

Guidelines for the clinical application of the *Xihuang* pill for the prevention and treatment of breast hyperplasia diseases

Hongmei Tang^a, Qin Lu^b, Shiyin Feng^a, Zhiwei Xiao^a, Wanyin Wu^c, Gaofeng Chen^d, Li Deng^e, Tianqi Yu^f, Junyan Wu^g, Hua Lin^c, Bo Ji^h, Jietao Lin^a, Chengguang Zhang^d, Liming Li^e, Tao Liuⁱ, Yong Ouyang^j, Kaijun Lei^k, Jun Chen^l, Weiwen Peng^m, Zhenwen Qiu^a, Qingqun Cai^a, Qi Liangⁿ, Cuiling Liuⁿ, Yuzhen Li^o, Lixia Zhu^o, Zexin Zhang^b, Xueting Liu^b, Lizhu Lin^a and Zhihua Zheng^p

^aThe First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China; ^bThe First Clinical Medical School of Guangzhou University of Chinese Medicine, Guangzhou, China; ^cGuangdong Provincial Hospital of Chinese Medicine, Guangzhou, China; ^dGuangdong Second Traditional Chinese Medicine Hospital, Guangzhou, China; ^eThe Affiliated Traditional Chinese Medicine Hospital of Guangzhou Medical University, Guangzhou, China; ^fThe Third Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China; ^gSun Yat-sen Memorial Hospital, Sun Yat-sen University, Guangzhou, China; ^hChinese PLA General Hospital of Southern Theater Command, Guangzhou, China; ⁱSun Yat-sen University Cancer Center, Guangzhou, China; ^jGuangzhou Hospital of Integrated Traditional and Western Medicine, Guangzhou, China; ^kFoshan Hospital of Traditional Chinese Medicine, Foshan, China; ^lShenzhen Traditional Chinese Medicine Hospital, Shenzhen, China; ^mZhongshan Hospital of Traditional Chinese Medicine, Zhongshan, China; ⁿShenzhen Bao'an Traditional Chinese Medicine Hospital Group, Shenzhen, China; ^oThe Eighth Affiliated Hospital, Sun Yat-sen University, Guangzhou, China; ^pGuangdong Pharmaceutical Association, Guangzhou, China

ABSTRACT

Context: The Xihuang pill (XHP) is a traditional Chinese medicine formulation that has been historically used in the prevention and treatment of proliferative breast diseases. However, there is a lack of guidelines that offer recommendations for its clinical use.

Objective: The task force from the Chinese Guangdong Pharmaceutical Association aims to develop evidence-based guidelines for XHP to prevent and treat proliferative breast diseases.

Methods: We searched six Chinese and English electronic databases, including the China National Knowledge Infrastructure, the Chinese Scientific Journal Database, the Wanfang Medical Database, PubMed, and Embase, up to November 1, 2022. Publications (case reports, clinical observation, clinical trials, reviews) on using XHP to treat proliferative breast diseases were manually searched. The search terms were Xihuang pill, hyperplasia of the mammary gland, breast lump, and mastalgia. The writing team developed recommendations based on the best available evidence.

Results: Treatment should be customized based on syndrome identification. We recommend using XHP for the prevention and treatment of breast hyperplasia disease when a patient presents the following syndromes: concurrent blood stasis syndrome, concurrent phlegm-stasis syndrome, and concurrent liver fire syndrome. Safety indicators, including blood analysis and liver and kidney function monitoring, should be performed regularly during treatment.

Conclusions: Current clinical evidence suggests that XHP can be used as a standalone treatment or in conjunction with other medications to prevent and manage breast hyperplasia diseases. More randomized controlled studies are warranted to establish high-quality evidence of its use.

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Clinical guideline; traditional Chinese medicine; syndrome differentiation

Introduction

Breast hyperplasia, also known as mammary gland hyperplasia (MGH), mammary gland adenosis, fibrocystic breast disease, fibrocystic changes in the breast, breast cyst, and cystic hyperplasia of the breast, is a degenerative condition characterized by the excessive growth of fibrous and epithelial tissues within the mammary gland (Zhang et al. 2020). In traditional Chinese medicine (TCM), MGH is classified into 'breast masses.' It is mainly attributed to *Qi* stagnation, phlegm accumulation, and blood stasis (Li et al. 2017). In recent years, there has been a noticeable increase in its prevalence, representing 75% of all breast

disorders, with the highest incidence observed among women 25 to 45 years old (Cowin and Wysolmerski 2010; Rungruang and Kelley 2011). The typical pathological progression of breast cancer has evolved into a gradual continuum, including stages such as 'normal epithelium-simple hyperplasia-atypical hyperplasia-*in situ* carcinoma-invasive carcinoma.' Breast hyperplasia, often accompanied by ductal and mammary epithelial and atypical hyperplasia, presents a risk of cancer transformation ranging from 1.25% to 50% (Shi et al. 2022). In the United States, women diagnosed with proliferative breast diseases by biopsy face nearly three times the risk of developing breast cancer than those with non-proliferative conditions (Cote et al. 2012). As a result, the

