

# Study on Herb Pairs for Breast Cancer Treatment Based on the Seven Emotions Compatibility Theory

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**Abstract:** The Seven Emotions constitute the original principle of traditional Chinese medicine (TCM) compatibility. Herb pairs, as the smallest unit of compatibility, connect single herbs and formulas, and their theory embodies the core of formula composition. Based on the medicinal properties of TCM, this paper sorts out herb pairs for breast cancer from the perspectives of mutual reinforcement and mutual assistance, and analyses their mechanisms via network pharmacology, so as to provide ideas for exploring the clinical value of herb pairs.

**Keywords:** Seven emotions; Breast cancer; Herb pairs; Network pharmacology

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## 1. Introduction

In 2020, breast cancer became the leading cause of cancer death among women worldwide. Its incidence in China has been rising year by year, accompanied by high recurrence rate, frequent drug resistance and numerous adverse reactions, which severely impair patients' quality of life. The core of TCM treatment for breast cancer is to regulate the "cancer state", achieve survival with tumor, and improve the body's microenvironment, rather than directly killing cancer cells.

Ancient TCM terms such as *ru yan* (breast rock), *shi yong* (stony abscess) and *fan hua shi liu* (blossoming pomegranate sore) correspond to modern breast cancer. Modern TCM holds that breast cancer is rooted in visceral deficiency and insufficient Qi and blood, marked by Qi stagnation, phlegm turbidity, blood stasis and heat-toxin, presenting a pathogenesis of intermingled deficiency and excess with mutual transformation. Treatment follows the principles of syndrome differentiation, holistic concept and Yin-Yang balance, with strengthening healthy Qi and eliminating pathogens as the core, and is implemented in stages: in the early stage with phlegm-stasis-toxin binding, eliminating pathogens is prioritized; after surgery, radiotherapy,

chemotherapy or in the metastatic stage, strengthening healthy Qi is essential.

Herb pairs are the smallest unit of TCM compatibility, a characteristic of TCM diagnosis and treatment, reflecting the pertinence and flexibility of syndrome-based treatment. Their compatibility takes “seeking by Qi and flavor” as the theoretical origin, aims at increasing efficacy and reducing toxicity, and relies on medicinal property theory and treatment thinking based on syndrome differentiation.

The Seven Emotions are the earliest criteria for TCM compatibility. Mutual reinforcement and mutual assistance can achieve synergistic efficacy enhancement, while mutual inhibition and mutual antagonism are contraindicated. Thus, herb pairs are mainly selected based on mutual reinforcement and mutual assistance<sup>[1]</sup>. Mutual reinforcement refers to the combination of herbs with similar effects to strengthen efficacy; mutual assistance means herbs cooperate to improve therapeutic effects. Modern herb pair compatibility follows a clear sovereign-vassal order. Summarizing breast cancer herb pairs based on the Seven Emotions and analyzing their mechanisms can provide evidence for clinical application.

## **2. Mutual reinforcement herb pairs of heat-clearing and detoxifying herbs**

The main causes of breast cancer are “latent toxin from six exogenous pathogens” and “depressive toxin from seven emotions”, leading to “endogenous cancer toxin”. The key pathogenesis after surgery is “uncleared residual toxin”, while recurrence and metastasis result from “spread of residual toxin”. Studies have found that heat-toxin accumulation is a common syndrome of breast cancer with high malignancy, which is insensitive to chemotherapy, endocrine therapy and molecular targeted therapy, making TCM the main treatment. Therefore, mutual reinforcement herb pairs of heat-clearing and detoxifying herbs are widely used in clinical practice.

### **2.1. Dandelion (Pugongying)–Selfheal (Xiakucao)**

*Compendium of Materia Medica* records: “For initial mammary abscess: equal parts of dandelion and selfheal, decocted with wine”. The combination clears heat and detoxifies, purges liver fire, and reduces swelling and masses, and is now widely used in tumor treatment. *New Revised Materia Medica* states dandelion treats women’s mammary abscess, which resolves when boiled in water. Studies show that dandelion-selfheal at a 4:3 ratio has strong anti-proliferative activity against breast cancer cells without obvious toxicity to normal mammary epithelial cells, and can intervene in breast cancer by regulating cell metabolism and apoptosis<sup>[2]</sup>.

### **2.2. *Cremastra Pseudobulbus* (Shancigu)–Uniflower Swisscentaury Root (Loulu)**

*Cremastra pseudobulbus* is cool-natured, sweet and slightly pungent in flavor, acting on the liver and spleen meridians; it clears heat, detoxifies, dissipates phlegm and reduces masses. Uniflower swisscentaury root is cold-natured, bitter in flavor, acting on the stomach meridian; it detoxifies, dissipates masses and treats abscesses. Their mutual reinforcement combination enhances the effects of clearing heat, detoxifying, dissipating stasis, reducing swelling, resisting tumors and diminishing inflammation. The clinical dosage is usually 12–15 g for *Cremastra pseudobulbus* and 15–30 g for uniflower swisscentaury root<sup>[3]</sup>. Network pharmacology confirms that the ethanol extract of this herb pair inhibits the PI3K/Akt pathway to induce breast cancer cell apoptosis and control tumor progression.

