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Potential molecular mechanisms of Huangqi in radiotherapy-induced kidney injury associated with chronic kidney disease: A network pharmacology study

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► ***Original article***

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ABSTRACT

Background: Radiotherapy is an important treatment for cancer but may cause renal injury, particularly in patients with pre-existing or treatment-related chronic kidney disease (CKD). Huangqi (Astragalus membranaceus) has been widely used in traditional Chinese medicine for kidney-related disorders. This study explored the potential molecular mechanisms of Huangqi in radiotherapy-induced kidney injury using network pharmacology. ***Materials and Methods:*** Active compounds of Huangqi were obtained from the TCMSP database and screened using oral bioavailability ≥30% and drug-likeness ≥0.18. Compound-related targets were standardized using UniProt and DrugBank. CKD-related targets were collected from GeneCards and DrugBank. Overlapping targets between Huangqi and CKD were identified as potential therapeutic targets. Protein-protein interaction analysis, GO enrichment, KEGG pathway enrichment, and compound-target-pathway network construction were performed using STRING, Cytoscape, and Metascape. ***Results:*** Twenty active compounds and 104 potential therapeutic targets were identified. Key targets included IL-6, TNF, AKT1, IL1B, TP53, MMP9, CASP3, PTGS2, JUN, and CXCL8. Enrichment analysis indicated that these targets were mainly involved in inflammatory response, apoptosis, oxidative stress, extracellular matrix remodeling, and cancer-related signaling pathways. These mechanisms are closely related to radiation-induced renal inflammation, fibrosis, and tissue injury. ***Conclusion:*** Huangqi may have potential mechanistic relevance in radiotherapy-induced kidney injury by regulating inflammation, apoptosis, oxidative stress, and fibrosis-related targets. These findings provide bioinformatics-based hypotheses for future experimental and clinical validation.

INTRODUCTION

As China's economy continues to grow and living standards improve, chronic diseases, including cancer, have emerged as significant public health challenges [1]. Cancer incidence rates are rising, and radiotherapy has become a common treatment option for various malignancies [2, 3]. However, cancer patients undergoing radiotherapy often experience numerous side effects, including kidney damage, immune suppression, and inflammation [4]. Chronic kidney disease (CKD), a progressive condition that affects kidney function, is commonly observed in cancer patients, especially those undergoing cancer treatments like radiotherapy. It is estimated that over 100 million individuals in China are affected by CKD [5, 6]. Many of these patients face increased risks and complications due to cancer treatments.

Radiotherapy is an effective tool for treating cancer and can also lead to renal toxicity and exacerbate existing kidney damage in patients, further complicating their management [7]. The progression from CKD to end-stage renal disease (ESRD) can significantly impact a patient's overall health, leading to multiple systemic complications such as metabolic abnormalities, water and electrolyte imbalances, and neurological dysfunction [8]. The cost of treating ESRD is high, and a complete cure remains elusive, particularly in the context of cancer patients who may also be dealing with the physical toll of chemotherapy and radiotherapy.

Astragalus membranaceus, also known as Huangqi, is a prominent herb in traditional Chinese medicine (TCM) with a rich history of use in treating a variety of ailments, including kidney diseases [9, 10]. Known for its immune-boosting, anti-inflammatory, and anti-cancer properties, Huangqi has been used to enhance the body's resistance to diseases and improve kidney function [11, 12]. Modern pharmacological studies have further revealed its ability to regulate cardiovascular function, reduce oxidative stress, and exhibit anti-tumor and anti-aging effects [11]. Several experts in TCM have highlighted the role of Huangqi in treating kidney diseases, particularly its potential in slowing CKD progression [11, 13].

