Archives of Medical Reports

1(2) (2024) 1-6

OPEN ACCESS

RESEARCH ARTICLE

Pharmacological mechanism of Cinnamic acid in the treatment of Prostate cancer by network pharmacology

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Articleinfo
Received: 19 May 2024
Accepted: 28 June 2024

Keywords: Cinnamic acid, Prostate cancer, Network pharmacology, Targeted genes.

How to cite this article: Jilani P Shaik, Ashfaq Ahmad. (2024). "Pharmacological mechanism of Cinnamic acid in the treatment of Prostate cancer by network pharmacology", *Archives of Medical Reports,* vol. 1, no. 2, pp. 1–6. Retrieved from https://archmedrep.com/index.php/amr/article/view/23

Abstract

Cinnamic acid (CM), a naturally occurring phenolic compound, has shown significant potential in therapeutic interventions for prostate cancer (PCa). Utilizing a network pharmacology approach, we investigated the molecular mechanisms underlying the anti-cancer properties of CM. A total of 78 potential targets were identified through integrating CM-related targets and PCa-related genes. The top 10 core hub targets were identified using protein-protein interaction (PPI) network analysis. Gene Ontology (GO) enrichment and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses revealed key biological processes and pathways associated with these targets, such as apoptosis regulation, cell proliferation, and PI3K-Akt signaling. Our findings suggest that CM exerts anti-prostate cancer effects by modulating critical molecular targets and signaling pathways, laying a foundation for further experimental validation and therapeutic applications.

1. Introduction

Prostate cancer (PCa) represents one of the most prevalent malignancies in men and a leading cause of cancer-related mortality worldwide (Badal et al., 2020). Epidemiological data indicate a significant burden of PCa, with its incidence steadily rising due to factors such as aging populations, lifestyle changes, and advancements in diagnostic technologies (Prathap et al., 2024). Despite advancements in treatment modalities, including surgery, radiation therapy, androgen deprivation therapy (ADT), and chemotherapy, resistance to therapies and disease recurrence pose significant challenges, particularly in advanced or metastatic stages. This necessitates the exploration of novel therapeutic agents and strategies. Molecular studies have identified several critical pathways involved in PCa progression, including the androgen receptor (AR) signalling axis, PI3K-Akt-mTOR pathway, MAPK pathway, and cell cycle regulatory networks (Hashemi et al., 2023; Pungsrinont et al., 2021). These pathways play pivotal roles in cell survival, proliferation, angiogenesis, and metastasis (Song et al., 2015). Targeting these pathways has emerged as a promising approach to mitigating therapy resistance and improving patient outcomes.

Natural products have gained significant attention in cancer research due to their structural diversity, bioavailability, and potential for multi-targeted therapeutic effects. Among these, cinnamic acid (CM), a naturally occurring phenolic acid present in various fruits, vegetables, and spices, has demonstrated substantial pharmacological properties, including anti-inflammatory, antioxidant, and anti-cancer effects (Freitas et al., 2024; Pontiki and Hadjipavlou-Litina, 2018). CM's structural simplicity and ability to modulate multiple biological pathways make it a candidate of interest in cancer therapeutics (Pontiki et al., 2014). Previous studies have highlighted CM's role in inducing apoptosis, suppressing angiogenesis, and modulating oxidative stress (Ravikumar et al., 2024). These effects are primarily mediated through the regulation of key signalling pathways, including NF-κB, PI3K-Akt, and MAPK. Furthermore, CM has been shown to interact with epigenetic regulators, providing a basis for its use in cancer therapy (Ciz et al., 2020). Despite these promising findings, the specific molecular mechanisms through which CM exerts its anti-cancer effects in PCa remain poorly understood. Network pharmacology offers a systems-level approach to elucidate the complex interactions between bioactive compounds and biological systems. By integrating multi-omics data and pathway analyses, network pharmacology can identify potential targets and signaling cascades involved in disease modulation (Mukherjee et al., 2021; Zhang et al., 2019). This study employs network pharmacology to investigate the pharmacological mechanisms of CM in PCa, focusing on its interaction with critical molecular targets and pathways. By delineating these mechanisms, we aim to provide a foundation for the development of CM-based therapeutic strategies for PCa management.

