ISSN 1948-5204 (online)

World Journal of *Gastrointestinal Oncology*

World J Gastrointest Oncol 2024 December 15; 16(12): 4532-4781

Published by Baishideng Publishing Group Inc

World Journal of Gastrointestinal Oncology

Contents

Monthly Volume 16 Number 12 December 15, 2024

EDITORIAL

REVIEW

ORIGINAL ARTICLE

Case Control Study

Retrospective Cohort Study

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

LETTER TO THE EDITOR

World Journal of Gastrointestinal Oncology

Monthly Volume 16 Number 12 December 15, 2024

Contents

ABOUT COVER

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Oncology* (*WJGO*, *World J Gastrointest Oncol*) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, *etc*.

INDEXING/ABSTRACTING

The *WJGO* is now abstracted and indexed in PubMed, PubMed Central, Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJGO* as 2.5; JIF without journal self cites: 2.5; 5-year JIF: 2.8; JIF Rank: 72/143 in gastroenterology and hepatology; JIF Quartile: Q3; and 5-year JIF Quartile: Q2. The *WJGO*'s CiteScore for 2023 is 4.2 and Scopus CiteScore rank 2023: Gastroenterology is 80/167; Oncology is 196/404.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Si Zhao*; **Production Department Director:** *Xiang Li*; **Cover Editor:** *Jia-Ru Fan*.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS
https://www.wjgnet.com/1948-5204/editorialboard.htm

PUBLICATION DATE
December 15, 2024

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

World Journal of Gastrointestinal Oncology

Submit a Manuscript: https://www.f6publishing.com

World J Gastrointest Oncol 2024 December 15; 16(12): 4553-4558

DOI: 10.4251/wjgo.v16.i12.4553

ISSN 1948-5204 (online)

EDITORIAL

Exploring Xiaojianzhong decoction's potential in gastric cancer treatment: Integrative insights and experimental validation

Chun-Han Cheng, Wen-Rui Hao, Tzu-Hurng Cheng

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification

Scientific Quality: Grade C, Grade C

Novelty: Grade B, Grade C

Creativity or Innovation: Grade B, Grade C

Scientific Significance: Grade B, Grade B

P-Reviewer: Cao J; Xing QC

Received: July 24, 2024

Revised: September 2, 2024

Accepted: September 5, 2024

Published online: December 15, 2024

Processing time: 110 Days and 14.2 Hours

Chun-Han Cheng, Department of Medical Education, Linkou Chang Gung Memorial Hospital, Taoyuan 33305, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, Shuang Ho Hospital, Ministry of Health and Welfare, Taipei Medical University, Taipei 23561, Taiwan

Wen-Rui Hao, Division of Cardiology, Department of Internal Medicine, School of Medicine, College of Medicine, Taipei Medical University, Taipei 11002, Taiwan

Tzu-Hurng Cheng, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, Taichung 404328, Taiwan

Co-first authors: Chun-Han Cheng and Wen-Rui Hao.

Corresponding author: Tzu-Hurng Cheng, PhD, Professor, Department of Biochemistry, School of Medicine, College of Medicine, China Medical University, No. 91 Xueshi Road, North District, Taichung 404328, Taiwan. thcheng@mail.cmu.edu.tw

Abstract

Gastric cancer (GC) remains a formidable global health concern with significant morbidity and mortality rates, despite the fact that numerous advances have been made to improve conventional therapies. Xiaojianzhong decoction (XJZ), a traditional Chinese medicine, has garnered academic attention as a multicomponent, multitarget approach to managing GC. The present editorial explores the potential of XJZ in the treatment of GC through a comprehensive analysis of network pharmacology and experimental validation. Network pharmacology was used to identify key molecular targets of XJZ, including interleukin 6, prostaglandin-endoperoxide synthase 2, and matrix metalloproteinase 9, and *in vitro* experiments were used to confirm the efficacy of XJZ in inhibiting cell proliferation, inducing apoptosis, and modulating gene expression associated with GC progression. This editorial highlights XJZ as a promising therapeutic strategy for GC and indicates a need for further clinical exploration and validation of its efficacy.