While Huangqi's use in kidney disease treatment is well-established, its potential to alleviate the side

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effects of radiotherapy and enhance cancer treatment outcomes remains underexplored. This study aims to leverage network pharmacology to examine the active ingredients, molecular targets, and disease pathways associated with Huangqi, with a particular focus on its implications for cancer therapy and radiotherapy. By constructing a drug-target-disease network, this research will explore how Huangqi's bioactive compounds may support cancer patients, mitigate the adverse effects of radiotherapy, and improve kidney function in the context of CKD. This approach seeks to integrate Huangqi's traditional medicinal value with modern pharmacological research, offering new insights into its potential as an adjunctive therapy in cancer treatment and radiotherapy. Radiotherapy-induced kidney injury, also known as radiation nephropathy, is a clinically important complication in patients whose kidneys are included in or exposed to the radiation field during cancer treatment. The kidney is highly sensitive to radiation-related microvascular and tubular injury. Radiation exposure can induce endothelial dysfunction, oxidative stress, inflammatory cytokine release, tubular epithelial cell apoptosis, glomerular injury, and progressive interstitial fibrosis, which may ultimately contribute to a decline in renal function and the development or worsening of CKD. These pathological processes overlap with several molecular mechanisms involved in CKD progression, including inflammation, apoptosis, oxidative stress, extracellular matrix remodeling, and fibrotic signaling. Therefore, identifying agents that can modulate these pathways may provide useful mechanistic insight into potential strategies for reducing radiotherapy-induced renal damage.

In this context, the present study used a network pharmacology approach to explore whether the bioactive compounds of Huangqi may interact with molecular targets and pathways involved in radiation -related renal injury and CKD progression. Rather than evaluating clinical renal function before and after radiotherapy, this study aimed to identify potential molecular mechanisms by integrating Huangqi-related targets with CKD-related targets and analyzing their enrichment in inflammation-, apoptosis-, oxidative stress-, fibrosis-, and cancer/ radiotherapy-associated pathways. This revised focus provides mechanistic hypotheses for future experimental and clinical studies evaluating Huangqi as an adjunctive intervention for cancer patients at risk of radiotherapy-induced kidney injury.

MATERIALS AND METHODS

Data collection

A computer-based search was conducted on several platforms, including CNKI (https://www.cnki.net/), Wanfang Data Knowledge Service Platform (https://www.wanfangdata.com.cn/index.html), VIP Chinese Journal Service Platform (https://qikan.cqvip.com/), and the Ancient and Modern Medical Case Cloud Platform (http://www.yiankb.com/), covering publications from January 1, 2012 to December 1, 2021. This search was based on the medical records of renowned doctors and experts, combined with the treatment experiences of mentors in managing chronic kidney disease (CKD). Additionally, relevant published books were manually reviewed to analyze Astragalus membranaceus (Huangqi) as a target drug for CKD treatment [14].

Inclusion and exclusion criteria

Studies were included if they: Focused on cancer patients receiving radiotherapy (including techniques such as IMRT, SBRT, or conventional radiotherapy). Reported on radiation-induced CKD or kidney toxicity.Investigated the use of Huangqi or its active compounds.Provided data on molecular targets or pathways related to Huangqi's effects.

Studies were excluded if they: Did not involve human subjects or clinical data. Lacked clear methodology or results.Were not peer-reviewed.

Screening of active ingredients and corresponding targets in astragalus membranaceus

Compounds from Astragalus membranaceus were retrieved from the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP) [15]. Preliminary screening of active ingredients was performed based on two pharmacokinetic parameters: oral bioavailability (OB) ≥ 30% and drug likeness (DL) ≥ 0.18. This screening process identified effective active compounds and their related protein targets. The obtained protein targets were then imported into the UniProt database (https://www.uniprot.org/) for name correction. If no relevant names were found in UniProt, alternative names were retrieved from the DrugBank Online database (https://go.drugbank.com/). After cross-referencing and correcting the names, duplicate targets and proteins without corresponding targets were removed.

Prediction of CKD targets and identification of potential targets for Huangdi treatment

The GeneCards database (https://www.genecards.org/) was used to search for the disease keyword "chronic kidney disease" in order to obtain CKD-related targets. Additionally, Western medicine targets for CKD treatment were supplemented using the DrugBank Online database. The targets associated with the active ingredients of Astragalus membranaceus (Huangqi) and the CKD-related targets were imported into Venny 2.1.0 (https://bioinfogp.cnb.csic.es/tools/venny/), where

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the intersection of these targets was identified. These intersecting targets were considered potential targets for Huangqi in treating CKD, and a Venn diagram was created to visualize the overlap.