CONTACT Lizhu Lin  gzuclmlnz@163.com  The First Affiliated Hospital of Guangzhou University of Chinese Medicine, Guangzhou, China; Zhihua Zheng  snownotrace@126.com  Guangdong Pharmaceutical Association, Guangzhou, China

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prevention and treatment of breast hyperplasia represent the most effective strategies for reducing the incidence of breast tumours (Ercan et al. 2011).

In clinical practice, Western medicine approaches patients with breast hyperplasia with surgical interventions and predominantly uses hormonal medications to regulate endocrine functions. Although this method is precise and effective, it is not without substantial side effects. Studies have indicated that using nonsteroidal antioestrogen agents such as tamoxifen in treating breast hyperplasia can lead to adverse reactions with an incidence of up to 49.39% (Bai 2010; Ryu et al. 2022).

During an extended period of clinical practice, TCM has developed a variety of treatment approaches for breast hyperplasia. These methods are effective and are associated with minimal side effects (Wang et al. 2011). Consequently, TCM and Chinese herbal medicine have become the primary modalities for treating breast hyperplasia in China (Fan et al. 2013). However, due to the absence of a precisely defined mechanism of action, the overall efficacy of these herbal remedies remains to be further verified using standardized and scientific methods.

Chinese medicine surgery has a rich developmental history and encompasses a broad spectrum of diseases. Along with societal progress and academic advancements, modern Chinese medicine surgery extends its scope to various conditions, including sores, carbuncles, galls, tumours, skin problems, breast problems, and disorders of the anus and intestines. Consistent with surgical pharmacy, we define surgical pharmacy of Chinese Medicine as a discipline that delves into the intricacies of TCM treatments for surgical diseases, analysing patient characteristics to identify optimal TCM treatment plans, addressing medication-related problems, and improving clinical outcomes. This guideline is an example of Chinese Medicine surgical pharmacy (Xie et al. 2021; Zheng et al. 2023).

The *Xihuang* pill (XHP) is a renowned therapeutic formula for the management of 'breast rocks' and 'phlegm nuclei'. Its substantial efficacy has been demonstrated in addressing precancerous breast lesions and breast cancer. Documented evidence firmly supports its clinical efficacy (Zheng et al. 2016; Mao et al. 2019). This formula was initially presented in 'The Encyclopaedia of Surgical Diagnosis and Treatment (authored by the famous Qing Dynasty physician Wang Hongxu, published in the fifth year of Kangxi reign, which is 1740 AD)'. XHP is recognized for improving blood circulation, alleviating stasis, clearing heat, facilitating detoxification, and reducing swelling and pain. It can regulate hormonal imbalances and free radical metabolism while restricting neovascularization and epithelial cell proliferation. Furthermore, XHP improves immune function, thus preventing and treating proliferative breast diseases (Lian 2019). This comprehensive approach demonstrates that XHP exerts anti-breast hyperplasia effects by addressing multiple stages and factors. Its therapeutic outcomes, ease of administration, and substantial clinical potential establish it as an ideal medication to prevent and treat breast hyperplasia.

However, there is a lack of guidelines that offer recommendations for the clinical use of XHP to prevent and treat proliferative breast diseases. This absence includes guidance on indications based on the TCM syndrome, dosage and administration, duration of treatment, concurrent medications, contraindications, and possible adverse reactions. Consequently, a critical research gap in these domains requires resolution by developing evidence-based guidelines. The Pharmaceutical Professional Committee of the Chinese Guangdong Pharmaceutical Association has launched an interdisciplinary guideline task force involving professionals in

areas such as TCM oncology, TCM, and clinical pharmacy. Their mission is to develop evidence-based guidelines for the prevention and treatment of proliferative breast diseases using XHP. These guidelines promote a more uniform and judicious application of XHP in clinical settings, promoting the effectiveness and safety of preventing and treating MGH.

