Imperata cylindrica L. Rhizome: network pharmacology and molecular docking analysis of active ingredients and their mechanisms of action in treating acute kidney injury

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Abstract. Acute kidney injury (AKI) is a significant health concern that can result in kidney impairment and failure. *Imperata cylindrica* L., a traditional medicinal plant, has shown potential in treating renal diseases, though its mechanisms in AKI remain unclear. This research integrated network pharmacology and molecular docking to analyze the active constituents of Imperata cylindrica rhizome in relation to AKI treatment. Pharmacological databases were used to identify the active compounds and their therapeutic targets, while Venny 2.1.0 was employed to determine the common targets shared with AKI-related drugs. A protein–protein interaction (PPI) network was generated to illustrate target associations. ShinyGo was utilized to perform Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses. Molecular docking assessed the binding affinity and stability of active compounds with core targets. Key compounds, including 6-Methoxyflavone, Beta-Sitosterol, Bifendate, Luteolinidin, and Stigmasterol, were identified alongside 131 core targets. The docking results indicated strong binding interactions, suggesting therapeutic potential. These results offer valuable insight into the molecular mechanisms of *I. cylindrica* in AKI treatment, emphasizing the importance of further in vivo studies to validate its clinical effectiveness.

1 Introduction

Acute Kidney Injury (AKI) has attracted significant attention in recent years, primarily because of its association with a heightened risk of complications for patients. It is estimated that one in five patients admitted to the emergency department presents with AKI, and approximately one in three patients develops chronic AKI during their hospital

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stay [1]. This condition is prevalent among hospitalized patients and is linked to substantial morbidity and mortality. AKI is characterized by an abrupt reduction in kidney function, often triggered by ischemia and exposure to toxic agents. Diagnosis and staging of AKI, as outlined by several criteria, usually focus on changes in serum creatinine levels, urine output volume, and the indication for renal replacement therapy (RRT). However, creatinine, as a marker of glomerular filtration rate (GFR), has limitations in sensitivity, as it does not rise significantly until there is a substantial reduction in GFR or significant parenchymal damage. In the pathophysiology of AKI, inflammation often plays a dual role, acting as both a cause and a consequence of kidney injury. For instance, systemic lupus erythematosus can trigger glomerulonephritis, while nephrotoxic drugs can induce local inflammation, leading to kidney injury.

Inflammation not only accelerates disease progression but also strengthens the inflammatory response, perpetuating a cycle that complicates the treatment process. The process involves the activation of immune and stromal tissue cells, which facilitates the migration of immune cells and proteins from the bloodstream to the site of injury or infection, aiding in the repair process [2]. The inflammatory response occurs in distinct phases, starting with a rapid initiation stage that triggers a pro-inflammatory reaction, which later transitions into a resolution phase. While a well-regulated inflammatory response is essential for eliminating pathogens, persistent inflammation can negatively impact affected organs as well as surrounding tissues [3]. Several studies have emphasized the crucial role of inflammation in the onset and progression of various complex diseases. In general, inflammation can be divided into two types: acute and chronic. Acute inflammation tends to be temporary and protective, whereas chronic inflammation is sustained and linked to the onset of numerous chronic diseases, including diabetes, obesity, arthritis, cardiovascular diseases, pancreatitis, metabolic disorders, neurological conditions, and even cancer.

Considering that inflammation is involved in the development and progression of various diseases, anti-inflammatory compounds have become a central focus in the search for effective treatments. Anti-inflammatory drugs, including steroidal (SAIDs) and nonsteroidal (NSAIDs) types, have been considered as potential options for treatment. However, the long-term use of these drugs has certain limitations, as it may lead to adverse side effects that impact multiple organs [4].

Imperata cylindrica L. is a traditional Asian medicinal plant, has benefits for stopping bleeding, relieving internal heat, and increasing diuresis in traditional medicine. Exhibiting significant therapeutic potential in both in vivo and in vitro settings, this herb helps reduce lipid levels, regulate immunity, and provides antibacterial, antitumor, anti-inflammatory, and hepatoprotective benefits [5]. In Acute Kidney Injury (AKI), the anti-inflammatory mechanism of *I. cylindrica* rhizome is not yet fully elucidated. Consequently, this study employs network pharmacology and molecular docking methods to investigate its potential mechanisms of action.