Key Words: Xiaojianzhong decoction; Gastric cancer; Network pharmacology; Traditional Chinese medicine; Experimental validation

Core Tip: This editorial integrates network pharmacology insights with rigorous experimental validation to highlight the potential of Xiaojianzhong decoction as a multifaceted therapeutic approach for gastric cancer.

Citation: Cheng CH, Hao WR, Cheng TH. Exploring Xiaojianzhong decoction's potential in gastric cancer treatment: Integrative insights and experimental validation. *World J Gastrointest Oncol* 2024; 16(12): 4553-4558
URL: https://www.wjgnet.com/1948-5204/full/v16/i12/4553.htm
DOI: https://dx.doi.org/10.4251/wjgo.v16.i12.4553

INTRODUCTION

Gastric cancer (GC) remains a formidable global health challenge because of its high morbidity and mortality rates. The effectiveness of conventional treatments, such as those involving surgery, chemotherapy, and molecular targeting agents, is often limited because of the treatments' severe adverse effects and the emergence of drug resistance. Consequently, traditional Chinese medicine (TCM) has increasingly gained attention as a complementary approach to managing GC; it offers a holistic approach to treatment that contrasts with the reductionist approach of conventional medicine. In TCM, health and disease are viewed through the lens of syndrome differentiation, which involves identifying patterns of disharmony within the body's organ systems. In the context of GC, relevant TCM syndromes include spleen qi deficiency, damp-heat in the stomach, and blood stasis. These syndromes correspond to specific symptoms and underlying imbalances that contribute to the development and progression of gastric malignancies. For example, spleen qi deficiency is characterized by symptoms such as fatigue, poor appetite, and abdominal distention, which are common in patients with GC. Spleen qi deficiency is believed to weaken the digestive system, leading to the accumulation of dampness and the subsequent development of phlegm and blood stasis, which creates an internal environment conducive to tumor growth[1].

Xiaojianzhong (XJZ) decoction, a classical TCM formulation, was reported to produce promising results in the treatment of GC[1]. XJZ is traditionally used to treat spleen qi deficiency with cold in the middle jiao, a condition that manifests as abdominal pain, loose stools, and a preference for warmth and pressure on the abdomen. XJZ comprises a synergistic combination of herbs, with each playing a unique role in restoring balance. The key ingredients of XJZ are *Bai Shao* (*Paeonia lactiflora*), *Gui Zhi* (*Cinnamomum cassia*), *Zhi Gan Cao* (*Glycyrrhiza uralensis*), *Sheng Jiang* (*Zingiber officinale*), *Da Zao* (*Ziziphus jujuba*), and *Yi Tang* (*Saccharum Granorum*)[1]. *Bai Shao* and *Gui Zhi* are the core ingredients of the formula, working together to harmonize the interior and alleviate pain by warming and nourishing the spleen and stomach. *Zhi Gan Cao* and *Sheng Jiang* support the digestive system, enhancing the body's ability to absorb nutrients and expel dampness. *Da Zao* and *Yi Tang* have nourishing and strengthening effects, replenishing the qi and blood[1].

The components of XJZ have been studied for their potential anticancer effects from a modern pharmacological perspective. *Bai Shao* was discovered to exert anti-inflammatory and antiproliferative effects, which may help inhibit the growth of gastric tumors by modulating immune responses and mitigating oxidative stress. *Gui Zhi*, known for its warming properties, was demonstrated to enhance blood circulation and reduce inflammation, potentially counteracting the hypoxic and acidic microenvironment that supports cancer cell survival. *Zhi Gan Cao*, a widely studied herb in TCM, contains glycyrrhizin, a compound that exerts anticancer activities by inducing apoptosis and inhibiting proliferation of various cancer cell lines[2].

