The Multidimensional Role and Molecular Mechanisms of Traditional Chinese Medicine in Adjuvant Therapy for Breast Cancer: Current Research Status

Hailin Zhang[1], Zhi Li[2,*]

[1] Shaanxi University of Chinese Medicine, Xianyang 712046, Shaanxi, China

[2] Department of Surgery, Xi'an Hospital of Traditional Chinese Medicine, Xi'an 710000, Shanxi, China

Abstract: Breast cancer is the most common malignancy among women worldwide, with incidence rates continuing to rise and a trend toward younger onset. As an important component of comprehensive breast cancer treatment, Traditional Chinese Medicine (TCM) plays a unique role in "enhancing efficacy and reducing toxicity" in adjuvant therapy. This article systematically reviews recent research progress on TCM in the adjuvant treatment of breast cancer. It summarizes the mechanisms of active ingredients and compound formulas from multiple dimensions, including the regulation of tumor cell apoptosis, intervention in key signaling pathways, modulation of metabolic reprogramming, improvement of the immune microenvironment, and reversal of endocrine resistance. Furthermore, combined with evidence-based medical evidence, the clinical value of TCM in conjunction with chemotherapy and endocrine therapy is analyzed. Research indicates that through a holistic regulatory mechanism involving multiple targets and pathways, TCM offers significant advantages in improving therapeutic efficacy, reducing adverse reactions, and enhancing quality of life. However, systematic elucidation of its mechanisms and the generation of high-quality clinical evidence still require further exploration.

***Keywords*:** breast cancer; traditional Chinese medicine; adjuvant therapy; molecular mechanism; signaling pathway; evidence-based medicine

1. Introduction

Breast cancer is the most common malignancy among women globally, with approximately 2.3 million new cases and 660,000 deaths in 2022. In China, incidence continues to rise with a trend toward younger onset. Current treatments include surgery, chemotherapy, radiotherapy, endocrine therapy, and targeted therapy. Although these improve survival, adverse effects such as bone marrow suppression, nausea, cardiotoxicity, and endocrine-related symptoms often impair treatment adherence and quality of life.

TCM has accumulated rich experience in oncology. Modern research shows that through multi-target, multi-pathway regulation, TCM offers advantages in inhibiting tumor growth, reversing drug resistance, alleviating adverse reactions, and improving quality of life. This article reviews the multidimensional role and molecular mechanisms of TCM in adjuvant breast cancer therapy.

2. Clinical Evidence for TCM in Adjuvant Breast Cancer Therapy

The clinical value of TCM in adjuvant breast cancer therapy has been preliminarily validated. A meta-analysis of 22 randomized controlled trials involving 1,834 postoperative breast cancer patients showed that TCM combined with chemotherapy significantly improved clinical efficacy, enhanced immune function, and reduced adverse reactions compared with chemotherapy alone[1]. Levels of $CD3^+$, $CD4^+$ T cells, and the $CD4^+/CD8^+$ ratio were significantly higher in the combination group, while the incidence of leukopenia and thrombocytopenia was significantly reduced ($P < 0.05$).

Several oral Chinese patent medicines in the National Medical Insurance Catalog are widely used in adjuvant therapy. Lai Baoyong et al. reviewed anti-tumor oral Chinese patent medicines and found that Xihuang Pill, Compound Kushen Injection, Aidi Injection, and Jinlong Capsule show good efficacy and safety[2]. Among these, Xihuang Pill has a unique effect in alleviating cancer-related fatigue, potentially through regulation of inflammatory factors and energy metabolism.

3. Molecular Mechanisms of Active TCM Ingredients Against Breast Cancer

3.1 Induction of Tumor Cell Apoptosis

Inducing apoptosis is a core mechanism of TCM against tumors. Erianin, a component from Dendrobium, has gained attention in triple-negative breast cancer research. It enhances sensitivity to death signals by activating intrinsic and extrinsic

apoptotic pathways, inducing mitochondrial dysfunction, promoting cytochrome c release, and activating caspase-dependent pathways[3]. Erianin regulates the Bax/Bcl-2 ratio, reshapes apoptotic networks, and overcomes drug resistance. It also modulates PI3K/Akt, MAPK, and NFATc1 pathways.