2 Material and methods

2.1 Prediction active ingredients of *I. cylindrica* rhizome and Acute Kidney Injury drug targets

The Traditional Chinese Medicine Database and Analysis Platform (TCMSP) and the Encyclopedia of Traditional Chinese Medicine (ETCM) were searched using the keywords "*Bai mao gen*," "*Imperata cylindrica*," or "Cogongrass.". The data derived from TCMSP and ETCM underwent additional screening based on oral bioavailability (OB) ≥ 30% and drug- likeness (DL) ≥ 0.18 to ensure relevance.

These refined results were further analyzed to uncover the active ingredients in *I. cylindrica* rhizome with potential therapeutic effects for AKI. PubChem was used to acquire the two-dimensional molecular structures of these active compounds to predict the potential targets of these compounds, the SwissTargetPrediction tool was used. Cytoscape 3.7.2 facilitated the visualization of the interaction network between the active ingredients of *I. cylindrica* rhizome and their targets.

The keyword acute kidney injury was used to identify disease targets in the DrugBank and GeneCards databases. The relevant disease targets were collected, organized, and then imported into the UniProt platform for gene standardization. The active compounds targets in *I. cylindrica* rhizome and Venny 2.1.0 were used to analyze AKI drug targets and identify common targets. The PPI network was created in STRING, visualized with Cytoscape 3.7.2.

2.1 Analysis of GO function and KEGG pathway enrichment

The target intersection between *I. cylindrica* rhizome and acute kidney injury was analyzed using ShinyGO v0.81 for GO function and KEGG pathway enrichment, with a P-value filter set at <0.01. ShinyGO is a web-based tool for GO term enrichment analysis, comparing uploaded data with gene or protein annotations. Built on R, it provides interactive visualizations to identify overrepresented functional categories.

2.2 Molecular docking simulation of active compounds

YASARA software was used to perform molecular docking simulations, enabling the assessment of binding interactions between active compounds and core targets. Selection of the protein receptor was determined by the highest median degree value in the PPI network and five bioactive compounds extracted from *I. cylindrica* rhizome were employed as small molecule ligands in the simulations. The selected core targets' crystal structures were downloaded from the RCSB Protein Data Bank and saved as PDB files. Meanwhile, the two-dimensional chemical structures of the active compounds from *I. cylindrica* rhizome were retrieved from the PubChem database.

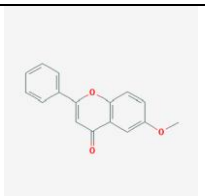
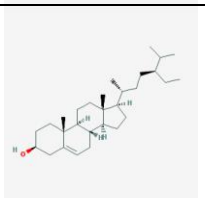
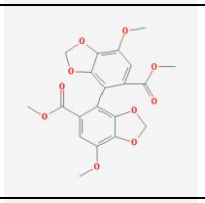
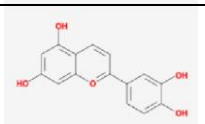
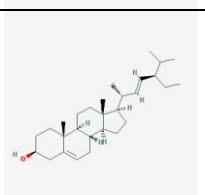
The molecular docking simulations were carried out with YASARA Structure software. The prepared protein file was reloaded into YASARA Structure, where the docking site was determined and saved in *.sce format. The docking was performed using the Extend setting, based on validation results with the best binding energy, which was used as the grid box. All test ligands in *.pdb format were then imported, and the protein structure was locked. The AMBER14 force field was selected to execute the docking process. The ligand-protein complex was subsequently saved in *.complex.sce format. Molecular docking was repeated 50 times to generate files in *.yob and *.txt formats, containing data on binding energy, dissociation constant (Kd), and contact residues.

3 Result and discussion

3.1 Bioactive compounds of *I. cylindrica* Rhizome and their potential targets

The TCMSP and ETCM databases were used to screen the active ingredients of *I. cylindrica* rhizome based on OB and DL criteria, identifying five active compounds (Table 1). These compounds were retrieved from PubChem to obtain their 2D structures in .sdf format. After importing the structures into the SwissTargetPrediction platform, 174 potential targets were predicted.

