Mechanism of Jiawei Qifang Weitong Granules Against Gastric Cancer Through Modulation of Tumor Cell Glycolysis via the PI3K/AKT/HIF-1α Pathway: A Postprint

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Abstract

Gastric cancer, as one of the common malignant tumors of the digestive tract, has a complex pathogenesis and limited treatment options, and the mechanism of Jiawei Qifang Weitong Granules in treating gastric cancer remains unclear.

To investigate the mechanism by which Jiawei Qifang Weitong Granules inhibit gastric cancer proliferation through phosphatidylinositol 3-kinase (PI3K)/protein kinase B (AKT)/hypoxia-inducible factor 1α (HIF-1α)-mediated tumor cell glycolysis.

From March 2024 to June 2025, 50 nude mice were selected to establish HGC-27 gastric cancer cell xenograft tumor models, and 40 were finally included in the study. They were randomly divided into a control group, and low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups, with 10 mice in each group. The treatment groups were administered 15.28 $g \cdot kg^{-1} \cdot d^{-1}$, 30.55 $g \cdot kg^{-1} \cdot d^{-1}$, and 61.1 $g \cdot kg^{-1} \cdot d^{-1}$ of the drug solution by gavage, respectively, while the control group received an equal volume of normal saline by gavage, once daily. After 14 days of administration, the xenograft tumor weight was measured to calculate the tumor inhibition rate, hematoxylin-eosin (HE) staining and immunohistochemical analysis of xenograft tumor tissues were performed, the generation of adenosine triphosphate (ATP) and lactate in xenograft tumor tissues was detected by micro-method, and the expression of hexokinase 2 (HK2) and lactate dehydrogenase A (LDHA) mRNA in xenograft tumor tissues was detected by real-time fluorescence quantitative polymerase chain reaction (RT-qPCR). Network pharmacology was used to analyze the key targets and pathways through which Jiawei Qifang Weitong Granules regulate glycolysis

in gastric cancer cells, and Western Blot was used to detect changes in the expression of PI3K/AKT/HIF-1α pathway-related proteins.

After 14 days of intervention, the xenograft tumor mass in the low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups was lower than that in the control group ($P<0.05$), with tumor inhibition rates of 11.90%, 33.61%, and 52.70%, respectively; HE staining showed varying degrees of tumor cell necrosis and nuclear fragmentation in the low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups compared with the control group; immunohistochemical results showed that the protein expression of glucose transporter 1 (GLUT1) and 6-phosphofructokinase 1 (PFK1) in xenograft tumors of the low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups was lower than that in the control group ($P<0.05$); micro-method and RT-qPCR detection results showed that the generation of ATP and lactate and the expression of HK2 and LDHA mRNA in xenograft tumors of the low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups were lower than those in the control group ($P<0.05$); network pharmacology analysis showed that the PI3K/AKT/HIF-1α signaling pathway was closely related to the regulation of glycolysis in gastric cancer cells by Jiawei Qifang Weitong Granules, and Western blot results showed that the p-PI3K/PI3K protein ratio and HIF-1α protein expression in xenograft tumor tissues of the low-, medium-, and high-dose Jiawei Qifang Weitong Granules groups were lower than those in the control group ($P<0.05$).

Jiawei Qifang Weitong Granules can inhibit the growth of xenograft tumors in HGC-27 tumor-bearing nude mice, and its mechanism is related to the inhibition of PI3K/AKT/HIF-1α pathway activation, reduction of GLUT1, PFK1, HK2, and LDHA expression, decrease in ATP and lactate generation, and regulation of glycolysis.

Full Text

Introduction

Gastric cancer (GC) is one of the most common malignant tumors of the digestive tract, with complex pathogenesis and limited therapeutic options. Helicobacter pylori infection is considered a major risk factor for its development [1]. According to global statistics, there were 968,350 new cases (4.9%) and 659,853 deaths (4.9%) from gastric cancer in 2022, ranking fifth in both incidence and mortality worldwide. Despite advances in chemotherapy, targeted therapy, and immune checkpoint inhibitors that have reduced overall incidence and mortality, the prognosis remains poor due to the insidious onset of the disease and drug resistance. The global burden of gastric cancer is projected to increase by 62% by 2040 [2], making the search for novel therapeutic approaches an urgent clinical priority.