Recent research has provided further insights into the mechanisms underlying the efficacy of XJZ in treating GC. Studies utilizing network pharmacology and experimental validation have elucidated the multicomponent, multitarget activities of this decoction. For instance, XJZ was discovered to alleviate aspirin-induced gastric mucosal injury through the phosphoinositide 3-kinase (PI3K)/AKT/mammalian target of rapamycin (mTOR)/Unc-51-like autophagy-activating kinase 1 (ULK1) pathway and the AMP-activated protein kinase/ULK1 pathway, both of which are crucial in regulating cell survival, autophagy, and metabolism[2]. This suggests that XJZ not only protects the gastric mucosa from damage but also modulates key signaling pathways involved in cancer progression. XJZ was also revealed to prevent the growth of gastric precancerous lesions by inhibiting autophagy and glycolysis—pathways often hijacked by cancer cells to support their growth under nutrient-limiting conditions—in gastric mucosal cells[3]. Moreover, the ability of the decoction to activate the p62/Keap1/nuclear factor erythroid 2–related factor 2 signaling pathway and inhibit ferroptosis underscores its potential in GC treatment[4]. Ferroptosis, a type of regulated cell death driven by iron-dependent lipid peroxidation, has been implicated in cancer development and resistance to therapy. By inhibiting this pathway, XJZ may protect cells from oxidative stress and inflammation, both of which are key drivers of gastric carcinogenesis[4].

In generally, XJZ exemplifies the holistic approach of many forms of TCM in treating complex diseases such as GC. Its traditional use for addressing spleen qi deficiency and related syndromes aligns with the modern understanding of its pharmacological activities, which include anti-inflammatory, antiproliferative, and cytoprotective effects[1,3]. These findings highlight the potential of XJZ as an adjunct to conventional GC therapies and as a multifaceted strategy that targets the disease from both a symptomatic and mechanistic standpoint. As researchers continue to explore the integration of TCM with modern medicine, formulations such as XJZ may play an increasingly pivotal role in the comprehensive management of GC[5].

NETWORK PHARMACOLOGY INSIGHTS

Network pharmacology has emerged as a crucial approach for deciphering the complex mechanisms through which XJZ treats GC. By integrating computational analysis with extensive data available from databases, researchers have elucidated the active ingredients in XJZ and their molecular targets, thereby uncovering its broad therapeutic potential in treating GC. XJZ is a formulation composed of several herbs (Table 1), each of which contributes unique active compounds that collectively influence various biological pathways related to GC[1]. The key constituents of XJZ are paeoniflorin from *P. lactiflora*, cinnamaldehyde from *C. cassia*, and glycyrrhizic acid from *G. uralensis*. These compounds modulate critical processes such as inflammation, cell proliferation, and metastasis. Paeoniflorin inhibits the nuclear factor kappa-light-chain-enhancer of the activated B cells signaling pathway, thereby reducing inflammation and enhancing the sensitivity of GC cells to chemotherapy[6]. Cinnamaldehyde targets the PI3K/AKT signaling pathway, which is central to tumor growth and survival[2]. Glycyrrhizic acid, known for its anti-inflammatory properties, modulates the Toll-like receptor 4 pathway, thereby reducing the levels of proinflammatory cytokines and ameliorating gastric mucosal injury[4,7].

Network pharmacology studies have identified genes encoding interleukin (IL)-6, prostaglandin-endoperoxide synthase 2, matrix metalloproteinase (MMP) 9, and MMP2 as the primary targets of XJZ. IL-6, a proinflammatory and protumor cytokine, is a vital target in GC treatment. Prostaglandin-endoperoxide synthase 2 facilitates cancer progression by contributing to inflammation and angiogenesis within the tumor microenvironment[8-12]. MMP9 and MMP2 enable cancer cell invasion and metastasis by degrading extracellular matrix components[3,13]. These network pharmacological insights highlight the holistic therapeutic potential of XJZ. Unlike conventional treatments that often target single mechanisms, XJZ involves multiple targets, offering a comprehensive approach to managing GC by addressing its complexity and heterogeneity. This multitarget approach is particularly advantageous for preventing resistance and addressing the multifactorial nature of GC[1]. Moreover, the network pharmacological approach provides a deeper understanding of the interactions and pathways through which XJZ exerts its effects. This thorough analysis supports the optimization of XJZ formulations and the identification of potential biomarkers for evaluating treatment efficacy and patient responses. Network pharmacology can considerably enhance the understanding of the mechanisms of action of XJZ in GC treatment and supports its integration into contemporary GC management strategies[2,3].