Table 1. Information on the 5 active components that were filtered

Mol ID	Molecule Name	OB (%)	DL	MW	Structure
MOL001876	*6-Methoxyflavone*	34.56	0.18	252.28	
MOL000358	*Beta-Sitosterol*	36.91	0.75	414.79	
MOL000387	*Bifendate*	31.1	0.67	418.38	
MOL001870	*Luteolinidin*	53.66	0.22	271.26	
MOL000449	*Stigmasterol*	43.83	0.76	412.77	

Cogongrass, scientifically known as *Imperata cylindrica* (L.) Beauv. and part of the Poaceae family, is a wild plant and agricultural pest that thrives in fertile soils, exhibiting aggressive growth year after year. Although *I. cylindrica* is considered invasive, it is also recognized as an important medicinal plant, particularly in Indonesia. A variety of phytochemical and biological research on *I. cylindrica*, especially in tropical areas, has been undertaken to better understand and improve its therapeutic potential [6].

The identification of *cylindol A*'s inhibitory effect on 5-lipoxygenase has led to an increased focus on exploring the anti-inflammatory potential of *I. cylindrica*. Consequently, two chromone compounds were successfully isolated, showing neuroprotective properties against glutamate-induced toxicity in rat cortical cell cultures [7]. These findings highlight the anti-inflammatory properties of *I. cylindrica* in vitro, further validating its traditional medicinal applications. While the active compounds show promise, the precise mechanisms of their action in treating AKI are still not well defined.

3.2 Analysis and construction of the PPI network

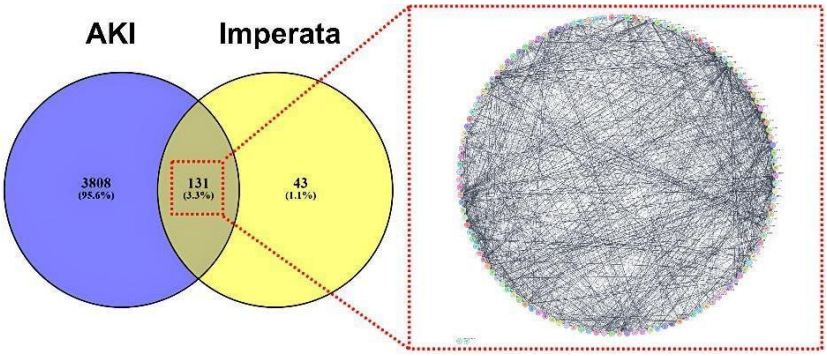


Fig. 1. Target Identification and PPI Network Diagram of *I. cylindrica* for AKI Treatment

The analysis of *I. cylindrica* rhizome targets and acute kidney injury-related targets was performed with Venny 2.1.0, leading to the creation of a Venn diagram (Fig. 1) that identified 174 overlapping targets. The STRING platform (Version 11.0) was used to import these targets, with *Homo sapiens* selected as the reference organism, to build a protein-protein interaction (PPI) network. Further analysis through SwissTargetPrediction and STITCH 5.0 databases revealed several proteins influenced by the active compounds of *I. cylindrica*. SwissTargetPrediction showed that 6-Methoxyflavone and Luteolinidin interacted with one protein with the highest probability score, while STITCH 5.0 identified interactions for beta- sitosterol with 10 proteins, bifendate with five, and stigmasterol with 10 proteins. The PPI network was visualized in Cytoscape 3.7.2 (Fig. 1) after importing all interaction data, followed by further evaluation using combination score parameters.

Table 2. Active compound-target proteins of *I. cylindrica* identified using STITCH 5.0.

Node 1	Node 2	Description	Combination Score
Beta-sitosterol	SREBF2	Sterol regulatory element-binding protein 2	0.926
	ABCG8	ATP-binding cassette sub-family G member 8	0.92
	ABCG5	ATP-binding cassette sub-family G member 5	0.879
	APOE	Apolipoprotein E	0.872
Beta-sitosterol	DHCR24	24-Dehydrocholesterol Reductase	0.841
	CASP3	Caspase-3	0.818
	SREBF1	Sterol Regulatory Element Binding Transcription Factor 1	0.816

Table 2. Active compound-target proteins of *I. cylindrica* identified using STITCH 5.0 (*continue*)