Tumor metabolic reprogramming is recognized as a key characteristic of gastric cancer development. Studies show that gastric cancer cells rely on glycolysis

to meet their energy demands regardless of oxygen availability, a phenomenon known as the Warburg effect [3-4]. As an inefficient energy production method, glycolysis allows tumor cells to competitively consume large amounts of glucose for growth while producing metabolites such as lactate and CO_2 that cause accumulation and acidification in the tumor microenvironment, facilitating proliferation, invasion, and migration of tumor cells including gastric cancer cells [5] and significantly affecting anti-tumor immune responses [6-7].

Traditional Chinese Medicine (TCM) can inhibit gastric cancer cell proliferation and overcome drug resistance by regulating glycolysis [8-9]. Professor Luo Weisheng, drawing on decades of clinical experience treating spleen and stomach diseases, formulated Modified Qifang Weitong Granules by recombining seven classical formulas including Danshen Drink, Four Gentlemen Decoction, and Free and Easy Wanderer Powder according to syndrome weighting [10]. This formula combines cold and warm properties, tonification and purgation, promoting blood circulation to relieve pain, soothing liver qi to relieve depression, and strengthening qi to support the spleen, supplemented with ingredients that eliminate masses and disperse stagnation. Our previous research found that Modified Qifang Weitong Granules can block the "inflammation-cancer transformation" process in the stomach [11] and inhibit gastric cancer cell proliferation, invasion, and migration while promoting apoptosis through multiple targets and pathways [10]. However, its effects on gastric cancer cell glycolysis remain unclear. This study employed network pharmacology and constructed an HGC-27 tumor-bearing nude mouse model to observe the pharmacological effects of Modified Qifang Weitong Granules against gastric cancer and its influence on glycolysis, analyzing relevant targets and mechanisms to provide theoretical support for clinical application.

Materials and Methods

Study Timeline and Ethical Approval

This study was conducted from March 2024 to June 2025 and approved by the Guangxi University of Chinese Medicine Ethics Committee (Approval No.: DW20240507-091).

Cells and Experimental Animals

The human gastric cancer cell line HGC-27 was purchased from Wuhan Procell Life Technology Co., Ltd. (Catalog No.: CL-0107). Four-week-old male Balb/c nude mice weighing 20$±2gweresuppliedbyHunanSlackJingdaCompany(LicenseNo.:SCXK(Xiang)2019−0004)andhousedattheGuangxiUniversityofChineseMedicineLaboratoryAnimalCenteSYXK(Gui)2024 − 0004)at24±$1°C with 50-60% relative humidity, 12-hour light/dark cycles, and ad libitum access to food and water.

Reagents and Drugs

Modified Qifang Weitong Granules contain: Red Ginseng 10g, Poria 10g, Stir-fried Atractylodes Macrocephala 10g, Honey-fried Licorice 9g, Coptis 6g, Auckland 6g, Processed Evodia 3g, Aurantium Immaturus 6g, Astragalus 30g, Polygonatum 6g, Trichosanthes Peel 20g, Trichosanthes Root 10g, White Peony 30g, Salvia 10g, Stir-fried Chicken Gizzard Lining 9g, Sparganium 15g, Curcuma Zedoaria 15g, Oldenlandia Diffusa 20g, and Pinellia 10g, all purchased from Jiangyin Tianjiang Pharmaceutical Co., Ltd. (various batch numbers). HGC-27 cell-specific culture medium, BCA protein assay kit, protease and phosphatase inhibitors, trypsin-EDTA solution, ATP detection kit, lactate detection kit, SDS-PAGE loading buffer, rapid blocking solution, primary and secondary antibody diluents, RIPA lysis buffer, PAGE gel kit, rapid transfer buffer, rapid electrophoresis buffer, ECL reagent, PI3K antibody, AKT antibody, p-PI3K antibody, p-AKT antibody, HIF-1α antibody, Taq SYBR Green qPCR Premix, and ALL-in-One First-Strand Synthesis MasterMix were obtained from various commercial sources as detailed in the original methods.

Experimental Instruments

Key equipment included vertical electrophoresis and transfer systems (Wuhan Servicebio Technology Co., Ltd., Models: SVE-2, SVT-2), chemiluminescence gel imaging system (Shanghai Qinxiang Scientific Instrument Co., Ltd., Model: ChemiScope6100), CO_2 incubator (PHCbi, Model: MCO-18AC), flow cytometer (Thermo Fisher Scientific, Model: Attune NxT), cryogenic high-throughput tissue homogenizer (Ningbo Xinzhi Biotechnology Co., Ltd., Model: Scientz-48L), high-speed refrigerated centrifuge (Eppendorf, Model: 5424R), electrophoresis power supply (Beijing Liuyi Instrument Factory, Model: DYY-6C), bioanalyzer (Agilent, Model: 5300), fluorometer (Thermo Fisher Scientific, Model: Qubit 4.0), and PCR thermal cycler (Bio-Rad, Model: T100).