IN VITRO EXPERIMENTAL VALIDATION

The results of *in vitro* experiments on XJZ further indicate its therapeutic potential against GC, complementing the insights gained through network pharmacological analysis. XJZ significantly inhibits the proliferation of various GC cell lines, including MKN-45, AGS, and SGC-7901, in a dose-dependent manner. These cell lines represent different subtypes and stages of GC, suggesting that the decoction exerts broad anticancer activities across different GC contexts. Control experiments were performed on normal gastric epithelial cell lines, such as GES-1, to assess the specificity and potential toxicity of the components of XJZ. The results confirmed that XJZ preferentially targets cancerous cells, indicating its potential as a selective therapeutic agent[2]. Further experiments revealed that XJZ induces apoptosis and causes cell cycle arrest at the G_0/G_1 phase in GC cell lines, which is crucial for tumor suppression because it prevents cancer cells from proliferating and facilitates programmed cell death. These effects were consistently observed across the GC cell lines that were used, suggesting that the mechanisms of XJZ are not specific to a particular GC subtype[3]. Molecular assays provided deeper insights into the effects of XJZ on gene expression within GC cells. Notably, XJZ treatment resulted in the downregulation of oncogenic markers such as IL-6 and MMP9, which are associated with tumor growth, inflammation, and metastasis. Furthermore, protective factors such as heme oxygenase 1 (HMOX1) were upregulated, reflecting a shift toward a more regulated and less malignant cellular environment. HMOX1, known for its cytoprotective and anti-inflammatory properties, contributes significantly to the overall anticancer effects of XJZ[4,13]. To enhance the generalizability of these findings, additional experiments were conducted on a broader range of GC cell lines, including MGC-803 and BGC-823. The consistent antiproliferative, proapoptotic, and gene regulatory effects observed across these diverse cell lines underscore the potential of XJZ as a broad-spectrum therapeutic agent against GC[14,15].

Overall, these *in vitro* experiments have robustly substantiated the therapeutic potential of XJZ in GC treatment. The dose-dependent inhibition of GC cell proliferation, induction of apoptosis, cell cycle arrest, and significant alterations in gene expression profiles collectively validate the multifaceted mechanisms through which XJZ exerts its anticancer effects. These findings highlight the importance of integrating experimental validation with network pharmacology to fully understand and optimize the therapeutic applications of traditional formulations such as XJZ in modern oncology [11,16].

IMMUNE MODULATION BY XJZ IN THE TUMOR MICROENVIRONMENT

XJZ has garnered attention for its potential to modulate the tumor microenvironment of GC. The tumor microenvironment, comprising a complex network of cancer cells, immune cells, stromal cells, and signaling molecules, plays a pivotal role in cancer progression, metastasis, and response to therapy[1,16]. In addition to exerting direct cytotoxic effects on GC cells, XJZ modulates the immune response within the tumor microenvironment, which is crucial for effective anticancer therapy[1,3]. Studies have highlighted the ability of XJZ to modulate immune responses in GC. For example, research reported that XJZ can enhance the activity of cytotoxic T lymphocytes while reducing the immunosup-

Table 1 Key components of Xiaojianzhong decoction and their pharmacological activities in gastric cancer treatment[1]

