactive components in inhibiting gastric, breast, ovarian, liver, and other tumors, there exist few studies[9-13] on the active components, molecular targets and mechanism of action of *Scutellaria baicalensis* in the treatment of RCC. This paper verifies the 36 main active chemical components and 500 drug targets within *Scutellaria baicalensis* through network pharmacology, among which wogonin, baicalein, acacetin, oroxylin A, moslosooflavone, and salvigenin serve as the major contributor as for its application in treating *RCC*. The anti-renal cancer active components mostly consist of flavonoids and polyphenolic compounds, which outperforms in inhibiting tumor cell proliferation and inducing tumor cell apoptosis[12,13,18-20]. Wogonin, acacetin, and baicalein can induce G0/G1 phase arrest, increase ROS levels, inhibit cell proliferation, and promote apoptosis in tumor cells[18-20]. *Oroxylin A*, *moslosooflavone*, and *salvigenin* perform anti-tumor role through *AKT*, *NF-κB*, *P53*, *EGFR* and other pathways[18-20].

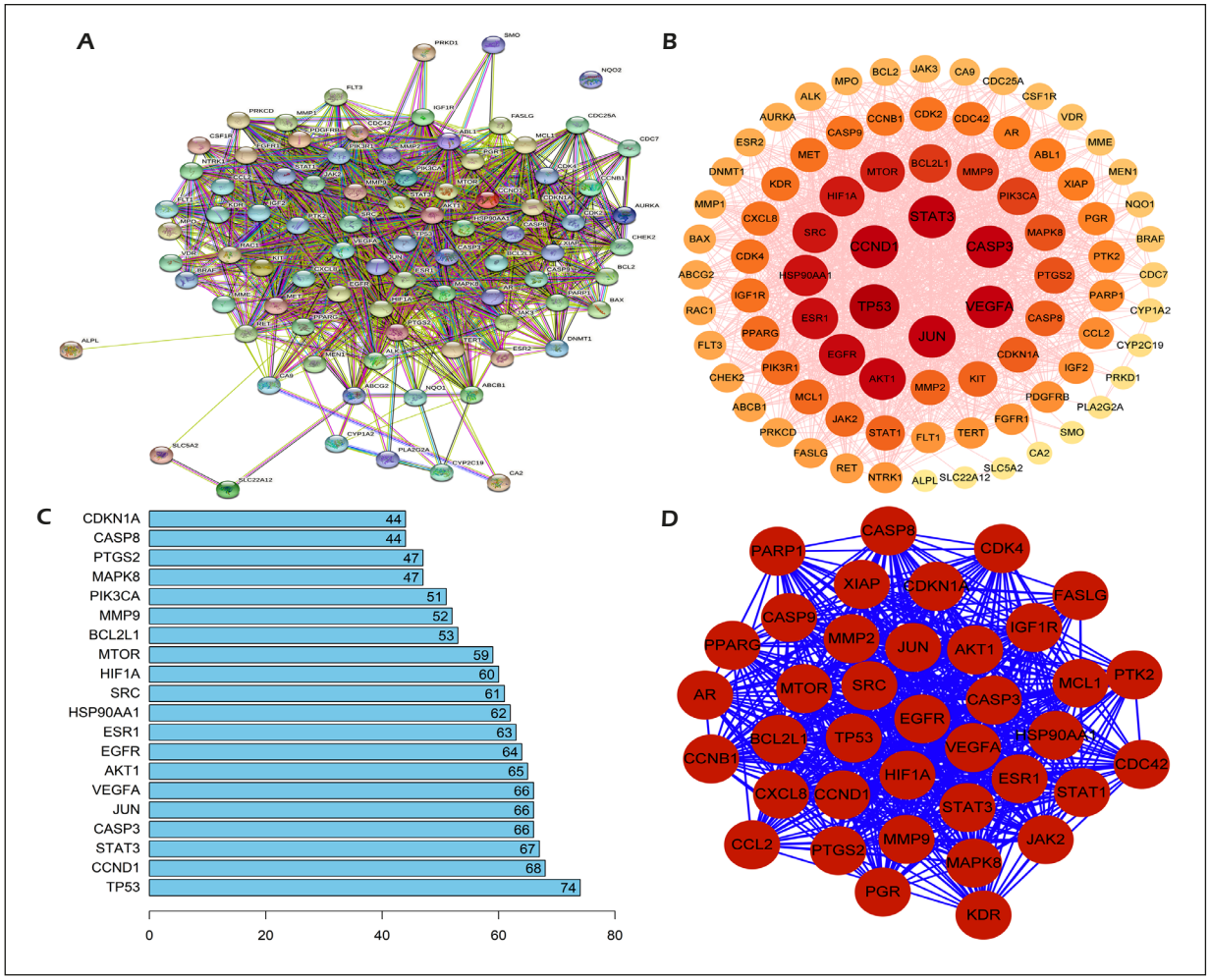

Figure 3. *Scutellaria baicalensis* and renal cancer common target protein interaction analysis, in which (**A**) depicts the core target protein PPI network diagram, (**B**) the core target protein interaction network diagram, (**C**) the top 20 core target molecular bar graph, while (**D**) the top 20 core target protein-protein interaction network diagram.

The main targets of *Scutellaria baicalensis* in the treatment of RCC, including TP53, CCND1, STAT3, CASP3, JUN, VEGFA, AKT1, and EGFR, are observed through *PPI* and protein network analysis. In this study, we found that wogonin, the most important active component of *Scutellaria baicalensis*, has good binding affinity with the core target molecules *CASP3, CCND1, JUN, STAT3, TP53* and *VEGFA* through molecular docking. Studies[20-24] suggest that Tp53 is one of the inhibitors of tumorigenesis, which affects the occurrence and development of renal cell carcinoma. *P53*, the protein of *Tp53*, fights against tumor by regulating tumor cell cycle and facilitating tumor apoptosis[20-24]. The role of wogonin and baicalein, the active biological species of *Scutellaria baicalensis*, in up-regulating the expression and activity of *p53* is proved, thus crippling tumor cell proliferation and benefiting apoptosis[20-26]. *VEGF*, which supposedly promote the growth of new blood vessels in ccRCC and its metastases, brings about inactivation or deletion of *VHL* gene through increased expression, bothering 50% to 60% of patients with ccRCC[27]. *VEGFA*, the main angiogenic factor of the *VEGF* family, is involved in the biological process of RCC occurrence and metastasis, the blocking of which performs obvious anti-RCC effect[27-29]. The active biological wogonin, baicalein, and oroxylin A within *Scutellaria baicalensis* are proved to shape *VEGFA* to display anti-tumor effect[27-29]. *CASP3*, as a key player downstream of caspase cascade activation in the apoptotic pathway, up-regulates its protein expression to facil-