Cell Culture and Tumor Model Establishment

HGC-27 cells were cultured in RPMI-1640 medium containing 10% fetal bovine serum and 1% penicillin-streptomycin at 37°C in a 5% CO_2 incubator. Cells at 80% confluence were passaged, and passages 3-5 were used for experiments. For tumor modeling, logarithmic-phase HGC-27 cells were prepared as a 1$×10^{7}$/ml suspension and mixed 1:1 with Matrigel matrix (0.1 ml each) before subcutaneous inoculation (0.2 ml/mouse) into the right lower limb of nude mice under sterile conditions. Successful modeling was confirmed when stable tumor masses were palpable upon weekly examination.

Grouping and Drug Administration

Forty successfully modeled tumor-bearing mice were randomly divided into four groups (n=10 each): control group, low-dose, medium-dose, and high-dose Mod-

ified Qifang Weitong Granules groups. Drug doses were calculated according to *Pharmacological Experimental Methodology* [12] with the medium dose equivalent to the clinical dose (30.55 $g \cdot kg^{-1} \cdot d^{-1}$), establishing low (15.28 $g \cdot kg^{-1} \cdot d^{-1}$), medium (30.55 $g \cdot kg^{-1} \cdot d^{-1}$), and high (61.1 $g \cdot kg^{-1} \cdot d^{-1}$) dose groups. Granules were dissolved in saline to prepare a 2 g/ml solution for gavage administration once daily for 14 days. The control group received equal volumes of saline. All granules were from the same batch.

Tumor Suppression Rate Measurement

After 14 days of treatment, mice were anesthetized and tumor tissues were excised, rinsed, and weighed. Tumor suppression rate was calculated as: (average tumor weight of model group - tumor weight of treatment group) / average tumor weight of model group × 100% [13].

Histopathological and Molecular Analyses

Hematoxylin-Eosin (HE) Staining: Tumor tissues were fixed in 4% paraformaldehyde, dehydrated, embedded, sectioned, and stained with HE for histopathological examination.

Immunohistochemistry: Sections were deparaffinized, subjected to antigen retrieval, blocked with 3% H_2O_2, and incubated overnight at 4°C with primary antibodies against GLUT1 and PFK1. After incubation with goat anti-rabbit IgG secondary antibody and DAB chromogen development, sections were counterstained with hematoxylin and examined microscopically. Positive area ratios were analyzed using ImageJ software.

ATP and Lactate Measurement: Tumor tissues were homogenized on ice, centrifuged, and supernatants were assayed for ATP and lactate content using commercial kits according to manufacturer instructions.

RT-qPCR Analysis: Total RNA was extracted from tumor tissues and reverse-transcribed using a 20 L reaction system (37°C for 2 min, 55°C for 15 min, 85°C for 5 min). PCR was performed in 20 L volumes with the following program: 95°C for 30 s, followed by 40 cycles of 95°C for 3 s and 60°C for 30 s, with a melting curve analysis. Relative mRNA expression was calculated using the 2^(-ΔΔCt) method with GAPDH as internal control. Primer sequences were: HK2 (forward: 5' -AAGGCCATCCAGAGGAGAGG-3' , reverse: 5' -GCCTTCCACCATGTCGATGT-3' , 180 bp); LDHA (forward: 5' -AACTGAAAACTCCAAGCTGGT-3', reverse: 5'-TCTTCCAAGCCACGTAGGTC-3' , 194 bp); GAPDH (forward: 5' -GGCTGCCCAGAACATCAT-3' , reverse: 5' -CGGACACATTGGGGGTAG-3' , 122 bp).

Network Pharmacology Analysis: Active ingredients were screened from TCMSP (oral bioavailability $ $30%, drug-likeness $ $0.18), ETCM (Drug-likeness Grading=Moderate or Good), HERB, and HIT databases. Targets for ingredients not in TCMSP were predicted using SwissTargetPrediction (proba-

bility $ $10%). Standardized gene names were obtained from UniProt. Gastric cancer-related targets were retrieved from GeneCards (Score $ 2×$median), OMIM, and Therapeutic Target Database using "gastric cancer" and "stomach neoplasms" keywords. Glycolysis-related targets were obtained from Coremine Medical. Intersection targets were identified using Venn diagrams. PPI networks were constructed using STRING 11.5 (Homo sapiens) and analyzed in Cytoscape 3.10.2 to identify core targets. GO and KEGG enrichment analyses were performed using Metascape ($P<0.05$) and visualized.