To strengthen the relevance of the analysis to radiotherapy-induced kidney injury, the identified Huangqi-CKD intersecting targets were further interpreted according to their known involvement in radiation-related biological processes, including oxidative stress, inflammatory response, endothelial injury, apoptosis, extracellular matrix remodeling, and renal fibrosis. Targets such as IL-6, TNF, IL1B, AKT1, TP53, CASP3, MMP9, and PTGS2 were considered particularly relevant because these molecules are closely associated with inflammation, apoptotic regulation, tissue injury, tumor response, and radiotherapy-related toxicity. Therefore, the subsequent PPI, GO, KEGG, and network analyses were interpreted not only as general CKD-related mechanisms but also in relation to the molecular events involved in radiotherapy-induced renal damage.

Construction of protein-protein interaction (PPI) network

The potential targets of Huangqi for treating CKD were imported into the STRING database (https://cn.string-db.org/) to construct a PPI network. The "Multiple proteins" option was selected, and the minimum interaction threshold was set to 0.9. All other settings were kept at default, with free nodes hidden. The PPI network diagram was generated and exported as a TSV format file. The results were then imported into Cytoscape 3.9.1 software for topological analysis, where degree values were calculated, and core targets for Huangqi in treating CKD were identified based on the median degree.

GO and KEGG enrichment analysis of core targets

GO functional enrichment analysis and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis were performed on the core targets of Huangqi for treating CKD using the Metascape database (https://metascape.org/gp/index.html) [16]. The GO functional enrichment analysis covered biological processes (BP), cellular components (CC), and molecular functions (MF).

"Astragalus membranaceus - Active Ingredients - Potential Targets - Signaling Pathways ".

Diseases" network diagram

Excel was used to create files representing the relationships between "Huangqi - active ingredients," "active ingredients - potential targets," "diseases - potential targets," and "potential targets - pathways." These files were imported into Cytoscape 3.9.1 software to construct a comprehensive network diagram that illustrates the connections between Huangqi, its active ingredients, potential targets, signaling pathways, and associated diseases.

RESULTS

Active ingredients and related targets of Astragalus membranaceus

Based on the Traditional Chinese Medicine Systems Pharmacology Database and Analysis Platform (TCMSP), a total of 20 active ingredients and 204 related targets were identified from Astragalus membranaceus. The top 10 active ingredients with the highest number of associated targets were quercetin (148 targets), kaempferol (62 targets), 7-O-methyl-isomucronulatol (45 targets), formononetin (39 targets), isorhamnetin (37 targets), jaranol (24 targets), 3,9-di-O-methylnisen pea rosewood phenol (23 targets), calycosin (23 targets), and mairin (13 targets). The chemical properties of all components were processed through the Chemical Source Network (https://www.chemsrc.com/). Using the UniProt database, 200 official gene names corresponding to 204 targets were retrieved. Three proteins were missing in human species data, and one protein did not have an official name in UniProt, leading to the removal of four targets from the dataset (figure 1).

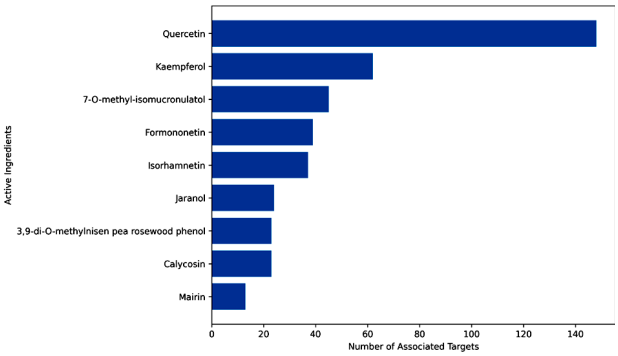


Figure 1. Active ingredients of astragalus membranaceus and their associated targets.