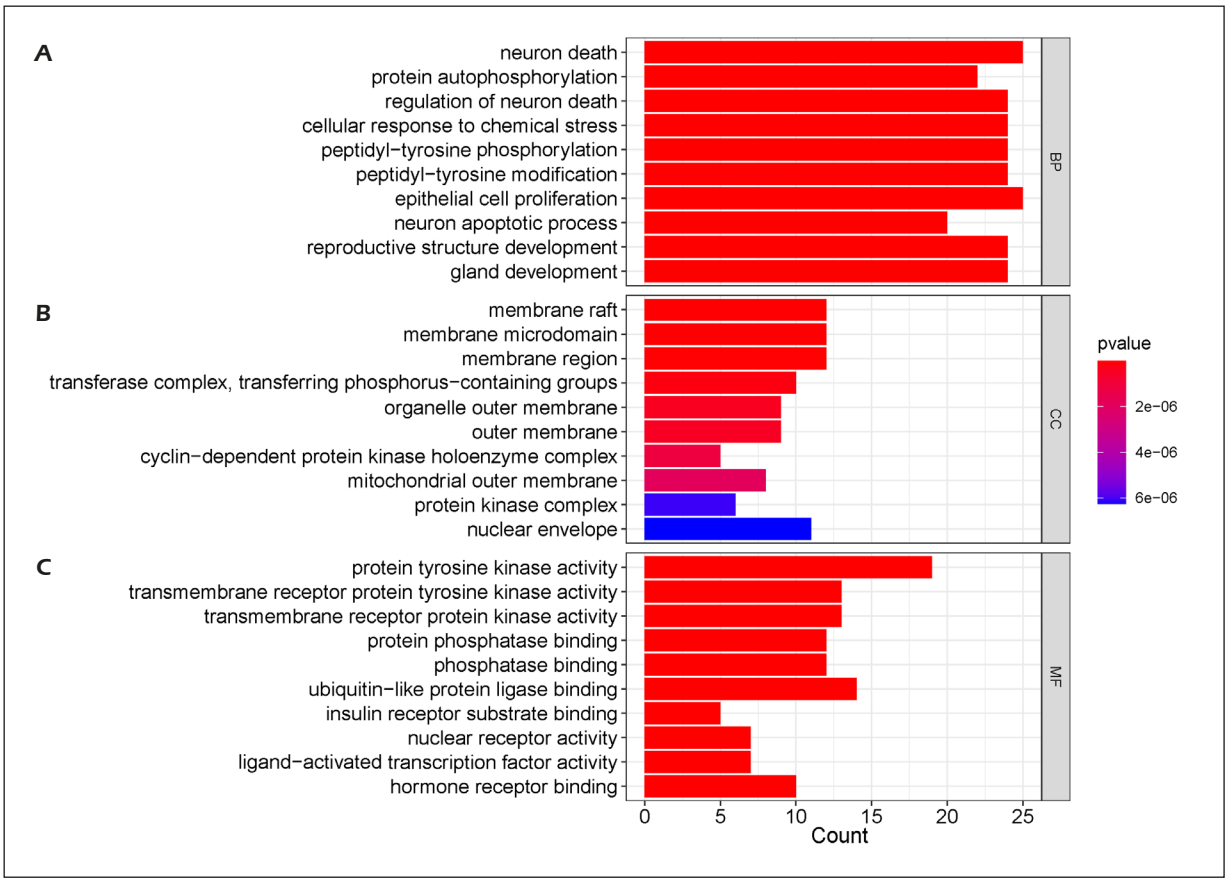

Figure 4. GO enrichment analysis of core targets of *Scutellaria baicalensis* and renal cancer (Top 10). **A**, Biological process. **B**, Cellular component. **C**, Molecular function.

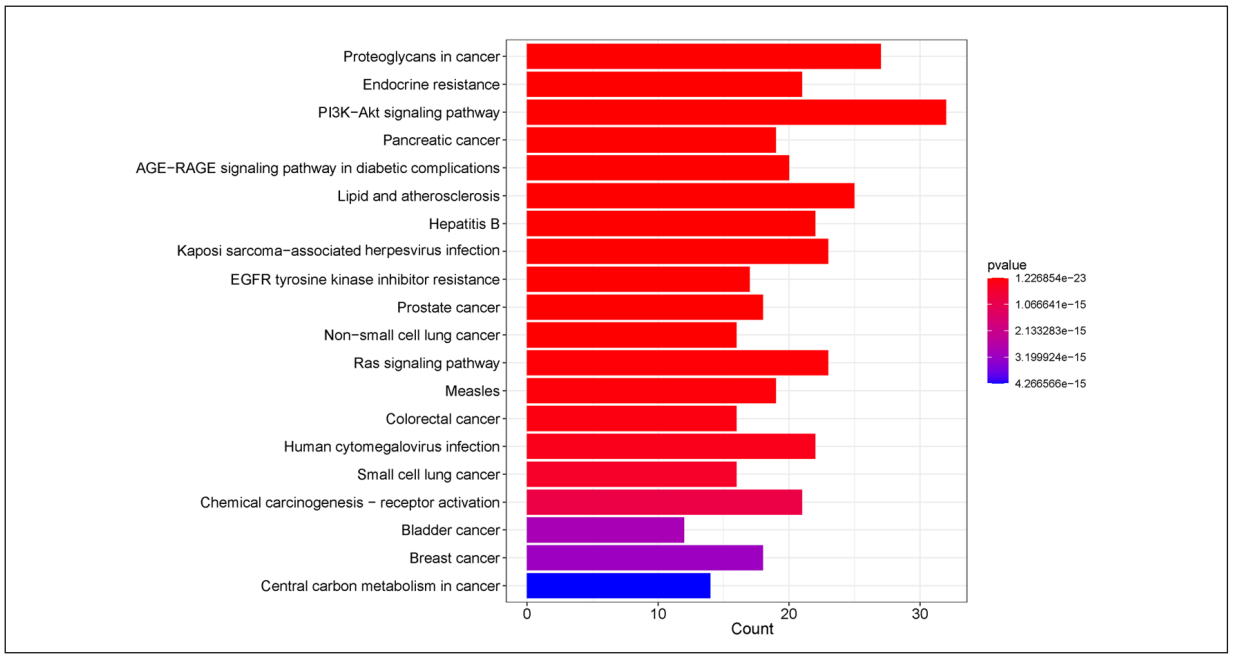

Figure 5. KEGG pathway enrichment analysis of core targets of *Scutellaria baicalensis* and renal cancer (top 20).