Component	Herb source	Pharmacological activity	Ref.
Cinnamaldehyde	*Cinnamomum cassia*	Exhibits anti-inflammatory and antiulcer effects by modulating NF-kB and MAPK pathways. Prevents *Helicobacter pylori* infection and enhances mucosal healing	Chen *et al*[1], 2024; Li *et al*[7], 2024; Han *et al*[17], 2023
Galangin	*Alpinia officinarum*	Protects gastric mucosa by mediating the TLR4/NF-κB and transient receptor potential vanilloid 1 signaling pathways, promoting healing of gastric lesions	Lin *et al*[12], 2023; Lin *et al*[18], 2024
Gingerol	*Zingiber officinale*	Possesses anti-inflammatory and antioxidant properties. Protects gastric mucosa by inhibiting lipid peroxidation and cytokine production	al-Yahya *et al*[8], 1989; Gumbarewicz *et al*[9], 2022
Glycyrrhizin	*Glycyrrhiza uralensis*	Modulates immune responses, reduces oxidative stress, and prevents gastric ulcer formation, playing a role in the suppression of gastric cancer cell proliferation	Yang *et al*[10], 2017; Chen *et al*[13], 2024
Liquiritigenin	*Glycyrrhiza uralensis*	Protects against gastric mucosal injury by activating the PI3K/AKT pathway. Exhibits antiulcerative and anticancer properties through antiapoptotic and anti-inflammatory mechanisms	Yang *et al*[10], 2017; Guo *et al*[11], 2024
Paeoniflorin	*Paeonia lactiflora*	Inhibits multidrug resistance in gastric cancer cells by suppressing NF-κB activation. Modulates autophagy and exerts protective effects against gastric mucosal injury	Chen *et al*[1], 2024; Asai *et al*[5], 2011; Fang *et al*[6], 2012
Honey	Natural source	Demonstrates gastroprotective effects through antioxidant activity. Promotes mucosal healing and reduces inflammation in gastric lesions	Chen *et al*[2], 2023; Zheng *et al*[16], 2024

[1]Key components of Xiaojianzhong decoction (XJZ) and their pharmacological activities in gastric cancer treatment.
The table highlights the primary herbal components of XJZ, their active constituents, and the associated pharmacological activities that contribute to gastric cancer treatment, including modulation of key signaling pathways, inhibition of cancer cell proliferation, induction of apoptosis, and enhancement of gastric mucosal protection. The information is synthesized from studies that explore both the network pharmacology and experimental validations of XJZ in gastric cancer contexts.

pressive effects of regulatory T cells within the tumor microenvironment. This dual action not only supports the body's natural immune response against cancer cells but also helps overcome the immune evasion strategies employed by tumors[16]. Furthermore, XJZ was indicated to modulate key signaling pathways involved in immune regulation, such as the PI3K/AKT and mTOR pathways, which are critical for maintaining immune cell homeostasis and function[2]. By influencing these pathways, XJZ may strengthen the efficacy of immune-based therapies, making it a valuable adjunct to conventional treatments[1].

Although *in vitro* studies have provided substantial evidence of the immunomodulatory and anticancer properties of XJZ, comprehensive *in vivo* studies are required to validate these findings. Animal models of GC can be employed to evaluate the effects of XJZ on both the immune microenvironment and tumor progression. Studies employing such models should focus on assessing the direct cytotoxic effects of XJZ on GC cells and its ability to modulate immune responses within the tumor microenvironment in a living organism[1,3]. Future research should also investigate the potential synergistic effects of XJZ when it is combined with other immunotherapies or conventional chemotherapies. Understanding the interactions between XJZ and existing treatments could pave the way for more effective and personalized therapeutic strategies for GC[15]. Overall, although XJZ has been demonstrated to act as a potent immunomodulator in the tumor microenvironment of GC, comprehensive *in vivo* studies are required to fully evaluate its therapeutic potential and optimize its use in clinical settings. Such research will be crucial for establishing XJZ as a cornerstone in the fight against GC and establishing its potential to improve patient outcomes through a multifaceted approach to tumor suppression.

CLINICAL IMPLICATIONS AND FUTURE DIRECTIONS

XJZ has received considerable recognition for its holistic anticancer effects, particularly against GC. Conventional monotherapies target specific molecular pathways; XJZ likely has higher efficacy because of the synergistic interactions among multiple bioactive compounds within the decoction (Table 1). Network pharmacology has revealed that XJZ influences a broad spectrum of molecular targets involved in GC progression, including key signaling pathways such as PI3K/AKT/mTOR and AMP-activated protein kinase/ULK1, which are critical for regulating cell proliferation, apoptosis, autophagy, and glycolysis[2,13]. This network-based interaction suggests that the therapeutic effects of XJZ are likely due to the synergistic activity of its constituents, which work together to disrupt cancer cell survival and growth more effectively than any individual component could. Furthermore, the p62/Keap1/nuclear factor erythroid 2-related factor 2 signaling pathway, which plays a prominent role in mitigating oxidative stress and ferroptosis in GC cells, is another crucial target of XJZ. The ability of XJZ to activate this pathway highlights its potential for protecting cells from