Western Blot Analysis: Tumor tissues were homogenized at low temperature, centrifuged, and protein concentrations were determined. Samples were separated by SDS-PAGE (160 V) and transferred to membranes (300 mA, 30 min). After blocking, membranes were incubated overnight at 4°C with primary antibodies against PI3K, AKT, p-PI3K, p-AKT, and HIF-1α, followed by HRP-conjugated secondary antibody and ECL detection. Protein bands were quantified using ImageJ.

Statistical Analysis

Data were processed using GraphPad Prism 9. All measurement data were normally distributed and expressed as mean ± standard deviation ($\bar{x}\pm s$). Intergroup comparisons were performed using one-way ANOVA. $P<0.05$ was considered statistically significant.

Results

Tumor Growth Inhibition

After modeling, nude mice showed reduced activity and lethargy. Following treatment, mice in the low-, medium-, and high-dose groups exhibited better mental status and higher activity compared to controls. After 14 days of intervention, significant differences in transplanted tumor mass were observed among the four groups ($F=74.64$, $P<0.001$). Tumor weights in all treatment groups were lower than in the control group ($P<0.05$), with tumor suppression rates of 11.90%, 33.61%, and 52.70% for low-, medium-, and high-dose groups, respectively .

Histopathological Changes

HE staining revealed tightly packed tumor cells with high nuclear-cytoplasmic ratios, nuclear atypia, and frequent pathological mitotic figures in the control group, indicating rapid proliferation. In contrast, treatment groups showed varying degrees of tumor cell necrosis and nuclear fragmentation, with the extent increasing dose-dependently. The high-dose group exhibited the most significant tumor necrosis [Figure 1: see original paper].

Glycolytic Protein Expression

Immunohistochemistry showed high GLUT1 and PFK1 protein expression (brown-yellow staining) in the control and low-dose groups, while medium- and high-dose groups displayed lower expression (light yellow staining). Significant differences were observed among groups ($P<0.001$), with all treatment groups showing reduced GLUT1 and PFK1 levels compared to controls ($P<0.05$) [Figure 2: see original paper], .

ATP and Lactate Production

ATP and lactate generation in tumor tissues differed significantly among groups ($P<0.001$). All treatment groups exhibited reduced glycolytic products compared to controls ($P<0.05$), with more pronounced reductions at higher doses .

Glycolytic Enzyme mRNA Expression

RT-qPCR analysis revealed significant differences in HK2 and LDHA mRNA expression among groups ($P<0.001$). Medium- and high-dose groups showed significantly lower expression than controls ($P<0.05$) .

Network Pharmacology Results

Target Screening: A total of 441 active ingredients were initially identified from databases, yielding 394 unique components after removing duplicates. These corresponded to 8,136 target genes, which were standardized to 985 valid targets. Gastric cancer-related genes (1,134) and glycolysis-related genes (6,819) were retrieved, resulting in 98 intersection targets after Venn analysis [Figure 3: see original paper].

PPI Network Construction: The PPI network contained 98 nodes and 2,332 edges. Core targets identified by Cytohubba included TP53, STAT3, AKT1, EGFR, CTNNB1, MYC, SRC, JUN, IL6, and BCL2, suggesting these as key nodes for the granules' intervention in gastric cancer glycolysis [Figure 4: see original paper].

Enrichment Analysis: GO analysis revealed 670 biological processes (e.g., insulin-like growth factor receptor signaling, MAPK cascade regulation, cell proliferation), 152 molecular functions (e.g., protein binding, tyrosine kinase activity), and 77 cellular components. KEGG analysis identified 165 pathways including cancer pathways, PI3K-AKT signaling, and HIF-1 signaling pathway [Figure 5: see original paper].

PI3K/AKT/HIF-1α Pathway Inhibition

Western blot analysis showed significant differences in p-PI3K/PI3K, p-AKT/AKT, and HIF-1α protein levels among groups ($P<0.001$). All treatment

groups had reduced p-PI3K/PI3K and HIF-1α compared to controls ($P<0.05$). The p-AKT/AKT ratio was significantly decreased in medium- and high-dose groups ($P<0.05$) but not in the low-dose group ($P>0.05$) , [Figure 6: see original paper].