2. Materials and Methods

2.1. Identification of Targets for Cinnamic Acid and Prostate Cancer

Cinnamic acid-associated targets were retrieved from online databases such as PubChem (https://pubchem.ncbi.nlm.nih.gov/) and SwissTargetPrediction (http://www.swisstargetprediction.ch/). Prostate cancer-related genes were extracted from GeneCards (https://www.genecards.org/), DisGeNET (https://disgenet.com/), and OMIM databases (https://www.omim.org/). Overlapping targets were identified using a Venn diagram to determine potential CM-PCa therapeutic targets (Huang, 2024; Wang et al., 2024).

2.2. Protein-Protein Interaction (PPI) Network Construction

The identified targets were analyzed using the STRING database to construct a PPI network. Core hub targets were identified based on degree centrality, closeness centrality, and betweenness centrality measures (Mei, 2018).

2.3. GO and KEGG Pathway Enrichment Analysis

GO enrichment analysis was performed to explore the biological processes, molecular functions, and cellular components associated with the targets (Xin et al., 2022). KEGG pathway analysis identified key signaling pathways implicated in PCa treatment, with significant emphasis on pathways such as apoptosis, oxidative stress response, and PI3K-Akt signaling (Du et al., 2016).

2.4. Visualization of Core Targets

The core targets were visualized using Cytoscape software (Kohl et al., 2011), and their role in PCa progression and treatment was analyzed in detail.

3. Results

3.1. Overlapping Targets of Cinnamic Acid and Prostate Cancer

A total of 78 overlapping targets were identified, signifying potential therapeutic targets for CM in PCa treatment. These targets include proteins involved in apoptosis, cell cycle regulation, and metastasis (Figure 1).

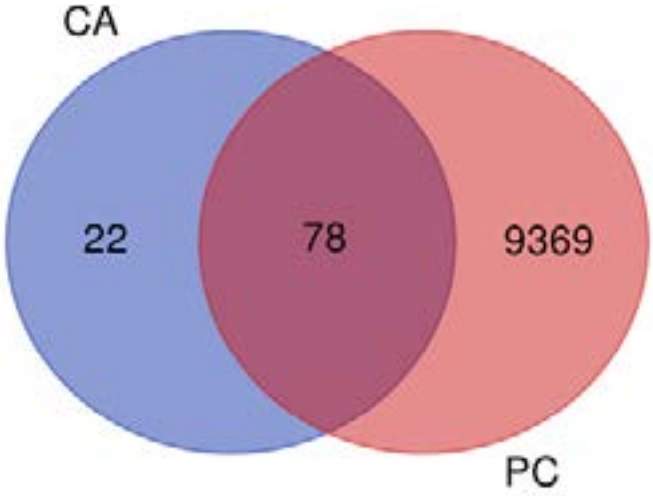

Figure 1: Venn diagram of CM and PCa to detect targets

3.2. PPI Network Analysis

The PPI network showed the direct or indirect protein-protein interaction. These targets were found to be highly interconnected and play pivotal roles in PCa pathophysiology (Figure 2).

3.3. GO Enrichment Analysis

GO analysis revealed significant biological processes such as regulation of apoptotic signaling pathways,