Methods

The guideline development process

Guideline scope, target professionals, and target patient population

This guideline applies to healthcare institutions at all levels. The target patient population includes individuals who have or are at risk of developing proliferative breast diseases. The target healthcare professionals include physicians, pharmacists, nurses, other healthcare professionals, and decision-makers who manage proliferative breast diseases.

Guideline development method

The guideline development process has previously been published elsewhere (Lin et al. 2023). A nominal group technique was used to discuss a specific topic (Xihuang pills for MGH) in an online conference format organized by an experienced facilitator with 24 relevant experts. The guideline development process and reporting adhered to the World Health Organization Guideline Development Handbook and the Statement of Reporting Items for Practice Guidelines in Healthcare (RIGHT). A copy of the complete RIGHT-TCM checklist is shown in [Supplementary material 1](#). Conflicts of interest and disclosure were handled under the Recommendations for the Conduct, Reporting, Editing, and Publication of Scholarly Work in Medical Journals of the International Committee of Medical Journal Editors.

Guidelines panels

The group members comprised experts from the following disciplines: TCM oncology, clinical pharmacy, and TCM. The composition and positions of the members are shown in [Table 1](#).

Evidence retrieval and data extraction

We searched six Chinese and English electronic databases, including the China National Knowledge Infrastructure (CNKI), the Chinese Scientific Journal Database (VIP), the Wanfang Medical Database (WANFANG), PubMed, and Embase, up to November 1, 2022. Publications (case reports, clinical observation, clinical trials, reviews) on using XHP to treat proliferative breast diseases were manually searched. Search languages were limited to Chinese and English. Chinese search terms included 西黄丸 (Xihuang pill), 乳腺增生 (hyperplasia of the mammary gland), 乳癖 (breast lump), and 乳痛 (mastalgia). English search terms included Xihuang pill, mammary gland hyperplasia, breast lump, and mastalgia.

Two reviewers independently screened potentially relevant studies based on titles, abstracts, and full-text records. Data were then extracted from included studies using a standardized data extraction form. Two reviewers cross-checked the screening results and the data extraction tables. Discrepancies were resolved through group discussions led by another senior researcher.

Table 1. Members of the guideline develop team.

	Work unit	Title
Consultant		
Zhihua Zheng	Guangdong Pharmaceutical Association	Vice Chairman and Secretary-General, Chief Pharmacist
Writing member		
Lizhu Lin	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Professor
Hongmei Tang	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Shiyin Feng	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Supervising Pharmacist of Traditional Chinese Medicine
Member		
Tianqi Yu	The Third Affiliated Hospital of Guangzhou University of Chinese Medicine	Chief Physician of Traditional Chinese Medicine
Li Deng	The Affiliated Traditional Chinese Medicine Hospital of Guangzhou Medical University	Chief Physician
Tao Liu	Sun Yat-sen University Cancer Center	Chief Pharmacist
Zhenwen Qiu	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Cuiling Liu	Shenzhen Bao'an Traditional Chinese Medicine Hospital Group	Associate Chief Pharmacist of Traditional Chinese Medicine
Junyan Wu	Sun Yat-sen Memorial Hospital, Sun Yat-sen University	Chief Pharmacist
Liming Li	The Affiliated Traditional Chinese Medicine Hospital of Guangzhou Medical University	Chief Pharmacist of Traditional Chinese Medicine
Yuzhen Li	The Eighth Affiliated Hospital, Sun Yat-sen University	Chief Pharmacist
Lixia Zhu	The Eighth Affiliated Hospital, Sun Yat-sen University	Associate Chief Pharmacist
Zhiwei Xiao	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Associate Chief Physician of Traditional Chinese Medicine
Wanyin Wu	Guangdong Provincial Hospital of Chinese Medicine	Chief Physician
Gaofeng Chen	Guangdong Second Traditional Chinese Medicine Hospital	Chief Physician of Traditional Chinese Medicine
Bo Ji	Chinese PLA General Hospital of Southern Theater Command	Chief Pharmacist
Chengguang Zhang	Guangdong Second Traditional Chinese Medicine Hospital	Chief Pharmacist of Traditional Chinese Medicine
Jun Chen	Shenzhen Traditional Chinese Medicine Hospital	Chief Pharmacist of Traditional Chinese Medicine
Hua Lin	Guangdong Provincial Hospital of Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Jietao Lin	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Chief Physician
Yong Ouyang	Guangzhou Hospital of Integrated Traditional and Western Medicine	Chief Pharmacist of Traditional Chinese Medicine
Qi Liang	Shenzhen Bao'an Traditional Chinese Medicine Hospital Group	Chief Pharmacist of Traditional Chinese Medicine
Weiwen Peng	Zhongshan Hospital of Traditional Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Kaijun Lei	Foshan Hospital of Traditional Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Qingqun Cai	The First Affiliated Hospital of Guangzhou University of Chinese Medicine	Chief Pharmacist of Traditional Chinese Medicine
Secretary		
Qin Lu	The First Clinical Medical School of Guangzhou University of Chinese Medicine	Master's student
Xueting Liu	The First Clinical Medical School of Guangzhou University of Chinese Medicine	Master's student
Zexin Zhang	The First Clinical Medical School of Guangzhou University of Chinese Medicine	Master's student