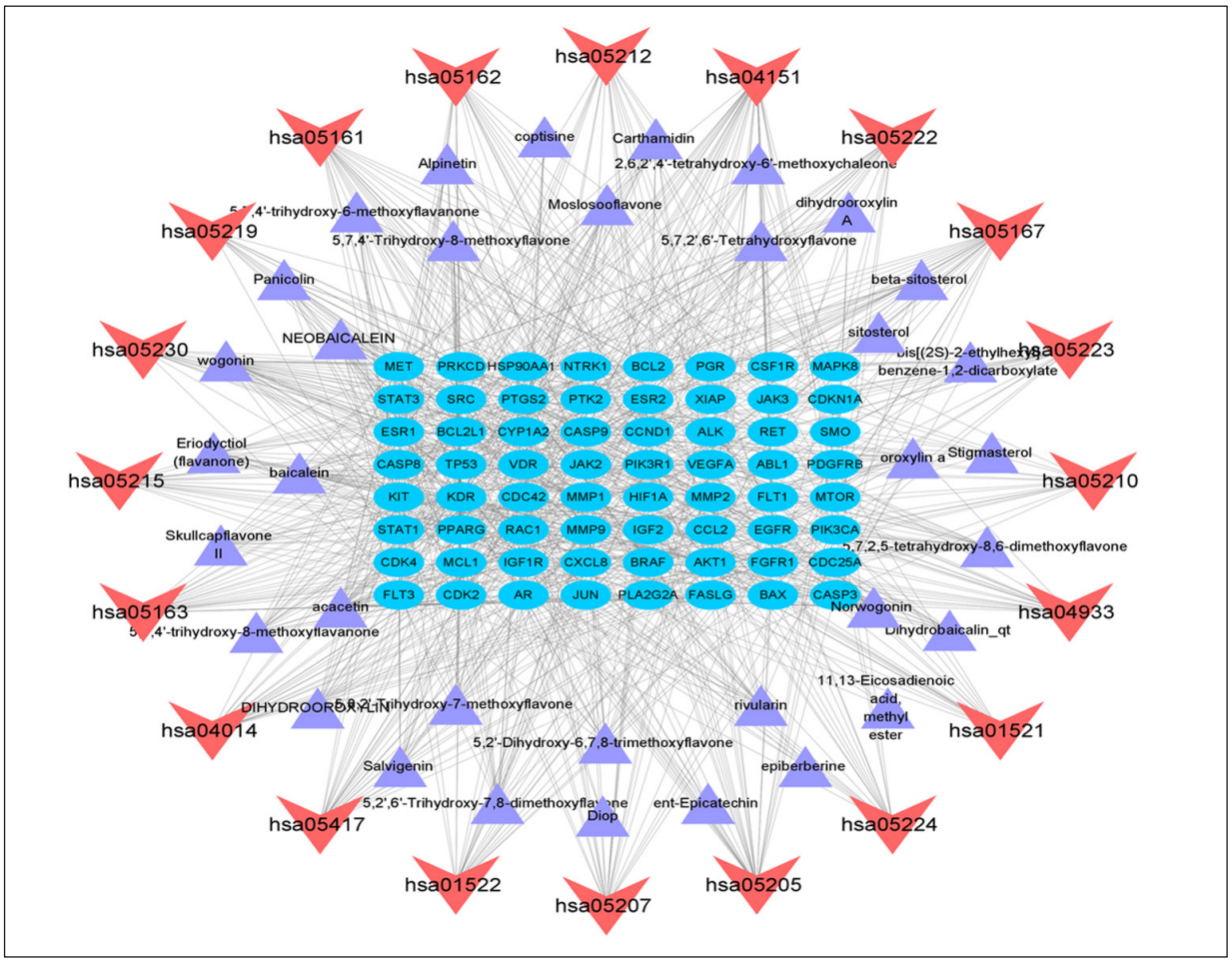

Figure 6. *Scutellaria baicalensis* and renal cancer interaction network diagram of Composition-Target-Pathway (blue refers to the active component, green is the target, and red to the *KEGG* pathway, while the size of the shape in the figure is that of the degree value).