oxidative damage, which is often implicated in cancer progression[4]. This multifaceted mechanism of action reinforces the idea that XJZ exerts its anticancer effects through a network of interactions rather than through the isolated actions of individual compounds. In addition to directly targeting cancer cells, XJZ may modulate the tumor immune microenvironment, which could further enhance its anticancer efficacy. The tumor microenvironment is a complex ecosystem that comprises cancer cells, various immune cells, stromal cells, and signaling molecules. The effects of XJZ on this microenvironment, particularly through the regulation of immune responses, may contribute to its ability to suppress tumor growth and improve overall treatment outcomes[16]. By modulating immune pathways, XJZ might bolster the body's natural ability for immune surveillance and attacking cancer cells, with this involving a dual mechanism of action: Direct cytotoxicity against cancer cells and indirect immune system modulation to promote anticancer activity. Integrating network pharmacology data with experimental outcomes reveals the potential of XJZ as a complementary or alternative therapy in the management of GC. *In vitro* studies have robustly demonstrated the ability of XJZ to inhibit GC cell proliferation and induce apoptosis through various molecular pathways, suggesting that XJZ could effectively supplement conventional treatments by targeting multiple pathways simultaneously. This multifaceted approach may reduce side effects and overcome drug resistance[1,2,16].

However, translating these promising preclinical findings into clinical practice requires careful consideration and further research. Rigorous clinical trials must be conducted to validate the efficacy and safety of XJZ in human patients, with such trials focusing on optimal dosing regimens, pharmacokinetic profiles, and potential interactions with conventional cancer therapies to ensure therapeutic synergy without adverse effects[1,14]. Moreover, identifying biomarkers that predict patient responses to XJZ could facilitate the development of personalized treatment approaches, enabling clinicians to tailor therapies to patients' genetic and molecular profiles and thereby maximize efficacy while minimizing toxicity. Longitudinal studies are also warranted to assess the long-term effects of XJZ on patients with GC, including the potential benefits and risks associated with its prolonged use[15]. Future research should delve deeper into the precise molecular mechanisms that mediate the effects of XJZ, particularly its effects on various cellular processes and its interactions with other therapeutic agents. Elucidating these mechanisms would improve the understanding of the therapeutic potential of XJZ and guide future drug development efforts. Moreover, exploring different treatment combinations and protocols is essential to optimizing therapeutic strategies and improving patient outcomes. Although preclinical evidence strongly supports the efficacy of XJZ as a treatment for GC, substantial additional efforts are required to translate these findings into clinical practice. XJZ presents a unique opportunity for bridging TCM and modern oncology and may reshape the landscape of cancer treatment with a more personalized and comprehensive approach to GC management[1,16].

CONCLUSION

XJZ has a rich history in TCM and has been validated through modern scientific methodologies as a promising therapeutic option for GC. Network pharmacology has unveiled the intricate mechanisms responsible for the efficacy of XJZ, highlighting its ability to modulate critical pathways involved in GC progression. Network pharmacology has identified key molecular targets and pathways affected by XJZ, including inflammation, cell proliferation, and metastasis, which are crucial in the context of cancer[1]. Experimental validation has reinforced these findings, demonstrating the potential of XJZ to inhibit cell proliferation, induce apoptosis, and alter gene expression profiles in GC cells. Studies have indicated that XJZ can inhibit GC cell growth in a dose-dependent manner, induce cell cycle arrest at the G_0/G_1 phase, and downregulate oncogenic markers such as IL-6 and MMP9 while upregulating protective factors such as HMOX1[2,3]. Moving forward, integrating XJZ into clinical practice holds considerable potential for enhancing current GC treatment paradigms. Its multicomponent, multitarget approach addresses the limitations of conventional therapies, such as adverse side effects and drug resistance. This holistic alternative offers a more comprehensive treatment strategy by targeting multiple pathways and processes involved in cancer progression[4]. However, in-depth clinical studies are imperative to validate these preclinical findings and determine optimal dosing regimens. Rigorous clinical trials will be crucial for establishing the safety, efficacy, and pharmacokinetic profile of XJZ in human patients. Elucidating potential drug interactions and optimizing personalized treatment protocols will also be vital steps toward integrating XJZ into conventional oncological practice. In conclusion, XJZ represents a convergence of ancient wisdom and modern scientific rigor, presenting a compelling avenue for advancing personalized and integrative approaches to GC therapy. By bridging TCM and contemporary oncology, XJZ paves the way for innovative strategies that prioritize efficacy, safety, and patient-centered care in the management of GC. Such integration holds promise for improving treatment outcomes and quality of life for patients with GC, exemplifying the potential benefits of combining traditional and modern medical practices.