Comprehensive analysis of evidence and compilation of evidence report

After analysing and summarizing the retrieved data, expert opinions were collected through meetings and online consultations to supplement the evidence. Finally, the writing team prepared an evidence report, which was reviewed by the consensus conference.

The process of formulating recommendations

The writing team developed recommendations based on the best available evidence. When direct supportive evidence was insufficient, expert clinical experience was collected online to supplement the recommendations. After discussions on expert evidence, the team formulated an initial draft of the expert consensus. The guideline members provided feedback on recommendations and the expert consensus statement, ultimately establishing linguistic consensus.

The Xihuang pill

XHP contains four rare Chinese herbs: artificial bezoar (Niu Huang, *Calculus Bovis*, from *Bos taurus domesticus* Gmelin [Bovidae]), artificial musk (*Moschus*, from *Moschus berezovskii* Flerov [Moschidae]), *Olibanum* (*Boswellia carterii* Birdw [Burseraceae]), and *Myrrha* (from *Commiphora myrrha* Engl.

[Burseraceae])). Niu Huang is the chief herb in the formula and has a cooling and sweet taste. It enters the meridians of the heart and liver, removes heat, detoxifies, reduces swelling, and alleviates pain. Frankincense and myrrh act as ministerial herbs, promoting blood circulation, resolving stasis, and alleviating pain. Musk is an adjuvant herb and has a pungent aroma. It improves blood and Qi circulation, relieves blood stasis, dispels stagnation, and reduces swelling and pain. When these herbs are combined, they synergistically work to remove heat, detoxify, reduce swelling, and disperse accumulations.

The diagnosis of MGH-related diseases

The diagnosis of MGH-related diseases is based on diagnostic criteria from 'Chinese Surgical Science,' 'Surgery,' and the 'Expert Consensus on Diagnosis and Treatment of Mammary Gland Hyperplasia' (Ma et al. 2016). Criteria include (1) persistent breast tenderness, stabbing pain, or dull pain of varying degrees in the breasts, associated with the menstrual cycle and emotional fluctuations, lasting for a continuous period of 3 months or intermittently for 3-6 months without relief; and (2) the development of one or multiple irregularly sized and variably shaped masses in unilateral or bilateral breasts, with indistinct boundaries from surrounding tissue. The skin color on the surface remains unchanged, and the size of the masses may fluctuate with

emotional changes. Some patients may also experience nipple discharge or itching. Other benign and malignant breast conditions, such as fibroadenoma and breast cancer, should be ruled out using additional diagnostic methods, including mammography and ultrasound (B-mode), fine needle aspiration, or histopathological examination.

The pharmacology of the Xihuang pill in treating MGH-related diseases

The Xihuang pill can regulate hormone levels and enhance immune function

Experimental animal studies (Lian et al. 2017; Li et al. 2021) have shown that XHP can down-regulate serum oestradiol, prolactin, and testosterone levels while increasing progesterone levels in rats. This modulation suppresses MGH and improves pathological changes in the morphology of mammary tissues. Additionally, XHP can regulate the levels of essential cytokines that reflect the body's immune function, such as interleukin-2 (IL-2) and tumour necrosis factor- α (TNF- α), in the serum of rats with MGH. It also significantly increases the spleen and thymus indices, indicating that XHP may exert anti-MGH effects by improving immune function.

The Xihuang pill can inhibit lipid peroxidation reactions

XHP reduces malondialdehyde (MDA) levels in the serum of MGH-treated rats and increases superoxide dismutase (SOD) activity. This regulation of free radical metabolism signifies a substantial impact in counteracting damage caused by free radicals. These findings suggest that XHP may exert its anti-MGH effects by inhibiting lipid peroxidation reactions (Chen 2007; Lian et al. 2017).