Node 1	Node 2	Description	Combination Score
Beta-sitosterol	SREBF2	Sterol regulatory element-binding protein 2	0.926
	ABCB11	ATP-binding cassette, sub-family B member 11	0.815
	ICAM1	Intercellular Adhesion Molecule 1	0.8
	CYP7A1	Cytochrome P450 Family 7 Subfamily A Member 1	0.771
Bifendate	PTHLH	Parathyroid Hormone-Like Hormone	0.697
	HOXD13	Homeobox D13	0.683
	F8	Coagulation Factor VIII	0.512
	FLNA	Filamine A	0.409
	HABP2	Hyaluronan Binding Protein 2	0.4
Stigmasterol	ABCA1	ATP Binding Cassette Subfamily A Member 1	0.88
	ABCG8	ATP Binding Cassette Subfamily G Member 8	0.811
	ABCG5	ATP Binding Cassette Subfamily G Member 5	0.711
	TNF	Tumor Necrosis Factor	0.7
	SLCO1B1	Solute Carrier Organic Anion Transporter Family Member 1B1	0.7
	IL10	Interleukin 10	0.7
	IL8	Interleukin 8	0.7
	SREBF2	Sterol Regulatory Element Binding Transcription Factor 2	0.622
	NR1H3	Nuclear Receptor Subfamily 1 Group H Member 3	0.476
	NR1H2	Nuclear Receptor Subfamily 1 Group H Member 2	0.437

Table 3. Active compound-target proteins of *I. cylindrica* identified using Swiss Target

Node 1	Node 2	Description	Combination Score
6-Methoxyflavone	ABCG2	ATP-binding cassette sub-family G member 2	0.995
LUTEOLINIDIN	CD38	Lymphocyte differentiation antigen CD38	0.731

A comprehensive analysis of the "bioactive ingredient-target" network was undertaken to explore the molecular mechanism of *I. cylindrica* in the treatment of AKI, uncovering important interactions between bioactive compounds and their molecular targets. The analysis indicated that 6-Methoxyflavone exhibited the strongest interaction with ABCG2, with a combined score of 0.995. ABCG2 is crucial in xenobiotic transport and protecting cells against oxidative stress, highlighting its role in mitigating kidney damage during AKI. Beta-sitosterol was found to interact with several important targets, including SREBF2, ICAM1, and CYP7A1, with combined scores of 0.926, 0.8, and 0.771, respectively. The interactions highlight its potential role in lipid metabolism regulation, inflammatory response modulation, and sterol balance, which are essential for restoring kidney function and structure
after acute injury.

Bifendate showed association with PTHLH (score 0.697) and HOXD13 (score 0.683), indicating its involvement in the regulation of mineral homeostasis and regenerative mechanisms of kidney tissue. Similarly, Stigmasterol interacts with key targets such as TNF (score 0.7), IL10 (score 0.7), and ABCA1 (score 0.88). These targets are important in modulating inflammatory responses and maintaining cellular cholesterol homeostasis, which supports cell survival and repair in AKI.

The interaction between luteolinidin and CD38 (score 0.731), which is central to immune regulation and energy metabolism, affirms its role in combating metabolic stress and immune responses during AKI. This network analysis highlighted that the bioactive compounds *of I. cylindrica,* including 6-Methoxyflavone, beta-sitosterol, stigmasterol, luteolinidin, and bifendate, interacted with key targets involved in oxidative stress regulation, inflammation modulation, and lipid metabolism. Key targets, including TNF, SREBF2, ABCG2, and CD38, were identified, indicating their importance as key therapeutic targets. These findings confirmed the nephroprotective potential *of I. cylindrica* in AKI through regulating key signaling pathways and molecular targets, providing a mechanistic basis for its therapeutic application.

As a result of the analysis, five active ingredients and 174 potential targets from *I. cylindrica* rhizome were identified using the database. The PPI network revealed 27 top core targets, which were derived from the overlap between the compounds in *I. cylindrica* rhizome and known AKI-related drug targets. To explore the potential mechanisms through which the rhizome of *I. cylindrica* may alleviate AKI, an 'active ingredient-target-pathway' network was developed. Several key targets, including TNF, IL-10, ABCG2, SREBF2, and CD38, were identified due to their strong associations with both active compounds and signaling pathways in the network. These results, in close agreement with the PPI network analysis, reinforce the concept that the active compounds in *I. cylindrica* rhizome may mediate therapeutic effects on AKI by modulating these targets and impacting five significant signaling pathways.