Discussion

Gastric cancer' s complex pathogenesis and limited treatment options necessitate novel therapeutic strategies. Tumor metabolic reprogramming, particularly the Warburg effect, promotes proliferation and creates an immunosuppressive microenvironment [14], making metabolic intervention a promising approach. In TCM theory, gastric cancer corresponds to conditions like "Fu Liang," "Ye Ge,""Zheng Jia,"and "Ji Ju,"with core pathogenesis of spleen-stomach deficiency and accumulation of phlegm, toxins, and stasis characterized by "root deficiency and branch excess" [15]. Modified Qifang Weitong Granules, derived from seven classical formulas [10], addresses both root and branch aspects through multiple actions: Red Ginseng, Astragalus, Atractylodes, Poria, Honey-fried Licorice, and Polygonatum strengthen the spleen and boost qi to support the "deficient root" ; Sparganium, Curcuma Zedoaria, Salvia, Aurantium Immaturus, Aucklandia, and Chicken Gizzard Lining promote qi and blood circulation to resolve masses; Oldenlandia Diffusa, Coptis, Trichosanthes Root clear heat and detoxify; Pinellia and Trichosanthes Peel resolve phlegm and disperse nodules; Evodia, Coptis, White Peony, and Pinellia harmonize liver-stomach and relieve nausea. This comprehensive approach treats both root and branch simultaneously.

Our previous in vitro studies demonstrated multi-target inhibition of gastric cancer cells by this formula [10]. The current in vivo study confirmed significant, dose-dependent tumor growth inhibition in HGC-27 xenograft models, consistent with our earlier findings. HE staining revealed dose-dependent increases in tumor necrosis and nuclear fragmentation. Moreover, treatment significantly reduced glycolytic markers including GLUT1, PFK1, HK2, LDHA, ATP, and lactate, confirming the formula' s ability to suppress glycolysis.

Network pharmacology identified 394 active components targeting 985 genes, with 98 core intersection targets related to both gastric cancer and glycolysis. The PPI network highlighted TP53, STAT3, AKT1, EGFR, CTNNB1, MYC, SRC, JUN, IL6, and BCL2 as key targets. Enrichment analysis revealed the PI3K/AKT/HIF-1α pathway as a critical signaling axis. The PI3K/AKT/HIF-1α pathway regulates multiple cancer processes including cell cycle, growth, proliferation, metastasis, apoptosis, and autophagy [18], and its dysregulation is closely linked to tumor glycolysis [19-20]. Our Western blot results confirmed that Modified Qifang Weitong Granules reduced p-PI3K/PI3K, p-AKT/AKT ratios and HIF-1α protein expression, thereby inhibiting this pathway.

This study has limitations. We only observed the inhibitory effects on tumor proliferation and glycolysis without identifying specific component-target relationships, and lacked in vitro validation. Future studies will employ high-

performance liquid chromatography to identify active components and conduct comprehensive cellular experiments to clarify mechanisms.

In conclusion, Modified Qifang Weitong Granules inhibit HGC-27 xenograft growth by suppressing the PI3K/AKT/HIF-1α pathway, downregulating GLUT1, PFK1, HK2, and LDHA expression, reducing ATP and lactate production, and modulating glycolysis. These findings enrich the scientific understanding of TCM "metabolic regulation" in cancer and provide a theoretical basis for clinical application.

References

[1] BRAY F, LAUVERSANNE M, SUNG H, et al. Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [J]. CA Cancer J Clin, 2024, 74(3): 229-263. DOI: 10.3322/caac.21834.

[2] THRIFT A P, WENKER T N, EL-SERAG H B. Global burden of gastric cancer: epidemiological trends, risk factors, screening and prevention [J]. Nat Rev Clin Oncol, 2023, 20(5): 338-349. DOI: 10.1038/s41571-023-00747-0.

[3] VAUPEL P, SCHMIDBERGER H, MAYER A. The Warburg effect: essential part of metabolic reprogramming and central contributor to cancer progression [J]. Int J Radiat Biol, 2019, 95(7): 912-919. DOI: 10.1080/09553002.2019.1589653.

[4] COURTNAY R, NGO D C, MALIK N, et al. Cancer metabolism and the Warburg effect: the role of HIF-1 and PI3K [J]. Mol Biol Rep, 2015, 42(4): 841-851. DOI: 10.1007/s11033-015-3858-x.

[5] CHEN S H, CAO G D, WU W, et al. Mining novel cell glycolysis related gene markers that can predict the survival of colon adenocarcinoma patients [J]. Biosci Rep, 2020, 40(8): BSR20201427. DOI: 10.1042/BSR20201427.