The Xihuang pill can inhibit neovascularization and promote cell apoptosis

XHP can decrease blood viscosity in MGH-treated rats and reduce the expression of vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), and proliferating cell nuclear antigen (PCNA) in mammary tissues. This inhibition inhibits neovascularization and epithelial cell proliferation. Excessive proliferation and decreased apoptosis of mammary epithelial cells are significant mechanisms in the development of MGH. XHP achieves substantial therapeutic effects by inhibiting the expression of the oestrogen receptor (ER) and progesterone receptor (PR), inducing mammary epithelial cell apoptosis through the mitochondrial pathway, preventing their proliferation, and effectively treating MGH. Furthermore, serum from subjects treated with XHP inhibits the growth of rat mammary epithelial cells induced by oestradiol (E2) and progesterone. This serum also enhances apoptosis in mammary cells by upregulating the transcription of the antiapoptotic Bcl-2-associated X-protein (Bax) and the pro-apoptotic B-cell lymphoma-2 (Bcl-2) protein on the cell surface (Lian et al. 2017; Han 2020), which indicates its significant role in the treatment of MGH.

Clinical application research of the Xihuang pill

We retrieved 45 studies, including 12 case reports and clinical observational/pilot studies (Table 2).

The Xihuang pill monotherapy treatment

XHP demonstrates remarkable efficacy in the treatment of MGH. Its administration is not limited to oral intake. It can also be applied externally, highlighting the convenience and cost-effectiveness of TCM treatment. In a study by Cheng et al. (2010), 117 patients with MGH were randomly divided into a treatment group (58 cases) and a control group (59 cases). The treatment group received oral XHP, while the control group received *Rupi Xiao* tablets for mammary lumps. The results revealed that patients in the XHP group experienced significant pain relief and reduced breast lumps, with an overall effective rate of 96.6%, markedly higher than the 72.9% control group. Han et al. (2009) used an external application of XHP by creating a paste with warm water and applying it to the breast lumps. They observed substantial improvements in breast tenderness, reduced nipple discharge, and decreased lump size. In the study by Gao et al. (2009), 120 patients with MGH were treated with XHP, and the results demonstrated its effectiveness in alleviating breast pain and lump symptoms in patients.

The Xihuang pill combination therapies

Zeng and Ding (2003) conducted a combined treatment study using XHP and tamoxifen in 132 cases of moderate to severe MGH. They compared it with a control group of 124 patients treated with *Rupi Xiao* or *Xiaojindan*. The results showed a total effective rate of 98.48% in the treatment group, significantly higher than the 81.45% in the control group. This indicates that the combination of tamoxifen and XHP is a safe and effective approach to treating MGH and can be considered a therapeutic option to treat the condition.

In another study by Zhang and Wen (2006), a combination of the *Xiaoyao* pill and XHP was used to treat MGH. The results demonstrated cure in 74 cases (62.7%), significant improvement in 32 patients (27.1%), and effectiveness in 10 cases (8.47%), resulting in an overall effective rate of 98.3%. Meanwhile, in a study by Jin (2009), the combination of *Xiaoyao* pill and XHP was also used in the treatment of MGH. The results showed that 61 cases (62.3%) were cured, 22 cases (22.5%) were significantly improved, and 12 cases (12.2%) were effective, with an overall effectiveness rate of 96.9%. Those suggest that the combined use of the *Xiaoyao* pill and XHP is an effective treatment approach for MGH. Clinical practice confirms that XHP, combined with Western medicine or TCM remedies to disperse swelling and eliminate accumulations, produces favourable therapeutic effects, and deserves further promotion.

The consensus recommendations for the prevention and treatment of breast hyperplasia diseases

TCM syndrome differentiation

According to TCM theory, breast hyperplasia falls under the category of 'breast affliction.' This condition primarily affects the breasts and has its root causes due to imbalances in the liver and kidneys. The development of these diseases is closely associated with the meridians of the liver, spleen, and kidney and the Chong and Ren channels. The liver promotes the body's smooth flow of energy (*Qi*). Emotional discomfort, mental depression, *Qi* imbalances, and liver *Qi* stagnation can disrupt the harmony of the Chong and Ren channels. Prolonged stagnation can transform into heat, scorching bodily fluids and leading to the formation of phlegm. Alternatively, liver *Qi* can invade the spleen, resulting in spleen deficiency and dampness accumulation,

Table 2. Summary of clinical studies of *xihuang* pill.