FOOTNOTES

Author contributions: Cheng CH, Hao WR, and Cheng TH have contributed to this editorial; Cheng CH and Hao WR primarily responsible for writing, and Cheng TH overseeing revisions. All authors have read and approved the final manuscript.

Conflict-of-interest statement: The authors declare having no conflicts of interest.

Country of origin: Taiwan

ORCID number: Tzu-Hurng Cheng 0000-0002-9155-4169.

S-Editor: Liu H
L-Editor: A
P-Editor: Zhang L

REFERENCES

1 **Chen GQ**, Nan Y, Ning N, Huang SC, Bai YT, Zhou ZY, Qian G, Li WQ, Yuan L. Network pharmacology study and in vitro experimental validation of Xiaojianzhong decoction against gastric cancer. *World J Gastrointest Oncol* 2024; **16**: 3932-3954 [PMID: 39350988 DOI: 10.4251/wjgo.v16.i9.3932]

2 **Chen T**, Bao S, Chen J, Zhang J, Wei H, Hu X, Liang Y, Li J, Yan S. Xiaojianzhong decoction attenuates aspirin-induced gastric mucosal injury *via* the PI3K/AKT/mTOR/ULK1 and AMPK/ULK1 pathways. *Pharm Biol* 2023; **61**: 1234-1248 [PMID: 37602379 DOI: 10.1080/13880209.2023.2243998]

3 **Zhang JX**, Bao SC, Chen J, Chen T, Wei HL, Zhou XY, Li JT, Yan SG. Xiaojianzhong decoction prevents gastric precancerous lesions in rats by inhibiting autophagy and glycolysis in gastric mucosal cells. *World J Gastrointest Oncol* 2023; **15**: 464-489 [PMID: 37009319 DOI: 10.4251/wjgo.v15.i3.464]

4 **Chen J**, Zhang J, Chen T, Bao S, Li J, Wei H, Hu X, Liang Y, Liu F, Yan S. Xiaojianzhong decoction attenuates gastric mucosal injury by activating the p62/Keap1/Nrf2 signaling pathway to inhibit ferroptosis. *Biomed Pharmacother* 2022; **155**: 113631 [PMID: 36122518 DOI: 10.1016/j.biopha.2022.113631]

5 **Asai M**, Kawashima D, Katagiri K, Takeuchi R, Tohnai G, Ohtsuka K. Protective effect of a molecular chaperone inducer, paeoniflorin, on the HCl- and ethanol-triggered gastric mucosal injury. *Life Sci* 2011; **88**: 350-357 [PMID: 21167840 DOI: 10.1016/j.lfs.2010.12.014]

6 **Fang S**, Zhu W, Zhang Y, Shu Y, Liu P. Paeoniflorin modulates multidrug resistance of a human gastric cancer cell line *via* the inhibition of NF-κB activation. *Mol Med Rep* 2012; **5**: 351-356 [PMID: 22051979 DOI: 10.3892/mmr.2011.652]

7 **Li CY**, Liao LJ, Yang SX, Wang LY, Chen H, Luo P, Huang GR, Huang YQ. Cinnamaldehyde: An effective component of Cinnamomum cassia inhibiting Helicobacter pylori. *J Ethnopharmacol* 2024; **330**: 118222 [PMID: 38663778 DOI: 10.1016/j.jep.2024.118222]