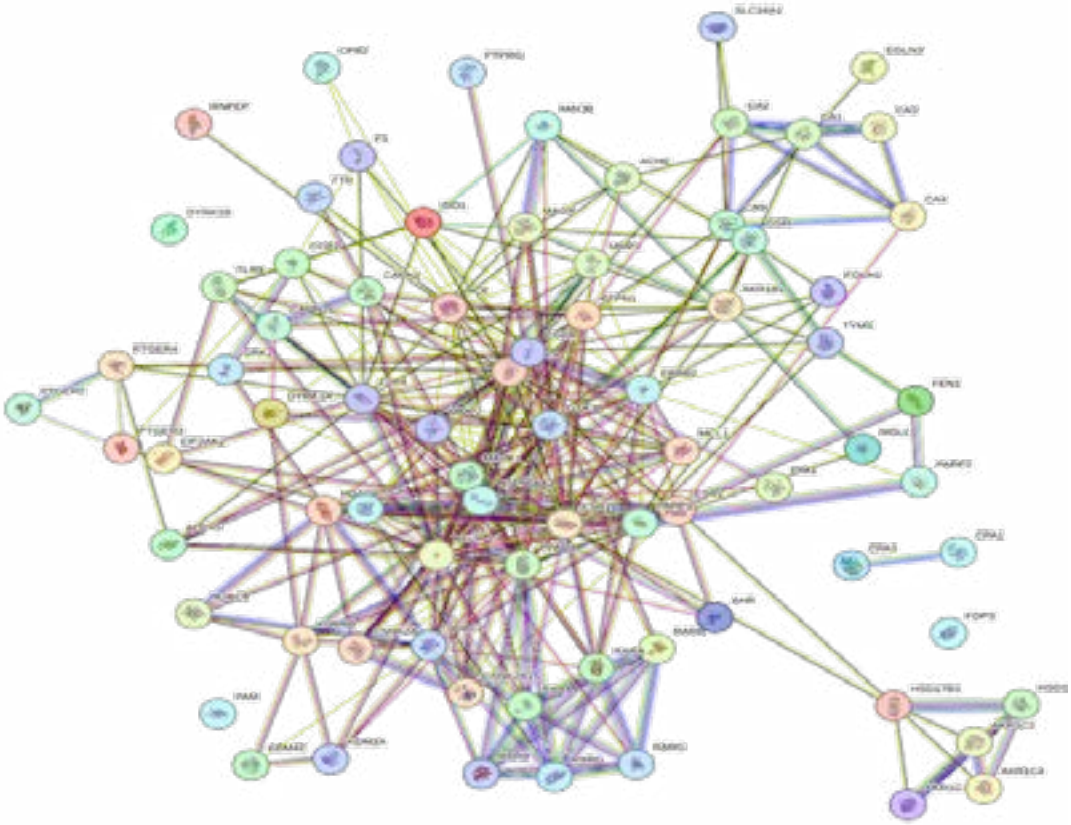

Figure 2: STRING database PPI network

inflammatory responses, and cell proliferation. Molecular function terms such as enzyme binding and receptor activity were prominently enriched (Figure 3).

3.4. KEGG Pathway Analysis

KEGG analysis identified pathways such as PI3K-Akt signaling, MAPK signaling, and oxidative phosphorylation