3.2 Intervention in Key Signaling Pathways

The Wnt/β-catenin pathway is crucial in breast cancer, linked to stem cell maintenance, epithelial-mesenchymal transition, and chemotherapy resistance. Ling Lu et al. reviewed 44 TCM monomers, one single herb, one herb pair, and eight compound formulas that exert anti-breast cancer effects via this pathway[4]. Terpenoids, flavonoids, phenolic compounds, and alkaloids inhibit proliferation and metastasis by suppressing β-catenin nuclear translocation and downregulating c-Myc and Cyclin D1. Xihuang Pill, Liuwei Dihuang Pill, and Huangqi Jiedu Decoction also act through this pathway.

3.3 Regulation of Metabolic Reprogramming

Metabolic reprogramming, including the Warburg effect, is a cancer hallmark. Wu Hui et al. reviewed that TCM components inhibit breast cancer proliferation and induce apoptosis by regulating enzymes in glucose, lipid, and amino acid metabolism. Some TCMs reduce glucose uptake and lactate production by inhibiting HK2 and PKM2. In lipid metabolism, they regulate FASN and ACC, interfering with lipid synthesis. Current research focuses mainly on glucose metabolism; lipid and amino acid mechanisms require further study[5].

3.4 Improvement of the Tumor Immune Microenvironment

The tumor immune microenvironment is critical in breast cancer. TCM regulates immune cell function to strengthen vital qi and eliminate pathogens. TCM combined with chemotherapy increases $CD3^+$ and $CD4^+$ T cells, reduces Tregs, and enhances anti-tumor immunity. Compound Kushen Injection and Aidi Injection enhance NK cell activity and promote IL-2 and IFN-γ secretion. Active ingredients like *Ganoderma* and *Astragalus* polysaccharides activate TLR pathways, promote dendritic cell maturation, and initiate adaptive immune responses[6].

4. Synergistic Effects of TCM in Different Stages of Breast Cancer Treatment

4.1 Combined with Chemotherapy: Enhancing Efficacy and Reducing Toxicity

Chemotherapy is an important adjuvant treatment for postoperative breast cancer, but its side effects often limit clinical application. TCM combined with chemotherapy can exert a "synergistic and toxicity-reducing" effect. Meta-analyses indicate that the combination of TCM and chemotherapy yields significantly higher clinical efficacy and better immune function improvement compared to chemotherapy alone, with a significantly lower incidence of adverse reactions such as leukopenia and thrombocytopenia. For instance, Fuzheng Xiaoliu Decoction combined with chemotherapy can significantly improve patients' quality of life and reduce the incidence of nausea, vomiting, and bone marrow suppression[7]. The mechanisms may be related to TCM's ability to alleviate chemotherapy-induced oxidative stress damage, promote hematopoietic stem cell recovery, and regulate the balance of the gut microbiota.

4.2 Combined with Endocrine Therapy: Reversing Drug Resistance

Endocrine therapy is a crucial treatment for hormone receptor-positive breast cancer, but drug resistance significantly affects efficacy. TCM shows potential in reversing endocrine resistance. Liu Jialing's study found that syndrome-differentiated TCM combined with endocrine therapy could regulate estradiol (E_2) levels in patients with estrogen receptor-positive breast cancer and alleviate endocrine therapy-related symptoms such as hot flashes and joint pain[8]. Some TCM compound formulas, such as Erxian Decoction and Guipi Decoction, can enhance endocrine therapy sensitivity by modulating the PI3K/Akt/mTOR signaling pathway and inhibiting ER phosphorylation[9]. Additionally, active TCM ingredients like curcumin and resveratrol can reverse tamoxifen resistance by inhibiting the expression of ERα co-activators.

4.3 Alleviating Cancer-Related Fatigue

Cancer-related fatigue is one of the most common accompanying symptoms in breast cancer patients, severely impacting quality of life. Lai Baoyong et al. used network pharmacology to predict the potential targets of Xihuang Pill in treating breast cancer-related fatigue, finding that it may act through regulating inflammatory factors (e.g., TNF-α, IL-6), neuroendocrine factors, and energy metabolism-related pathways. Animal experiments further confirmed that Xihuang Pill significantly improved fatigue-related behavior in tumor-bearing mice, reduced serum inflammatory factor levels, and potentially exerted its effects by regulating the hypothalamic-pituitary-adrenal axis function. Clinical studies have also shown that Xihuang Pill combined with conventional therapy effectively alleviates fatigue symptoms in breast cancer patients and improves quality of life.