### 2.3. Barbed Skullcap Herb (Banzhilian)–*Hedyotis Diffusa* (Baihuasheshecao)

Barbed skullcap herb is cold-natured, pungent and bitter in flavor, acting on the lung, liver and kidney meridians; it clears heat, detoxifies, removes stasis and reduces swelling. *Hedyotis diffusa* is cold-natured, bitter and sweet in flavor, acting on the heart, liver and spleen meridians; it clears heat, detoxifies, drains dampness and reduces swelling. Their mutual reinforcement combination is suitable for tumors with excessive heat-toxin, resisting cancer without impairing healthy Qi, and is applicable to postoperative or advanced patients with deficient healthy Qi to prevent recurrence and metastasis. Clinical dosage is 12–15 g for barbed skullcap herb and 15–30 g for *Hedyotis diffusa*<sup>[3]</sup>. The dosage can be increased to 60–120 g when tumor markers are elevated. This herb pair induces cell apoptosis, enhances immunity, inhibits proliferation, acts on MYC and CASP3 targets, and participates in transcriptional regulation<sup>[4,5]</sup>.

## 3. Mutual reinforcement herb pairs of blood-stasis-resolving herbs

*Lingshu-Bing Bai Ji Sheng* states: “When blood coagulates and accumulates without dispersing, body fluids seep stagnantly and adhere without leaving, leading to masses”. In TCM, cancer mostly arises from prolonged illness entering the collaterals, latent pathogenic toxin, and intractable blood stasis, leading to cancer toxin formation. Eliminating turbid pathogens and blood stasis, resolving phlegm and detoxifying are critical in treatment.

### 3.1. *Frankincense* (Ruxiang)–Myrrh (Moyao)

Both *Frankincense* and myrrh act on the liver, spleen and heart meridians. *Frankincense* regulates Qi, while myrrh enters blood; their mutual reinforcement combination treats both Qi and blood, and strengthens blood circulation and stasis resolution. *Complete Collection of Surgical Diseases* records their combination promotes pus discharge and wound healing, and they are the core compatibility of Xihuang Wan. The total dosage of this pair does not exceed 6 g; the 1:1 and 2:1 ratio yield the optimal dissolution of components, with the 1:1 ratio most widely used<sup>[6,7]</sup>. This herb pair regulates breast cancer-related microRNAs and the MAPK pathway, inhibits angiogenesis, invasion and metastasis, and improves chemosensitivity<sup>[8]</sup>.

### 3.2. Common Burreed Rhizome (Sanleng)–*Zedoary Turmeric* (Ezhu)

Both common burreed rhizome and *Zedoary turmeric* act on the liver and spleen meridians, dispersing cold, draining stagnation and unblocking collaterals, regulating both Qi and blood. They are derived from Sanleng Wan in *Experienced Prescriptions*. The clinical dosage for hyperplasia of mammary glands is 6–20 g at a 1:1 ratio; the 2:1 ratio achieves the highest dissolution of active components<sup>[9]</sup>. They induce tumor apoptosis and regulate the tumor microenvironment<sup>[10]</sup>. ESR1 is a key target for their anti-breast cancer effect, and its mutation causes endocrine therapy resistance<sup>[11]</sup>.

## 4. Mutual assistance herb pairs of other categories

### 4.1. *Astragalus membranaceus* (HuangQi)–*Zedoary Turmeric* (Ezhu)

Replenishing Qi and activating blood is a common tumor treatment. The astragalus-zedoary pair is derived from Lichong Tang in *Records of Traditional Chinese and Western Medicine*, primarily treating Qi deficiency and blood stasis at a 1:1 ratio in the original formula. *Astragalus* invigorates the spleen, replenishes Qi,

dissipates phlegm and resolves stasis; zedoary turmeric moves Qi, breaks blood, eliminates accumulation and relieves pain. Their combination replenishes Qi without stagnation and breaks blood without impairing healthy Qi. For severe Qi deficiency, 30–60 g of *Astragalus* is used; for severe blood stasis, 10–15 g of *Zedoary turmeric* is applied<sup>[11]</sup>. The 3:1 ratio shows the best anti-tumor and anti-angiogenesis effects<sup>[12]</sup>.

#### **4.2. *Cremastra Pseudobulbus* (Shancigu)–Thunberg Fritillary Bulb (Zhebeimu)**

Thunberg fritillary bulb is bitter and cold, clearing heat, resolving phlegm, dissipating masses and treating abscesses. *Cremastra pseudobulbus* is sweet, slightly pungent and cool, clearing heat, detoxifying, resolving phlegm and dissipating masses. Their combination disperses and drains with synergistic efficacy. The common component  $\beta$ -sitosterol inhibits the proliferation of breast cancer T47D cells<sup>[13]</sup>.

### **5. Discussion**

Herb pairs are a distinctive advantage of TCM treatment, reflecting the pertinence and flexibility of TCM syndrome differentiation. Proper compatibility achieves doubled results with half effort. For complex diseases like breast cancer, combining herb pairs with disease-specific formulas can resolve masses, detoxify and resist cancer, prevent recurrence and metastasis, and assist Western medicine to achieve optimal efficacy, providing new methods and ideas for breast cancer diagnosis and treatment worthy of further research and promotion.

However, the challenge of medication lies in herb selection and compatibility. Starting from TCM properties, this paper summarizes breast cancer herb pairs by mutual reinforcement and mutual assistance based on the connotation of herb pairs, and explains their anti-breast cancer mechanisms via network pharmacology, aiming to provide ideas for in-depth exploration of the academic and practical value of herb pairs. Further interpretation of herb pair connotation may be a path to TCM modernization.

In summary, the induction and analysis of the above herb pairs suggest that many clinically effective and frequently used herb pairs have not been systematically summarized. Meanwhile, discussions on mutual assistance herb pairs for breast cancer are scattered, and further research is needed to identify more effective herb pairs.

Many known herb pair combinations have not been studied by network pharmacology, and their main components, targets and mechanisms need to be clarified. Current theoretical research on breast cancer herb pairs is insufficient and unsystematic, mostly limited to formal examples without in-depth exploration of the internal laws of compatibility, which restricts the further development of herb pairs to some extent.

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## Disclosure statement

The authors declare no conflict of interest.

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