Prediction of CKD targets and collection of potential targets for Huangqi treatment of CKD

The GeneCards database (https://www.genecards.org/) was searched using the keyword "chronic kidney disease," identifying 13,955 targets related to CKD. By setting the score value to greater than 20%, 1,266 relevant targets were screened. These active ingredient-related targets from Astragalus membranaceus were introduced into Venny 2.1.0, alongside the CKD-related targets, resulting in 104 potential targets for Astragalus membranaceus in the treatment of CKD. These targets included MMP2 (matrix metalloproteinase 2), BCL2L1 (apoptosis regulator Bcl-X), CASP8 (cystathionine 8), CASP9 (cystathionine 9), CTSD (tissue protease D), CAV1 (caveolin 1), CD40LG (CD40 ligand), TP53 (tumor protein p53), COL3A1 (collagen, III, α 1), CRP (C-reactive protein), and

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stress proteins, among others.

PPI network

The 104 potential targets for Huangqi treatment of CKD were imported into the STRING database (https://cn.string-db.org/) to construct a protein-protein interaction (PPI) network. The resulting network comprised 103 nodes and 2,067 edges, with an average degree of 40.14. Using the median degree value as the threshold, 53 core targets were identified. The top 10 targets with the highest degree values were interleukin-6 (degree value 88), TNF (degree value 87), AKT1 (serine/threonine protein kinase 1, degree value 84), IL1B (degree value 83), TP53 (degree value 79), MMP9 (degree value 77), CASP3 (degree value 76), PTGS2 (degree value 73), JUN (degree value 73), and CXCL8 (degree value 72). These targets are central to the network and are likely to be the core targets of Huangqi in the treatment of chronic kidney disease (figure 2).

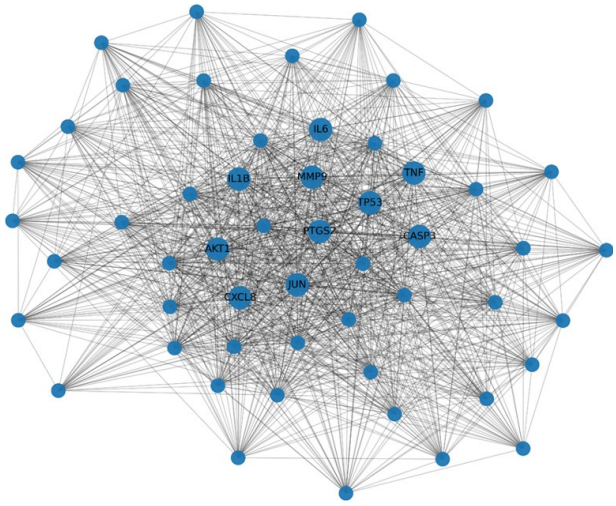


Figure 2. Core target subnetwork extracted using the median degree threshold.

Radiation-related interpretation of core targets

Although the initial screening identified active ingredients and CKD-related targets of Huangqi, the key purpose of this study was to determine whether these targets were relevant to radiotherapy-induced kidney injury. The core targets identified in the PPI network showed strong biological relevance to radiation-associated renal damage. IL-6, TNF, and IL1B are major inflammatory cytokines that can be activated after radiation exposure and contribute to tissue inflammation, endothelial dysfunction, and progressive renal injury. AKT1 and TP53 are involved in cell survival, DNA damage response, apoptosis, and radiation sensitivity. CASP3 is a central executor of apoptosis and may participate in radiation-induced tubular epithelial cell injury. MMP9 is involved in extracellular matrix remodeling and may contribute to tissue injury and fibrosis. PTGS2 is associated with prostaglandin-mediated inflammation and may participate in radiation-related inflammatory responses.

These findings indicate that the predicted Huangqi targets are not limited to general CKD mechanisms but are also closely linked to biological processes relevant to radiation-induced renal toxicity. Therefore, the network pharmacology results suggest that Huangqi may exert a protective effect against radiotherapy-related kidney injury mainly through regulation of inflammatory cytokine signaling, apoptosis, oxidative stress response, and fibrotic remodeling.