Based on the degree and closeness centrality values, 27 core targets inthe protein-protein interaction (PPI) network were identified. These targets include SREBF2,

ABCG8, ABCG5, APOE, DHCR24, CASP3, SREBF1, ABCB11, ICAM1, CYP7A1, PTHLH, HOXD13, F8, FLNA, HABP2, ABCA1, ABCG8, ABCG5, TNF, SLCO1B1, IL10, IL8, SREBF2, NR1H3, NR1H2, ABCG2, and CD38. These targets play a key role in regulating pathways related to oxidative stress, inflammation, lipid metabolism, and other biological processes essential to the development of AKI [8]. Previous studies have shown that the main active compounds of *I. cylindrica*, such as beta-sitosterol, stigmasterol, 6-Methoxyflavone, and luteolinidin, have significant therapeutic effects through their interactions with these targets. Beta-sitosterol, for example, is known to modulate lipid metabolism by regulating SREBF2, ABCG8, ABCG5, and ABCA1, which play important roles in maintaining lipid homeostasis, enhancing cell membrane integrity, and supporting kidney tissue repair after injury [9].

Stigmasterol has also been found to inhibit inflammation by downregulating proinflammatory cytokines, including IL-1β, IL-6, and TNF-α. The regulation of the NF-κB signaling pathway, a major mediator of inflammation, is thought to be responsible for this effect. Luteolinidin, another flavonoid compound found in *I. cylindrica*, exhibits antioxidant effects through its interaction with CASP3 and ICAM1, which helps reduce oxidative stress and prevent cellular apoptosis. Meanwhile, 6-Methoxyflavone is known to bind to transporter proteins such as ABCB11 and ABCG8. These proteins play an important role in detoxification and lipid transport, helping to reduce toxin accumulation in injured kidney tissue [10]. This compound also showed strong interactions with SREBF1, SREBF2, and CYP7A1, which are essential for the regulation of cholesterol biosynthesis and maintaining lipid homeostasis.

3.3 GO function and KEGG pathway enrichment analysis of common targets

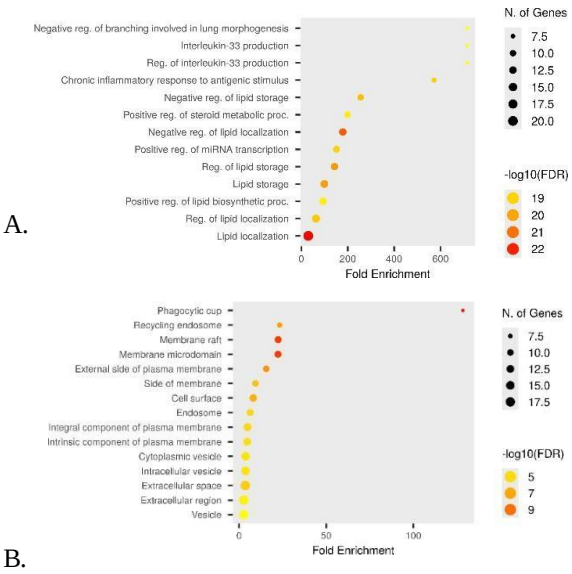


Fig. 2. GO and KEGG Enrichment Analysis Bubble Diagram: Biological Processes (A), Cellular Components (B), Molecular Functions (C), and KEGG Pathways (D).

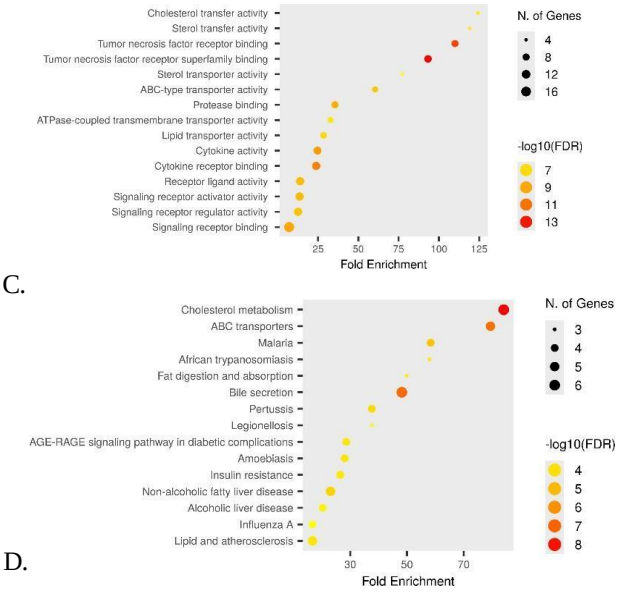


Fig. 2. GO and KEGG Enrichment Analysis Bubble Diagram: Biological Processes (A), Cellular Components (B), Molecular Functions (C), and KEGG Pathways (D) (*continue*)