itate tumor cell apoptosis in RCC[30]. Fortunately, both wogonin and baicalein, the active biologics of *Scutellariab aicalensis*, can perform such up-regulation, thus fight against prostate cancer and cervical cancer[31,32]. Given the close relation between the *EGFR* overexpression or mutation with the proliferation, metastasis, malignancy, and invasion of RCC, the active biological *wo*gonin, baicalein, oroxylin A, moslosooflavone, and salvigenin of *Scutellaria baicalensis* realize anti-tumor effects through the *EGFR* pathway[21-23,33,34]. Blocking the expression and activation of target molecules including *STAT3*, *JUN*, and *AKT1* that are significantly activated in RCC also undermines the proliferation and differentiation of RCC, thus relieving tumor[35,36]. Various bioactive components in *Scutellaria baicalensis* also benefit from such target molecules for anti-tumor effect[12,13,18-20].

The role of active components of *Scutellaria baicalensis* in throttling renal cancer in the cytoplasm, mitochondria, and the nucleus is verified thanks to GO enrichment analysis, which cannot be realized with cellular response to stress, protein tyrosine kinase activity, epithelial cell proliferation, nuclear receptor activity, and protein phosphatase binding. The combination of literature reports[12,13,18-20,24-36] and *KEGG* enrichment analysis makes clear the main molecular mechanisms of *Scutellaria baicalensis* against RCC, including *PI3K-Akt*, *Ras*, *MAPK*, *p53*, *VEGF*, *and JAK-STAT* signaling pathway. The involvement of *PI3K-Akt* and *p53* signaling pathways in the occurrence and development of tumors, including RCC, is proved, which explains the rising popularity of research on the usage of gene knockout or small molecule drugs to inhibit *PI3K*, *Akt*, *p53,* and related genes, block