5. Challenges and Future Perspectives

Although TCM shows promising prospects in adjuvant breast cancer therapy, several challenges remain:

First, systematic elucidation of the mechanisms of TCM action is still insufficient. Current research mostly focuses on single herbs or active ingredients, lacking in-depth analysis of the overall network regulatory mechanisms underlying the multi-target, multi-pathway synergistic effects of TCM compound formulas. Future research should integrate systems biology, network pharmacology, and multi-omics technologies to construct a "component-target-pathway-disease" network map of TCM intervention in breast cancer, revealing its holistic regulatory principles.

Second, the quality of clinical research needs improvement. Most existing clinical trials are small-sample, single-center studies, and the randomization methods, allocation concealment, and blinding designs in randomized controlled trials are often not standardized, affecting the level of evidence. Future efforts should focus on conducting more rigorously designed, adequately powered multi-center randomized controlled trials and establishing efficacy evaluation systems tailored to TCM characteristics, incorporating patient-reported outcomes and quality of life as core indicators.

Third, the optimal model of integrated traditional Chinese and Western medicine is not yet clearly defined. Further exploration is needed to determine how to develop individualized integrated treatment plans based on patients' molecular subtypes, treatment stages, and constitutional characteristics[10]. Additionally, the interactions and potential risks between TCM and chemotherapeutic or targeted drugs require systematic assessment.

6. Conclusion

TCM plays a multidimensional, multi-target holistic regulatory role in the adjuvant treatment of breast cancer. Through mechanisms such as inducing apoptosis, modulating signaling pathways, intervening in metabolic reprogramming, and reshaping the immune microenvironment, active TCM ingredients and compound formulas can not only directly inhibit tumor growth but also enhance sensitivity to chemotherapy and endocrine therapy, alleviate treatment-related adverse reactions, and improve patients' quality of life. With the deepening integration of modern biotechnology and TCM research, the unique value of TCM in comprehensive breast cancer treatment will be further demonstrated, providing optimized therapeutic options for breast cancer patients.

References

[1] Traditional Chinese medicine combined with chemotherapy for breast cancer after operation: A systematic review and meta-analysis[J]. Medicine, 2024, 103(46): e40264.

[2] Lai BY. Evidence-based evaluation of oral Chinese patent medicines in breast cancer intervention and a study on the effect of Xihuang Pill on cancer-related fatigue in breast cancer [D]. Beijing University of Chinese Medicine, 2022.

[3] Li JS, Liu SS, Guo HW. Research progress on the mechanism of erianin-induced apoptosis in breast cancer cells and its therapeutic potential[J]. Journal of Practical Medicine, 2025, 41(14): 2132-2137.

[4] Ling L, Xu JY, Zhao JF, et al. Research progress on traditional Chinese medicine regulating the Wnt/β-catenin signaling pathway in breast cancer intervention[J]. Chinese Journal of Experimental Traditional Medical Formulae, 2025, 31(8): 320-330.

[5] Wu H, Lei YT, Yang Y, et al. Research progress on the mechanism of traditional Chinese medicine in improving breast cancer by regulating metabolic reprogramming[J]. China Pharmacy, 2026, 37(2): 250-256.

[6] Research progress on pharmacological mechanisms and clinical application of traditional Chinese medicine in breast cancer treatment[J]. Chinese Herbal Medicine, 2025(21): 7983-7994.

[7] Li M, Liang ZX, Li GN, et al. Research progress on traditional Chinese medicine in treating breast cancer[J]. Journal of Traditional Chinese Medicine, 2023(2).

[8] Liu JL. Effect of syndrome-differentiated Chinese medicine on estrogen levels in women with ER+/PR+ breast cancer [D]. Beijing University of Chinese Medicine, 2017.

[9] Song P, et al. Traditional Chinese medicine in the treatment of breast cancer[J]. Mol Cancer, 2025.

[10] Research progress on traditional Chinese medicine in the prevention and treatment of breast cancer[J]. Guiding Journal of Traditional Chinese Medicine and Pharmacy, 2019(23).