Type of Research	Number of patients	Medications	Results	Reference
Case Report	1	Oral <i>Xihuang</i> pill+ <i>Jiawei Xiaoyao</i> Pill	Stabilized mood stability, increased menstrual flow, decreased blood clots.	Shao JF. 2018. Clinical application of <i>Xihuang</i> pill. <i>Smart Healthcare</i> . 4(09):119-120. (Chinese).
	1	Oral <i>Xihuang</i> pill	Soften lumps in both breasts and reduce pain	Zhu DS. 2009. A case of breast hyperplasia treated with <i>Xihuang</i> pill. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing(China): Chinese Association of Chinese Medicine. p.127. (Chinese).
	1	Oral <i>Xihuang</i> pill	Improve the degree of glandular disorder, without pain and discomfort	Zhu DS. 2009. A case of breast atypical hyperplasia treated with <i>Xihuang</i> pill. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing(China): Chinese Association of Chinese Medicine. p.128. (Chinese).
	1	Oral <i>Xihuang</i> pill	Glands of both breasts showed no significant abnormality after treatment	Zhang DX. 2009. Report of a case of cystic hyperplasia of the breast treated with <i>Xihuang</i> pill. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing (China): Chinese Association of Chinese Medicine. p.148-149. (Chinese).
	1	Oral <i>Xihuang</i> pill+ Prescription based on differential diagnosis	Breast swelling and pain improved and the lumps shrunk.	Liu L. 2009. <i>Xihuang</i> pill Clinical Experiments. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing (China): Chinese Association of Chinese Medicine. p.91. (Chinese).
Clinical Observation/Trials	58	Intervention: Oral <i>Xihuang</i> pills Control group: Oral <i>Rupi Xiao</i> tablet	<i>Xihuang</i> pills were more effective than <i>Rupi Xiao</i> tablet in treating breast hyperplasia	Chen ZH, Chen ZR, Zeng LH, Yang HC, Lu FH. 2010. Observation on the efficacy of <i>Xihuang</i> pill in treating 58 cases of breast hyperplasia. <i>Chinese Journal of Traditional Chinese Medicine and Pharmacy</i> . 25(11):1919-1920. (Chinese).
	132	Oral <i>Xihuang</i> Pills + Tamoxifen Control Group: <i>Rupi Xiao</i> tablet	Combination of <i>Xihuang</i> pill and tamoxifen was more effective than <i>Rupi Xiao</i> tablet	Zeng LZ, Ding ZS. 2003. Clinical observation on 132 cases of breast hyperplasia treated by <i>Xihuang</i> pill with tamoxifen. <i>Chinese Journal of Primary Medicine and Pharmacy</i> . (02):77. (Chinese).
	118	Oral <i>Xihuang</i> Pills + <i>Xiaoyao</i> Pills	Combination of two drugs was simple and effective in treating breast hyperplasia.	Zhang Q, Wen HB. 2006. Clinical observation on the treatment of breast hyperplasia by <i>Xihuang</i> pill together with <i>Xiaoyao</i> Pills. <i>Journal of Practical Medical Technology</i> . (14):2448-2449. (Chinese).
	120	Oral <i>Xihuang</i> Pills	More effective in treating breast enlargement disease	Gao YH, Tian Z, Wang XX, Yuan HE, Gao QZ. 2009. Observation on the therapeutic effect of <i>Xihuang</i> pill in the treatment of breast hyperplasia disease. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing(China): Chinese Association of Chinese Medicine. p.114. (Chinese).
	160	External application of <i>Xihuang</i> Pills + oral administration of <i>Rupi Xiao</i> Tablets Control group: Oral <i>Rupi Xiao</i> tablet	External application of <i>Xihuang</i> pill in the treatment of breast hyperplasia with good clinical efficacy.	Han T, Lan YM, Han P, Cheng ZQ. 2009. Clinical study on the treatment of breast hyperplasia by external application of <i>Xihuang</i> pill. <i>Journal of Chinese Medicinal Materials</i> . 32(11):1793-1794. (Chinese).
	56	Oral <i>Xihuang</i> Pills Control group: Oral <i>Rupi Xiao</i> tablet	<i>Xihuang</i> Pills were more effective than <i>Rupi Xiao</i> tablet in treating breast hyperplasia.	Sui YB. 2010. Clinical observation on the treatment of breast hyperplasia disease by <i>Xihuang</i> pill. <i>Chinese Journal of Traditional Chinese Medicine and Pharmacy</i> . 25(04):618-619. (Chinese).
	98	Oral <i>Xihuang</i> Pills + <i>Xiaoyao</i> pills	Combination of two drugs was simple and effective in treating breast hyperplasia.	Jin J. 2009. Clinical study on the treatment of breast hyperplasia by <i>Xihuang</i> pill together with <i>Xiaoyao</i> Pill. In: Beijing Tongrentang Science and Technology Development Co., Chinese Journal of Traditional Chinese Medicine, editors. [Proceedings of the Research on Clinical Application of <i>Xihuang</i> Pills]. Beijing(China): Chinese Association of Chinese Medicine. p.79. (Chinese).