[6] HUSAIN Z, SETH P, SUKHATME V P. Tumor-derived lactate and myeloid-derived suppressor cells: Linking metabolism to cancer immunology [J]. Oncoimmunology, 2013, 2(11): e26383. DOI: 10.4161/onci.26383.

[7] XIA L Z, OYANG L, LIN J G, et al. The cancer metabolic reprogramming and immune response [J]. Mol Cancer, 2021, 20(1): 28. DOI: 10.1186/s12943-021-01316-8.

[8] Tao HY, Liu YJ, Li JP, et al. Effects of Jianpi Yangzheng Xiaozheng Decoction on proliferation and stem cell characteristics of gastric cancer HGC-27 cells by inhibiting aerobic glycolysis [J]. Chinese Journal of Experimental Traditional Medical Formulae, 2023, 29(11): 82-88. DOI: 10.13422/j.cnki.syfjx.202202421.

[9] Cheng FE, Li Z, Liu CY, et al. Study on the effect and mechanism of Compound Xiyi Powder in regulating glycolysis to reduce cisplatin resistance in gastric cancer [J]. China Pharmacy, 2024, 35(10): 1421-1431. DOI:

10.16438/j.0513-4870.2024-1136.

[10] Xiong CZ, Chen XY, Wang T, et al. Research progress on the mechanism and signaling pathways of Qifang Weitong Granules in treating gastric cancer [J]. Chinese Journal of Medicinal Guide, 2024, 26(11): 1251-1257.

[11] Xiong CZ, Gu WS, Fang YJ, et al. Exploration of the mechanism of Modified Qifang Weitong Granules against chronic atrophic gastritis based on transcriptomics and proteomics [J]. Lishizhen Medicine and Materia Medica Research, 2025, 36(04): 601-608.

[12] Wei W, Wu XM, Li YJ. Pharmacological Experimental Methodology [M]. 4th ed. Beijing: People' s Medical Publishing House, 2010: 69-73.

[13] Gan P, Tan YH, Jin WH, et al. Inhibitory activity of CJ016 on human lung cancer xenografts in nude mice [J]. Chinese Pharmacological Bulletin, 2017, 33(3): 384-388. DOI: 10.3969/j.issn.1001-1978.2017.03.018.

[14] Li YT, Li WB, Zhang YJ, et al. Study on anti-gastric cancer effect of 2' ,4' -dimethoxychalcone inhibiting c-Myc-mediated glucose uptake and glycolysis [J]. Acta Pharmaceutica Sinica, 2025, (05): 1251-1257. DOI: 10.13863/j.issn1001-4454.2025.05.030.

[15] Jiang Y. Summary of National TCM Master Liu Jiaxiang' s clinical experience in treating gastric cancer [J/OL]. Liaoning Journal of Traditional Chinese Medicine, [2025-08-13]. https://link.cnki.net/urlid/21.1128.R.20250717.0913.010.

[16] (Qing) Gao SZ. Direct Explanation of Huangdi Neijing Suwen [M]. Sun GZ, Fang XH, collated. Beijing: Xueyuan Press, 2001: 230.

[17] Li Z, Liu CY, Zhang ZY, et al. Study on the effect of Eremias multiocellata in inhibiting cisplatin resistance in gastric cancer by regulating glycolysis through Akt/mTOR pathway [J]. Journal of Chinese Medicinal Materials, 2025, (05): 1251-1257. DOI: 10.13863/j.issn1001-4454.2025.05.030.

[18] MORGOS D T, STEFANI C, MIRICESCU D, et al. Targeting PI3K/AKT/mTOR and MAPK signaling pathways in gastric cancer [J]. Int J Mol Sci, 2024, 25(3): 1848. DOI: 10.3390/ijms25031848.

[19] Ma L, Yang YP, Bai M, et al. Exploration of the mechanism of Shenqi Yiliu Formula in reversing cisplatin resistance in ovarian cancer cells through PI3K/Akt/mTOR-regulated glycolysis [J/OL]. Chinese Journal of Experimental Traditional Medical Formulae, 1-13 [2025-08-11]. https://doi.org/10.13422/j.cnki.syfjx.20251121.

[20] Wen RJ, Dong X, Mai YX, et al. Taohong Siwu Decoction inhibits osteosarcoma proliferation and migration through PI3K/AKT/HIF-1α pathway-mediated glycolysis [J]. China Journal of Traditional Chinese Medicine and Pharmacy, 2024, 39(07): 3705-3710.

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