GO functional enrichment analysis and KEGG pathway enrichment analysis

KEGG pathway enrichment analysis identified 32 signaling pathways primarily involving cancer-related pathways such as the IL-17 signaling pathway, cancer pathways in cancer, lipids and atherosclerosis, prostate cancer, chemical carcinogenesis, ROS (reactive oxygen species) pathways, and pathways related to small cell lung cancer. Additionally, pathways related to hypoxia-inducible factor 1 (HIF-1) signaling and transcriptional disorders in cancer were also highlighted. The top 20 pathways, sorted by corrected P-value, were selected for visualization in a bar chart.

GO functional enrichment analysis revealed biological processes (BP), cellular components (CC), and molecular functions (MF) associated with the core targets of Huangqi in CKD treatment. BP primarily involved responses to inorganic substances, response to lipopolysaccharides, positive regulation of cell migration, positive regulation of cell death, gland development, and regulation of cell adhesion. CC mainly involved membrane rafts, extracellular matrix, transcription regulator complexes, vesicle lumen, and the external side of the plasma membrane. MF was enriched for functions like DNA binding, transcription factor binding, cytokine receptor binding, kinase binding, protein homodimerization activity, and phosphatase binding. The results were sorted by P-value, and the top 20 enriched terms were selected for visualization in bar charts.

Drug ingredient disease target pathway disease network diagram

To visualize the interactions between Astragalus membranaceus and its therapeutic effects, a network diagram of "Huangqi active ingredients - potential targets - signaling pathways - diseases" was constructed using CytoScape 3.9.1 software. In the network, the yellow circle represents Astragalus membranaceus, the green triangle represents its active ingredients, the blue quadrilaterals represent potential targets, the red V-shapes represent signaling pathways, and the purple hexagons represent diseases. This network diagram illustrates the complex relationships between Huangqi's active components, their molecular targets, related signaling pathways, and the diseases it potentially impacts

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(figure 3).

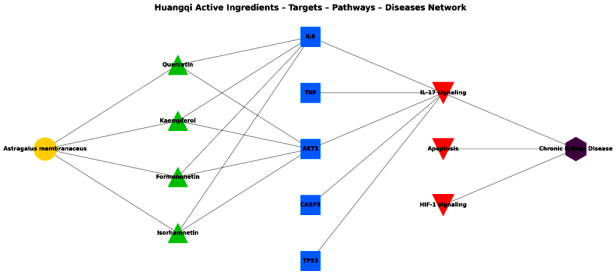


Figure 3. Network diagram of Astragalus membranaceus active ingredients, potential targets, signaling pathways, and disease.

DISCUSSION

The present study investigated the potential molecular mechanisms by which Huangqi may affect radiotherapy-induced kidney injury in the context of CKD. In response to the concern that active ingredient analysis alone does not sufficiently address radiotherapy-induced renal damage, we reinterpreted the network pharmacology results around radiation-related renal injury mechanisms. Radiotherapy can damage renal tissue through oxidative stress, endothelial dysfunction, inflammatory cytokine activation, tubular epithelial apoptosis, extracellular matrix remodeling, and fibrosis. The core targets identified in our PPI network, including IL-6, TNF, AKT1, IL1B, TP53, MMP9, CASP3, and PTGS2, are closely involved in these processes. Therefore, although the study began with the identification of Huangqi active compounds, the main significance of the analysis lies in showing that these compounds may interact with molecular targets associated with radiotherapy-induced inflammation, apoptosis, and fibrotic kidney damage.

In this study, we conducted a protein-protein interaction (PPI) network analysis to identify key molecular targets through which Huangqi exerts its effects. Targets such as IL-6, TNF, AKT1, IL1B, TP53, MMP9, CASP3, and PTGS2 were identified, all of which have been implicated in inflammation, fibrosis, apoptosis, and cancer progression. These targets are particularly relevant in the context of radiotherapy, as they are associated with the major side effects of radiotherapy, including tissue damage, inflammation, fibrosis, and resistance to cancer treatment. Our results provide valuable insight into how Huangqi's active compounds could potentially modulate these pathways to reduce the harmful effects of radiotherapy and improve overall treatment outcomes, aligning with previous studies.