contributing to phlegm formation. When *Qi* movement is hindered, and the harmony of *Qi* and blood is disrupted, blood stasis may occur as circulation becomes obstructed. The interaction of phlegm and stasis can block the mammary ducts, leading to breast affliction. The characteristic pathological features of this condition include the coexistence of internal deficiency and toxic accumulation. Internal deficiency encompasses Chong and Ren channel imbalances, liver damage due to emotional distress,

spleen impairment due to excessive worry and liver *Qi* stagnation leading to liver-kidney *Yin* deficiency. On the other hand, toxic accumulation refers to stagnation of the *Qi* in the liver, which transforms into heat, refining bodily fluids into phlegm, which becomes turbid and stagnant. Toxic stasis accumulates, leading to the formation of congealed masses in the breasts.

Pathological factors in breast hyperplasia include *Qi* stagnation, phlegm congestion, and blood stasis. As a result, the

Table 3. The syndrome differentiation based on concurrent clinical and relevant symptoms.

Combination of symptoms	Clinical symptom	Tongue Diagnosis	Pulse
Concurrent Blood Stasis Syndrome	Breast soreness, delayed menstruation, dark menstrual blood with clots, and premenstrual abdominal pain.	The tongue may appear dark with stasis spots or ecchymosis.	The pulse may be tight or astringent.
Concurrent Phlegm-Stasis Syndrome	An overweight body, less prominent breast pain, and a tough lump texture. They may also show fatigue, phlegm presence, poor appetite, and symptoms of chest congestion, hypochondriac fullness, irritability, and restlessness.	The tongue coating could be thin or greasy.	With a yellow coating and a slippery pulse.
Concurrent Liver-Fire Syndrome	Breast swelling and pain, possibly with the sensation of burning heat. Other symptoms include irritability, early menstruation with dark and heavy flow, dry and bitter mouth.	A red tongue, yellow or greasy coating.	A wiry or rapid pulse.

primary treatment principles revolve around soothing the liver, resolving stagnation, dispersing masses, and reducing swelling. In cases where long-term medication does not reduce the lump and the lump exhibits a rigid texture with unclear edges, raising suspicion of malignant transformation, it is advisable to consider a timely pathological diagnosis or surgical removal.

XHP removes heat, resolves toxicity, reduces swelling, and disperses masses. It is particularly suitable for patients with breast affliction who have patterns of accumulation of heat toxins or liver depression with phlegm congestion. The primary symptoms include hidden pain and discomfort in breast lumps, pain radiating to the sides of the chest, restlessness, poor sleep, dry and bitter mouth, constipation, a red tongue, a yellow or thick and greasy coating of the tongue, and a rapid, wet or slippery pulse.

The main therapeutic effects of XHP include ‘clearing’ and ‘dispersing.’ It can be combined with other herbal formulas. Treatment should be tailored based on syndrome identification, and the prescription should be adjusted accordingly. Safety indicators such as liver and kidney function monitoring should be performed regularly during treatment. The syndrome differentiation based on relevant and concurrent clinical symptoms is summarized in Table 3.

Consensus recommendations

XHP is suitable for preventing and treating breast hyperplasia diseases. TCM syndrome differentiation primarily includes heat-toxin accumulation syndrome (a group of symptoms

characterized by the accumulation of toxins or heat in the body) or liver depression with phlegm congestion syndrome. Additionally, concurrent clinical symptoms can consist of blood stasis syndrome (a condition where the flow of blood is disrupted, leading to the stagnation, accumulation, and congestion of blood in the body), phlegm stasis syndrome (the accumulation of phlegm and dampness in the body), and liver fire syndrome (a group of symptoms characterized by an excess of heat or fire in the liver, often causing emotional or physical disturbances). We recommend using XHP for the prevention and treatment of breast hyperplasia disease when a patient presents the following syndromes:

- When the TCM syndrome differentiation indicates the heat-toxin accumulation syndrome or relevant concurrent clinical syndromes.
- When the TCM syndrome differentiation indicates liver depression with phlegm congestion syndrome or relevant concurrent clinical syndromes.
- When the concurrent clinical syndrome differentiation indicates blood stasis syndrome.
- When concurrent clinical syndrome differentiation indicates phlegm-stasis syndrome.
- When the concurrent clinical syndrome differentiation indicates liver-fire syndrome.