The enriched biological and molecular pathways identified are closely associated with the pathogenesis and progression of AKI. Proteins such as SREBF2, ABCG8, ABCG5, ABCA1, and DHCR24, which are involved in lipid metabolism pathways, play a significant role in maintaining lipid homeostasis and supporting cell membrane integrity during kidney recovery after injury. Disruption of these pathways during AKI may affect mitochondrial function and membrane stability, contributing to further tissue damage. The inflammatory pathway is significantly influenced by proteins such as TNF, IL10, and IL8, suggesting that *I. cylindrica*'s active compounds might help suppress proinflammatory cytokines while enhancing the release of anti-inflammatory cytokines. This is relevant to reduce inflammation that often worsens kidney damage during AKI.

Other pathways, such as the response to oxidative stress, are regulated by proteins such as CASP3 and ICAM1, which contribute to the prevention of excessive apoptosis and repair of tissue damage. ABCG2, an essential transporter protein, plays a key role in the detoxification of xenobiotics and the reduction of toxin accumulation, which may help safeguard the kidney from additional damage. At the molecular level, the interaction with CD38 protein suggests potential regulation of energy metabolism and modulation of immune responses, which are important in reducing inflammation and improving kidney function. Enriched KEGG pathways, such as regulation of inflammation and apoptosis, support the hypothesis that active compounds such as beta-sitosterol, 6-Methoxyflavone, and luteolinidin may modulate important signaling pathways during AKI.

AKI is widely acknowledged as a condition defined by inflammation and oxidative stress, both of which contribute significantly to its progression. Several studies highlight that *I. cylindrica* has potent anti-inflammatory and antioxidant properties. Stigmasterol and beta- sitosterol, the key active compounds, exert anti-inflammatory effects by blocking cytokines such as TNF-α, IL-1β, and IL-6, which significantly contribute to inflammation via the NF- κB signaling pathway. In addition, luteolinidin has demonstrated the ability to suppress COX-2 and iNOS expression, highlighting its

potential to regulate essential inflammatory mediators [11].

Studies have also shown that oxidative stress contributes significantly to the development of AKI. 6-Methoxyflavone and beta-sitosterol are known to have antioxidant effects, which are mediated through the upregulation of ABCG2, a transporter protein that plays a pivotal role in cellular detoxification and managing oxidative stress [12]. This interaction helps reduce the accumulation of toxins and oxidative damage to kidney tissue during AKI. In addition to anti-inflammatory and antioxidant properties, compounds in *I. cylindrica* also have significant effects on vascular and cellular functions. Beta-sitosterol and stigmasterol, for example, have been reported to regulate lipid metabolism by interacting with targets such as SREBF2 and ABCA1 [13]. This interaction maintains the integrity of cell membranes and supports recovery from AKI-induced lipid dysfunction.

In the context of biological processes, it was found that several critical processes were involved, including the regulation of inflammatory responses, oxidative stress responses, lipid metabolism processes, detoxification, and apoptosis, all of which are closely related to the pathogenesis of AKI. Considering that inflammation, oxidative stress, and lipid dysfunction are major drivers of AKI, we hypothesize that these biological processes are involved in the therapeutic mechanisms of *I. cylindrica* rhizome in treating AKI.

3.4 Molecular docking analysis of active compounds and core targets

Based on the KEGG pathway enrichment and PPI network analysis, 11 core targets showing the highest combination scores were selected for detailed investigation (Table 3, Table 4). The molecular docking analysis of these targets was carried out using the active ingredients of *I. cylindrica*, such as 6-Methoxyflavone, beta-sitosterol, bifendate, luteolinidin, and stigmasterol, in line with drug-target interactions. The most stable conformation was identified by the lowest binding energy.