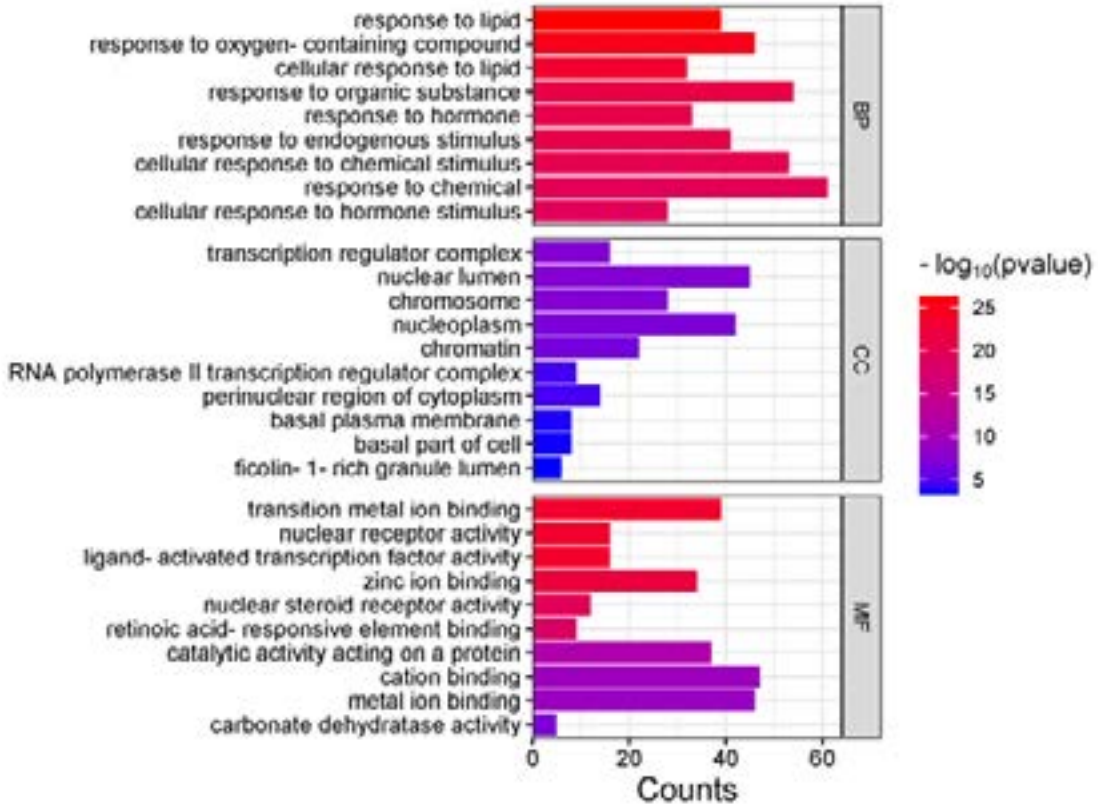

Figure 3: GO enrichment analysis

as key mechanisms through which CM exerts its anti-cancer effects. The modulation of these pathways suggests a multi-targeted therapeutic potential for CM (Figure 4 & 5).

3.5 Core Targets Analysis

Visualization of core targets highlighted their central role in disrup

to signaling networks that regulate cellular homeostasis and oncogenesis (Figure 6).

4. Discussion

The network pharmacology approach provides a comprehensive understanding of CM's pharmacological