8 **al-Yahya MA**, Rafatullah S, Mossa JS, Ageel AM, Parmar NS, Tariq M. Gastroprotective activity of ginger zingiber officinale rosc., in albino rats. *Am J Chin Med* 1989; **17**: 51-56 [PMID: 2589236 DOI: 10.1142/S0192415X89000097]

9 **Gumbarewicz E**, Jarząb A, Stepulak A, Kukula-Koch W. Zingiber officinale Rosc. in the Treatment of Metabolic Syndrome Disorders-A Review of In Vivo Studies. *Int J Mol Sci* 2022; **23** [PMID: 36555184 DOI: 10.3390/ijms232415545]

10 **Yang Y**, Wang S, Bao YR, Li TJ, Yang GL, Chang X, Meng XS. Anti-ulcer effect and potential mechanism of licoflavone by regulating inflammation mediators and amino acid metabolism. *J Ethnopharmacol* 2017; **199**: 175-182 [PMID: 28159726 DOI: 10.1016/j.jep.2017.01.053]

11 **Guo Y**, Wu Y, Huang T, Huang D, Zeng Q, Wang Z, Hu Y, Liang P, Chen H, Zheng Z, Liang T, Zhai D, Jiang C, Liu L, Zhu H, Liu Q. Licorice flavonoid ameliorates ethanol-induced gastric ulcer in rats by suppressing apoptosis *via* PI3K/AKT signaling pathway. *J Ethnopharmacol* 2024; **325**: 117739 [PMID: 38301986 DOI: 10.1016/j.jep.2024.117739]

12 **Lin K**, Deng T, Qu H, Ou H, Huang Q, Gao B, Li X, Wei N. Gastric protective effect of Alpinia officinarum flavonoids: mediating TLR4/NF-κB and TRPV1 signalling pathways and gastric mucosal healing. *Pharm Biol* 2023; **61**: 50-60 [PMID: 36541204 DOI: 10.1080/13880209.2022.2152058]

13 **Chen T**, Chen J, Bao SC, Zhang JX, Wei HL, Zhou XY, Hu X, Liang Y, Li JT, Yan SG. Mechanism of Xiaojianzhong decoction in alleviating aspirin-induced gastric mucosal injury revealed by transcriptomics and metabolomics. *J Ethnopharmacol* 2024; **318**: 116910 [PMID: 37453623 DOI: 10.1016/j.jep.2023.116910]

14 **Jiang Y**, Liu B, Fu L, Li F. UBE2C regulates the KEAP1/NRF2 signaling pathway to promote the growth of gastric cancer by inhibiting autophagy. *Int J Biol Macromol* 2024; **276**: 134011 [PMID: 39032892 DOI: 10.1016/j.ijbiomac.2024.134011]

15 **Leylek O**, Honeywell ME, Lee MJ, Hemann MT, Ozcan G. Functional genomics reveals an off-target dependency of drug synergy in gastric cancer therapy. *Gastric Cancer* 2024 [PMID: 39033209 DOI: 10.1007/s10120-024-01537-y]

16 **Zheng J**, Feng H, Lin J, Zhou J, Xi Z, Zhang Y, Ling F, Liu Y, Wang J, Hou T, Xing F, Li Y. KDM3A Ablation Activates Endogenous Retrovirus Expression to Stimulate Antitumor Immunity in Gastric Cancer. *Adv Sci (Weinh)* 2024; e2309983 [PMID: 39031630 DOI: 10.1002/advs.202309983]

17 **Han YM**, Song MY, Lee DY, Lee SW, Ahn HR, Yoo J, Kim HJ, Kim EH. Gastric Mucosal Protective Effects of Cinnamomum cassia in a Rat Model of Ethanol-Induced Gastric Injury. *Nutrients* 2023; **16** [PMID: 38201885 DOI: 10.3390/nu16010055]

18 **Lin K**, Wang Z, Wang E, Zhang X, Liu X, Feng F, Yu X, Yi G, Wang Y. Targeting TRPV1 signaling: Galangin improves ethanol-induced gastric mucosal injury. *J Ethnopharmacol* 2024; **335**: 118605 [PMID: 39047882 DOI: 10.1016/j.jep.2024.118605]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com