Table 4. Molecular docking simulation results

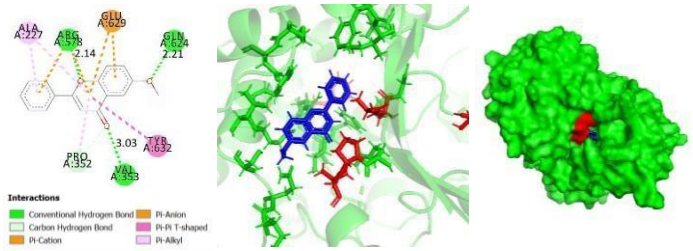
Ligand	Effi[kcal/(mol*Atom)	Bind.energy[kcal/mol]	Dissoc. constant [pM]
RM5	0.3658	-10.6080	16758.41
beta-sitosterol	0.3200	-9.5990	92010.99
stigmasterol	0.3150	-9.4500	118320
6-Methoxyflavone	0.4234	-8.0450	1267467
luteolinidin	0.3974	-7.9470	1495450
bifendate	0.2584	-7.7553	2074797

Caption: green box = natural ligand

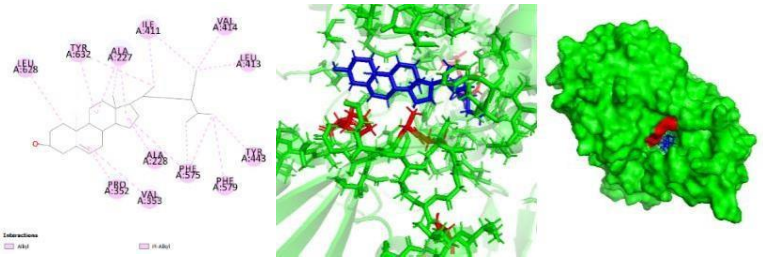
Table 4 shows the virtual screening results of several ligands with a specific protein target, where parameters such as binding energy efficiency, binding energy, and dissociation constant *are* used to evaluate the performance of each ligand. Evaluating binding energy in molecular docking is essential, where ligand exhibited the strongest binding affinity among tested compounds, a strategy also applied in this study to assess nephroprotective compounds from *I. cylindrica* against AKI-related targets [14]. Ligand RM5, which is marked with a green box as a natural ligand, shows the best performance in all parameters. With an efficiency of 0.3658 kcal/(mol*Atom), a binding energy of -10.6080 kcal/mol, and a dissociation constant of 16758.41 pM, RM5 has the most stable interaction and the highest affinity to the protein target.

Beta-sitosterol showed a binding energy of -9.5990 kcal/mol and a dissociation

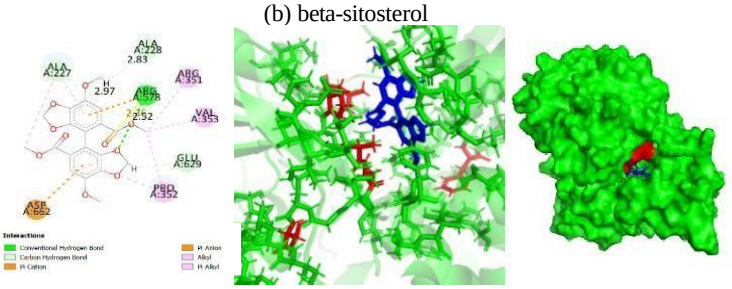
constant of 92010.99 pM, indicating good performance, although its efficiency was lower than that of RM5. Meanwhile, 6-Methoxyflavone and luteolinidin had higher efficiency values (0.4234 and 0.3974, respectively) but their binding energy and dissociation constant were weaker than RM5. Stigmasterol showed similar performance to beta-sitosterol, but still below RM5. On the other hand, bifendate showed the lowest performance, with a binding energy of only -7.7553 kcal/mol and the largest dissociation constant of 2074797 pM, indicating low affinity for the protein target. These binding characteristics were further validated using PyMOL, which was employed to visualize and analyze the interactions between bioactive compounds from *Imperata cylindrica* roots and target enzymes [15].