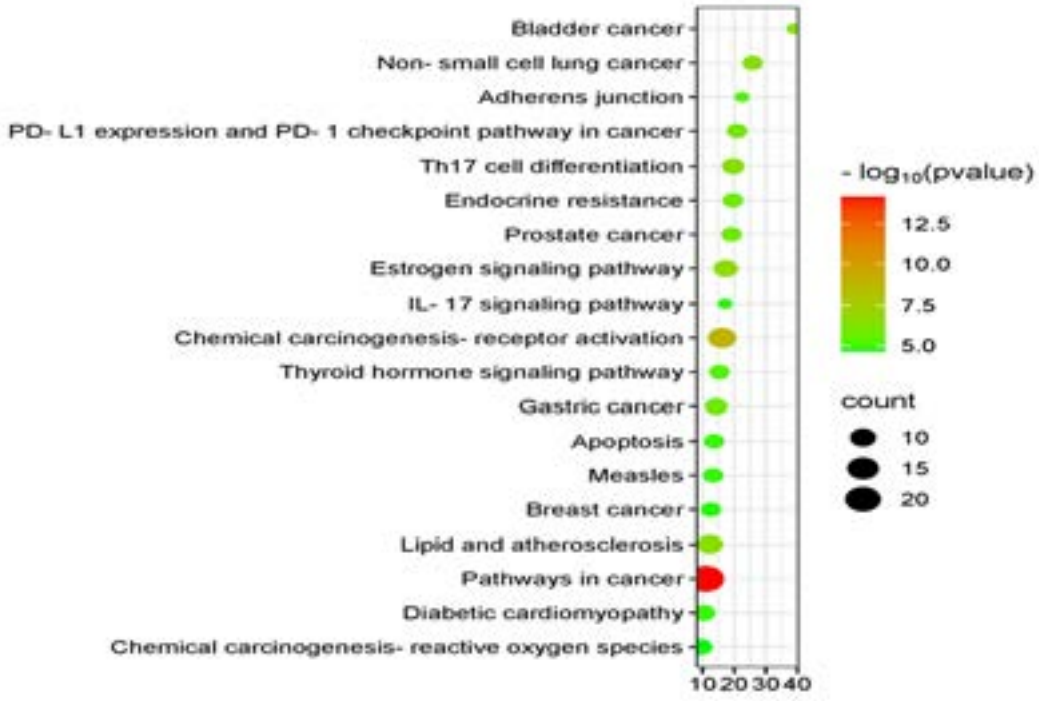

Figure 4: KEGG Enrichment analysis

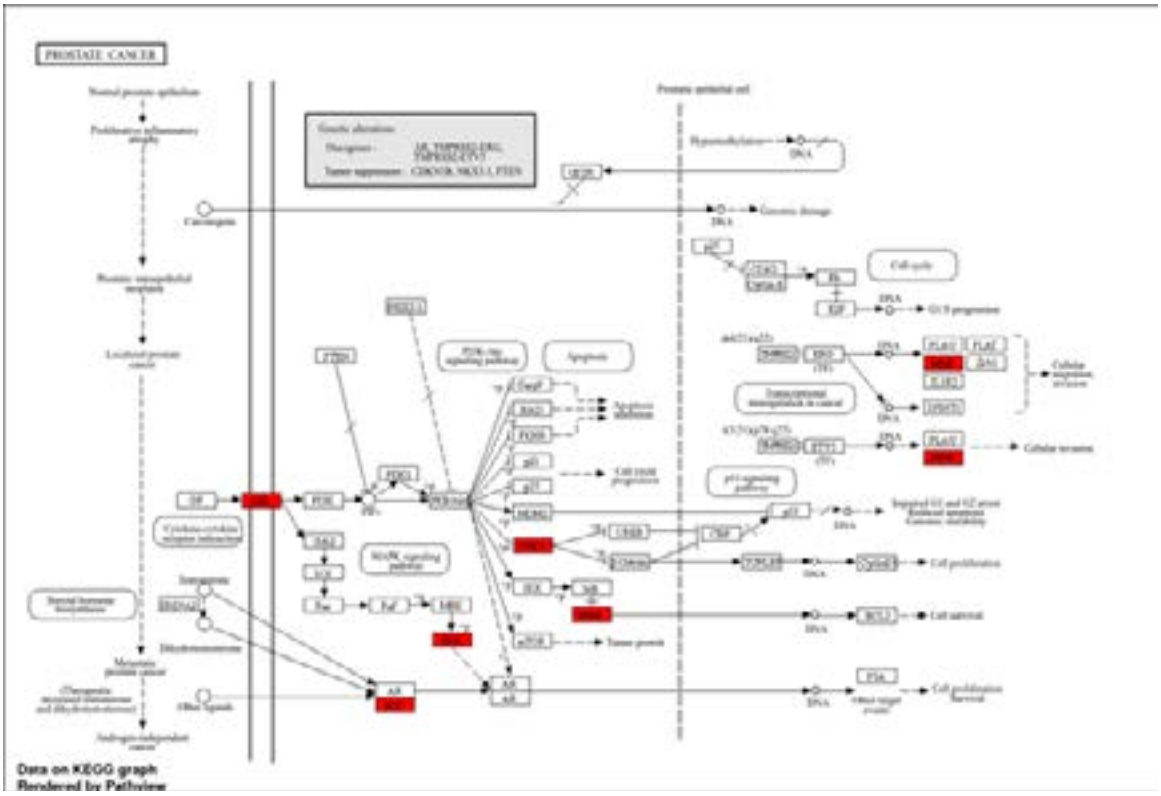

Figure 5: KEGG Pathway analysis and the red labelled detect the target for treating prostate cancer