Administration and dosage of the Xihuang pill

The specification of the XHP bottle is 3 g. Usage and dosage: For oral administration, take one bottle (3g) per dose twice daily. When it needs to be used in conjunction with other medications, it should be done in accordance with the guidance of a physician or pharmacist. Treatment should be customized based on syndrome identification, and the prescription should be adjusted accordingly. Safety indicators, including blood analysis and liver and kidney function monitoring, should be performed regularly during treatment.

Safety of the Xihuang pill

Contraindications: Do not use during pregnancy. Athletes should use it with caution. Smoking, alcohol consumption, and spicy, raw, and greasy foods should be avoided during the medication period.

Adverse reactions: Occasionally, cardiorespiratory, gastrointestinal, and urinary disturbances, as well as drug-induced rashes, are reported. These effects may be attributed to sensitizing ingredients in the XHP prescription and its suboptimal compounding standards (Zhang et al. 2009). Typically, these reactions will subside after discontinuing the medication. Symptomatic treatment may be required if necessary.

Conclusions

Current clinical evidence suggests that XHP can be used as a standalone treatment or in conjunction with other medications to prevent and manage breast hyperplasia diseases. The drug is well tolerated. However, more randomized controlled studies are warranted to establish high-quality evidence of its use.

Author contributions

Hongmei Tang: Conceptualization, Data Curation, Project Administration, Resources, Visualization, Writing-Review & Editing; Qin Lu: Formal Analysis, Investigation, Visualization, Writing-Original Draft, Software, Data Curation; Shiyin Feng: Methodology, Resources, Visualization, Writing-Original Draft, Software, Data Curation; Zhiwei Xiao: Methodology, Resources, Writing-Original Draft, Software, Data Curation; Wanyin Wu: Conceptualization, Investigation, Methodology, Writing-Original Draft; Gaofeng Chen: Data Curation, Methodology, Resources, Writing-Review & Editing; Li Deng: Conceptualization, Formal Analysis, Methodology, Validation, Visualization; Tianqi Yu: Conceptualization, Data Curation, Project Administration, Resources; Junyan Wu: Data Curation, Investigation, Project Administration, Resources; Hua Lin: Conceptualization, Investigation, Validation; Bo Ji: Conceptualization, Project Administration, Supervision, Validation, Writing-Review & Editing; Jietao Lin: Formal Analysis, Methodology, Supervision, Validation, Writing-Original Draft; Chengguang Zhang: Project Administration, Resources, Software, Supervision, Validation; Liming Li: Conceptualization, Investigation, Methodology, Software, Supervision; Tao Liu: Investigation, Methodology, Project Administration, Resources, Validation; Yong Ouyang: Formal Analysis, Methodology, Project Administration, Supervision; Kaijun Lei: Conceptualization, Resources, Software, Supervision; Jun Chen: Formal Analysis, Investigation, Methodology, Supervision, Validation; Weiwen Peng: Data Curation, Methodology, Project Administration, Resources, Supervision; Zhenwen Qiu: Conceptualization, Project Administration, Software, Supervision, Visualization; Qingqun Cai: Conceptualization, Investigation, Supervision, Writing-Review & Editing; Qi Liang: Resources, Software, Visualization, Writing-Review & Editing; Cuiling Liu: Data Curation, Investigation, Methodology, Writing-Review & Editing; Yuzhen Li: Conceptualization, Data Curation, Resources, Writing-Review & Editing; Lixia Zhu: Conceptualization, Data Curation, Software, Supervision, Visualization; Zexin Zhang: Investigation, Methodology, Validation, Writing-Original Draft; Xueting Liu: Investigation, Methodology, Writing-Original Draft, Validation; Lizhu Lin: Conceptualization, Formal Analysis, Project Administration, Resources, Supervision, Visualization, Writing-Review & Editing; Zhihua Zheng: Conceptualization, Methodology, Project Administration, Resources, Software, Validation, Writing-Review & Editing.

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