Interleukin-6 (IL-6) has been widely studied for its role in immune regulation, tissue regeneration, and cancer progression. As a pro-inflammatory cytokine, IL-6 plays a central role in the tumor microenvironment by promoting angiogenesis and supporting cancer cell survival and proliferation [17]. Its elevated expression is commonly observed in cancer patients undergoing radiotherapy, contributing to tumor resistance and poor therapeutic outcomes. Previous research has established that IL-6 overproduction can lead to resistance in cancer cells to both chemotherapy and radiotherapy [18, 19]. This finding is consistent with our results, where we identified IL-6 as a crucial target of Huangqi, suggesting that Huangqi's modulation of IL-6 activity may help reduce radiotherapy-induced inflammation and promote tissue regeneration. By mitigating the detrimental effects of IL-6 overexpression, Huangqi could enhance the efficacy of radiotherapy and potentially improve the recovery process post-treatment.

Tumor necrosis factor (TNF) is another inflammatory cytokine that has a dual role in cancer. While TNF can induce apoptosis in tumor cells, it can also foster tumor progression, metastasis, and resistance to treatment [20, 21]. Previous studies have shown that TNF-induced inflammation plays a significant role in radiotherapy-related side effects, such as pain, fatigue, and tissue damage [22, 23]. TNF is also involved in the induction of cachexia, a common complication in cancer patients undergoing treatment [24]. Our study supports these findings, as TNF was identified as a key target in the PPI network. The identification of TNF as a target of Huangqi suggests that the herb may play a role in managing radiotherapy-induced inflammation and tumor recurrence by modulating inflammatory pathways. This aligns with earlier studies that suggested the potential of Huangqi in regulating the inflammatory response to enhance cancer therapy [25, 26].

The AKT1 protein, a key component of the PI3K/AKT pathway, plays a significant role in regulating cell survival, proliferation, and metabolism. In the context of both CKD and cancer, AKT1 activation has been associated with fibrosis, inflammation, and resistance to treatment [27]. In radiotherapy, AKT1 serves as a protective mechanism for cancer cells, preventing apoptosis and contributing to radio resistance [28]. Studies have shown that targeting AKT1 can sensitize cancer cells to radiation therapy, enhancing the therapeutic effects of radiotherapy [29-31]. Additionally, AKT1 has been implicated in renal fibrosis, a complication that arises in CKD patients undergoing cancer treatments [32]. Our findings support these conclusions, showing that Huangqi can modulate AKT1 activity to potentially reduce renal fibrosis and improve the response to radiotherapy in CKD and cancer patients. By targeting AKT1, Huangqi could enhance the effectiveness of radiotherapy and mitigate its adverse effects, especially in CKD patients who are already predisposed to kidney dysfunction.

Both IL1B and PTGS2 (COX-2) are critical inflammatory mediators that contribute to cancer progression, tumor growth, and resistance to

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treatment. IL1B is involved in the induction of various inflammatory responses, while PTGS2 is responsible for the production of prostaglandins, which are implicated in cancer pain and inflammation [33, 34]. Previous studies have shown that PTGS2 inhibition can reduce tumor growth and enhance the response to radiotherapy by alleviating inflammation in the tumor microenvironment [35, 36]. Our results corroborate these findings, as we identified both IL1B and PTGS2 as key targets of Huangqi. By regulating these targets, Huangqi may offer therapeutic benefits in both CKD and cancer treatment by reducing inflammation, enhancing tissue repair, and improving the efficacy of radiotherapy.

Our study's findings align with and extend the insights provided by previous research on Astragalus membranaceus in CKD and cancer treatment. A number of studies have reported that Astragalus membranaceus and its active compounds, such as flavonoids, saponins, and polysaccharides, exert anti-inflammatory, anti-cancer, and immune-regulating effects [37, 38]. For example, studies demonstrated that Astragalus membranaceus could inhibit tumor progression and enhance the efficacy of chemotherapy by modulating key inflammatory cytokines, including TNF and IL-6 [37, 39]. Similarly, another study highlighted the role of Astragalus membranaceus in ameliorating kidney fibrosis in CKD patients through the regulation of inflammatory pathways, including those mediated by IL-6 and TNF [40]. Our study builds upon these findings by using network pharmacology to identify and validate the molecular targets of Huangqi in both CKD and cancer treatment, specifically focusing on its potential role in managing radiotherapy-induced inflammation and fibrosis.