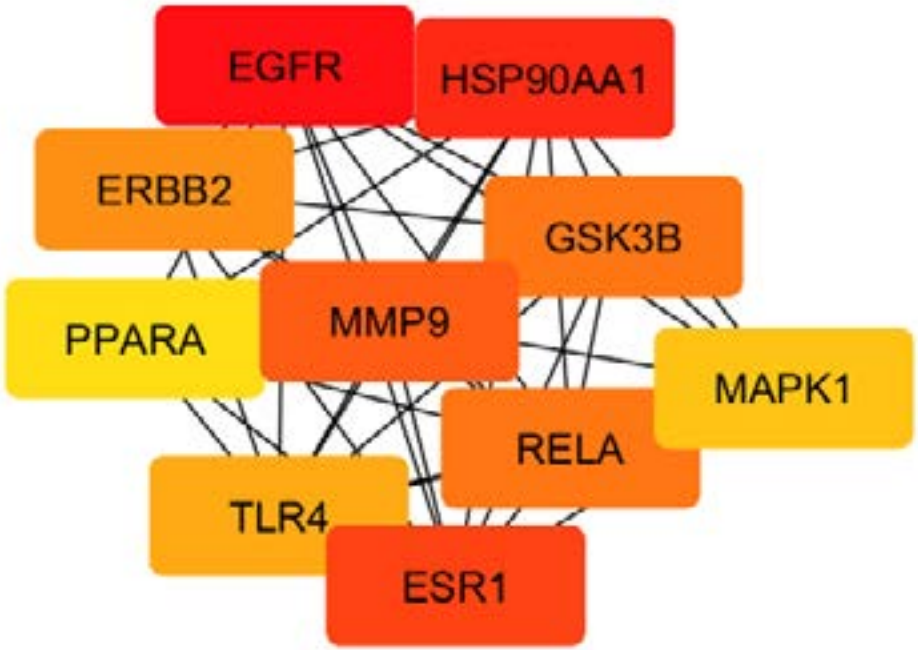

Figure 6: Inverted structures depict the top 10 core hub targets of CM on PCa

mechanisms in PCa. The identification of core hub targets such as TP53 and AKT1 underscores their significance in mediating anti-cancer effects. The enrichment analyses further corroborate the therapeutic potential of CM in regulating apoptosis, cell proliferation, and angiogenesis.

KEGG pathway analysis highlights the critical role of PI3K-Akt signaling in PCa, a pathway known to mediate survival, growth, and resistance mechanisms. CM's ability to modulate this pathway suggests its utility in overcoming drug resistance and enhancing treatment efficacy. Moreover, the anti-inflammatory and antioxidant properties of CM provide additional benefits in mitigating PCa progression and associated comorbidities. Future studies should focus on validating these findings through in

vitro and in vivo experiments. Additionally, exploring the synergistic effects of CM with existing therapies could pave the way for integrated treatment strategies.

5. Conclusion

This study elucidates the pharmacological mechanisms of cinnamic acid in prostate cancer treatment through a network pharmacology approach. By identifying key molecular targets and pathways, our findings provide a scientific basis for further experimental validation and clinical translation of CM as a promising anti-PCa agent. These results highlight the potential of natural compounds in addressing complex diseases like prostate cancer.

Declarations

Ethics approval statement

No ethical approval was required for the current study as it did not deal with any human or animal samples.

Consent to participate

Not applicable

Consent to publish

Not applicable

Data Availability Statement

The data are available from the corresponding author upon reasonable request

Competing Interests

The authors declare that they have no conflict of interest

Funding

Not Applicable

Author contribution

Conceptualization, Data curation, Investigation: J.P.S. Formal analysis: A.A. Writing—review and editing: J.P.S. All authors have read and agreed to the published version of the manuscript

Acknowledgements

Not Applicable

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