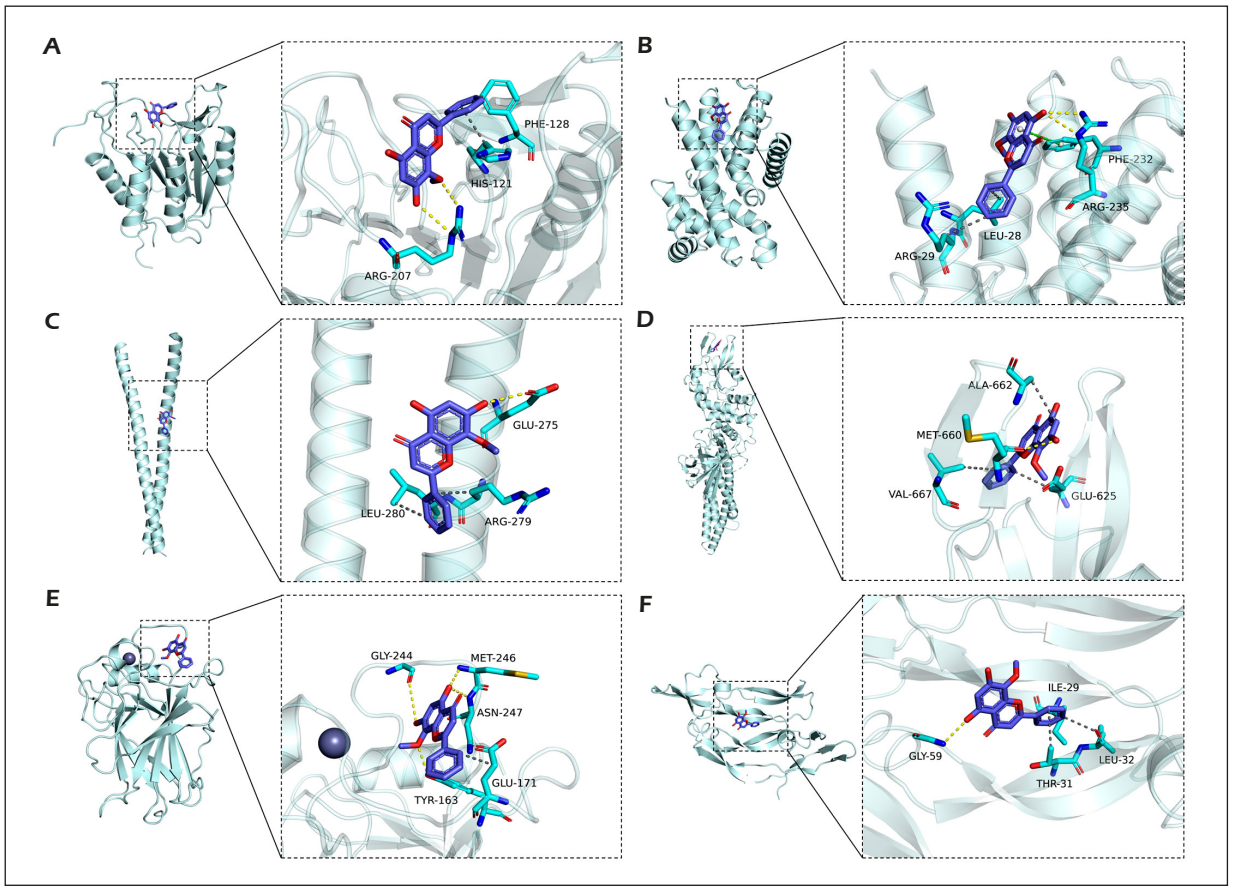

Figure 7. Core target and Wogonin molecular docking analysis. **A**, *CASP3*-Wogonin; (**B**), *CCND1*-Wogonin; (**C**), *JUN*-Wogonin; (**D**), *STAT3*-Wogonin; (**E**), *TP53*-Wogonin; (**F**), *VEGFA*-Wogonin.

the activation of various downstream effector molecules, undermine tumor proliferation, and promote tumor cell apoptosis in tumor treatment field[24,25,36-38]. The essential part of active components wogonin, baicalein, and oroxylin A within *Scutellaria baicalensis* in dampening the growth of tumor cells and promote tumor cell apoptosis by blocking *PI3K-Akt* and *p53* signals[18-20,24,25,37,38], as well as the activation of the *MAPK* signal transduction pathway which contributes to the proliferation, differentiation, apoptosis, angiogenesis, and tumor metastasis of RCC, explains the active components' ability to combat tumor diseases through blocking the *MAPK*[39-41]. Research[42,43] on the molecular biology of RCC reveals that the activation of *VEGF* signaling pathway and *Ras* signaling pathway promotes the proliferation and metastasis of RCC, which can be prevented thanks to drugs that constrain the expression and function of the two pathways. It is worth mentioning that the bioactive components of *Scutellaria baicalensis* are also equipped with such ability[44,45]. The persistent activation of *STAT3*, which smooths tumor cell survival, proliferation, angiogenesis, invasion and metastasis, immune escape, and other physiological functions by regulating the transcription of target genes, can be found in various tumor cells including RCC, which for-

Table IV. Ligand-receptor binding affinity scores and protein crystal structures for each target.