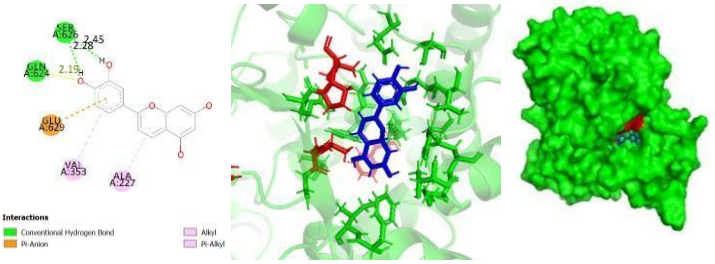
(a) 6-Methoxyflavone



(b) beta-sitosterol

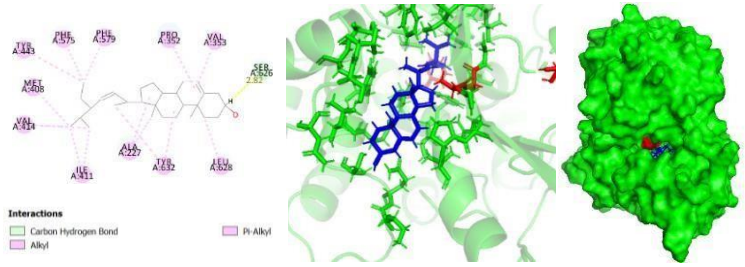


(c) bifendate

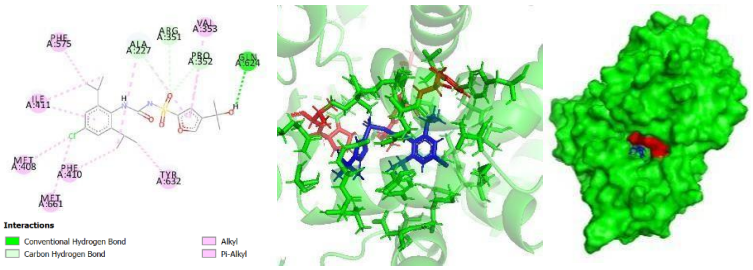


(d) Luteolinidin

Fig. 3. Interaction of Active Compounds with Core Targets of *I. cylindrica* Rhizome via Molecular Docking



(e) stigmasterol



(f) RM5

Fig. 3. Interaction of Active Compounds with Core Targets of *I. cylindrica* Rhizome via Molecular Docking (*continue*)

The therapeutic potential of *I. cylindrica* is also attributed to its capacity to influence signaling pathways associated with AKI. Molecular docking studies have revealed that compounds like 6-Methoxyflavone exhibit strong interactions with key proteins such as ABCG2 and TNF, demonstrating significant binding affinity, with calculated binding energies of -10.6 kcal/mol and -9.5 kcal/mol, respectively. Through this interaction, I. cylindrica demonstrates its potential to modulate the TNF signaling pathway, crucial for maintaining cell survival and managing inflammation and oxidative stress in AKI [34]. This interaction highlights the ability of *I. cylindrica* to regulate the TNF signaling pathway, which is an integral component of cell survival, inflammation, and response to oxidative stress during AKI.

Molecular docking analysis conducted on the active compounds of *I. cylindrica* rhizome, including 6-Methoxyflavone, beta-sitosterol, and luteolinidin, demonstrated strong binding interactions with key target proteins. Notably, 6-Methoxyflavone exhibited the highest binding affinity to ABCG2, with a binding energy of -10.6 kcal/mol, suggesting its potential role in regulating oxidative stress and detoxification pathways. These results indicate that *I. cylindrica* may exert nephroprotective effects through its bioactive compounds by influencing KEGG pathways and associated biological mechanisms. To confirm the results obtained from network pharmacology and molecular docking, in vivo experiments were performed, showing that *I. cylindrica* rhizome effectively alleviated kidney damage, reduced inflammatory markers, and improved lipid metabolism. These outcomes suggest that *I. cylindrica* could contribute to AKI recovery by modulating lipid metabolism, minimizing oxidative stress, and exhibiting anti- inflammatory properties. However, more research is needed to investigate the precise molecular mechanisms that underlie its therapeutic effects in AKI treatment.

4 Conclusions

Several bioactive compounds from *I. cylindrica* rhizomes show promising potential for treating Acute Kidney Injury (AKI). Key compounds, including 6-Methoxyflavone, beta- sitosterol, bifendate, luteolinidin, and stigmasterol, are believed to offer therapeutic effects by targeting oxidative stress, inflammation, and lipid metabolism. Through their interaction with targets such as SREBF2, ABCG2, and IL10, these compounds may modulate the TNF signaling pathway, decrease proinflammatory cytokines like TNF-α and IL-6, and enhance lipid regulation. Molecular docking studies confirm significant binding affinity between these compounds and their targets, supporting their therapeutic potential. Additionally, animal model experiments align with network pharmacology and docking findings, showing that *I. cylindrica* can reduce kidney injury, inflammation, and lipid disorders. Although these results offer a solid basis for the use of *I. cylindrica* in AKI treatment, additional research is required to explore the underlying mechanisms and confirm these findings.

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