Moreover, several studies have pointed out the importance of modulating inflammatory cytokines, such as IL-6, TNF, and IL1B, to reduce the adverse effects of radiotherapy. For instance, research demonstrated that targeting the IL-6/STAT3 signaling pathway could reduce the side effects of radiotherapy in cancer patients by suppressing inflammation and promoting tissue repair [41, 42]. Our study's identification of IL-6 and TNF as key targets further supports the potential of Huangqi in mitigating radiotherapy-induced inflammation and improving the recovery process.

Radiotherapy, while an effective treatment for cancer, often leads to significant side effects, including inflammation, fibrosis, and damage to healthy tissues, especially the kidneys. This is particularly problematic for cancer patients with pre-existing conditions such as CKD. The findings from this study suggest that Huangqi could provide a multifaceted approach to addressing these issues by targeting key inflammatory and fibrotic pathways. By modulating IL-6, TNF, AKT1, IL1B, and PTGS2, Huangqi can potentially reduce radiotherapy-induced inflammation, prevent renal fibrosis, and enhance the efficacy of cancer treatment. These findings open the door for further exploration of Huangqi as an adjunctive therapy in cancer treatment, particularly for patients undergoing radiotherapy who are at risk of kidney damage and other complications.

This study has several limitations. First, this was a network pharmacology study based on public databases and bioinformatics analysis, not a prospective clinical study. Therefore, we did not collect patient-level renal function data before and after radiotherapy, and we cannot directly conclude that Huangqi improves renal outcomes in patients receiving radiotherapy. Second, the active ingredients and predicted targets were obtained from existing databases, which may be incomplete or updated over time. Third, the predicted interactions among Huangqi compounds, CKD targets, and radiation-related pathways require validation through molecular docking, cell experiments, animal models of radiation nephropathy, and clinical studies. Future clinical studies should evaluate renal function indicators before and after radiotherapy, including serum creatinine, estimated glomerular filtration rate, blood urea nitrogen, urinary protein, and biomarkers of inflammation, oxidative stress, apoptosis, and fibrosis, to determine whether Huangqi has measurable protective effects against radiotherapy-induced kidney injury.

CONCLUSION

This network pharmacology study suggests that Huangqi may have potential mechanistic relevance in radiotherapy-induced kidney injury by targeting molecules involved in inflammation, apoptosis, oxidative stress, and fibrosis. Core targets including IL-6, TNF, AKT1, IL1B, TP53, CASP3, MMP9, and PTGS2 were identified as possible mediators linking Huangqi to CKD progression and radiation-related renal damage. These findings provide a mechanistic basis for future studies but do not constitute direct clinical evidence of efficacy. Well-designed experimental and clinical studies are required to determine whether Huangqi can protect renal function in cancer patients before and after radiotherapy.

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Data availability: The datasets used and/or analyzed during this study are available from the corresponding author on reasonable request.

Competing interests: No financial competing interests include family associations, political, religious, academic or any other.

Conflict of interest: No conflicts of interest, financial or otherwise, are declared by the authors.

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***Ethical statement*:** This network pharmacology - based study used publicly available databases for data retrieval, without involving direct human or animal experiments. As no personal or identifying patient information was collected, and in compliance with the databases' usage terms, no institutional review board approval was required. The research adhered to academic integrity and scientific responsibility, aiming to enhance understanding of Huangqi's mechanism in treating chronic kidney disease for future patient benefit.

***Authors contributions*:** Xiaofei Chen, designed the study. Baoxia Zhang, wrote the original draft. Lanying Zhuang, collected raw data. Haibo Ding and Wenjia Chen performed statistical and bioinformatics analyses. Xiaofei Chen, supervised the study. All authors have given consent to publish.

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