Target name	Ligand name	Docking score (kcal/mol)	PDB ID
CASP3	Wogonin	-6.9	7DHZ
CCND1	Wogonin	-6.9	6P8E
JUN	Wogonin	-6.1	6NJS
STAT3	Wogonin	-6.8	5T01
TP53	Wogonin	-6.6	3DEK
VEGFA	Wogonin	-6.2	1BJ1

tunately can be made up for thanks to various bioactive components of *Scutellaria baicalensis* that block the conduction of *STAT3* signaling pathway in tumors, thus realizing anti-cancer effect[46,47].

Conclusions

The role of *Scutellaria baicalensis* in the treatment of RCC in a multi-component, multi-target, and multi-pathway is proved in the paper. The main active components of *Scutellaria baicalensis* in the treatment of *RCC* include wogonin, baicalein, acacetin, oroxylin A, moslosooflavone, salvigenin, and neobaicakein, the major targets cover *TP53*, *CCND1*, *STAT3*, *CASP3*, *JUN*, *VEGFA*, *AKT1*, and *EGFR*, while the main molecular mechanisms consist of *PI3K-Akt*, *Ras*, *MAPK*, *p53*, *VEGF*, and *JAK-STAT* signaling pathway. However, there exist flaws, including the failure to take low-abundance active ingredients into consideration, and the disparity between the potential targets and signaling pathways of database mining, which requires further expansion and experimental verification.

Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Ethics Approval

Not applicable.

Informed Consent

Not applicable.

Availability of Data and Materials

The datasets are available from the corresponding author upon reasonable request.

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Authors' Contribution

GJ and QJ wrote the manuscript; MZW, and WXJ contributed, reviewed, and edited the manuscript; GJ, QJ, and LQ contributed to the content, discussion, review, and editing of the manuscript.

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