



## Review Article

# Traditional Chinese medicine treatment for benign thyroid nodules: Literature review

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### ABSTRACT

Thyroid nodules (TNs) are pathological changes characterized by abnormal proliferation of thyroid gland tissue. Approximately 19% to 67% of asymptomatic individuals are diagnosed with TNs, with the majority being benign nodules and 4% to 6.5% being thyroid cancer nodules. Western medicine recommends regular examinations and surgery, while traditional Chinese medicine (TCM) provides an alternative choice to maintain thyroid function and reduce the need for surgery. However, in Taiwan, research on TCM treatment for benign TNs is primarily limited to case reports, lacking large-scale and systematic clinical studies. We conducted a search of electronic databases including PubMed, Google Scholar, Wanfang Data, and China National Knowledge Infrastructure to collect clinical trials related to TCM treatment for TNs. Our goal is to provide new treatment options, further validate the value of TCM in the treatment of TNs, and lay a foundation for future clinical research.

**KEYWORDS:** *Benign thyroid nodules, Chinese herbs, Traditional Chinese medicine*

### INTRODUCTION

Thyroid nodules (TNs) are characterized by abnormal growth of thyroid tissue, with a higher incidence rate among women. The majority of nodules are benign, but some may be malignant [1]. Common clinical presentations include the presence of a neck mass, swelling, throat obstruction, or hoarseness of voice. Benign diseases include multinodular goiter, Hashimoto's thyroiditis, cysts, adenomatous nodules, colloid (macrofollicular) adenomas, microfollicular or macrofollicular adenomas, Noninvasive follicular thyroid neoplasm with papillary-like nuclear features (NIFTP) is an encapsulated or clearly delimited, noninvasive neoplasm with a follicular growth pattern and nuclear features of papillary thyroid carcinoma (PTC), but without well-formed papillae or psammoma bodies and without typical findings of the aggressive subtypes of PTC or poorly differentiated carcinoma and Hürthle cell adenomas [2]. Malignant diseases include papillary carcinoma, follicular carcinoma, Hürthle cell carcinoma, medullary carcinoma, poorly differentiated carcinoma, minimally or widely invasive carcinoma, primary thyroid lymphoma, and metastatic carcinoma. According to guidelines, the risk of malignancy is very low for benign TNs (BTNs), and surgical treatment of BTNs may be overly invasive, with currently no widely used effective therapy [3].

Traditional Chinese medicine (TCM) practitioners in Taiwan and other countries utilize herbal medicine to treat

various diseases. TCM believes that TNs can be prevented and treated through various approaches, potentially resulting in fewer adverse reactions. The treatment of BTNs in TCM is typically individualized, based on the etiology, pathogenesis, pattern differentiation, and patient's condition. TCM research has demonstrated that herbal medicine can effectively reduce the size of TNs without causing significant adverse events.

Recent clinical studies have confirmed the efficacy of herbal medicine decoctions, whether used alone or in combination with Western medicine, in treating BTNs and reducing their maximum diameter. However, current research on TCM treatment for BTNs in Taiwan primarily consists of case reports, indicating the need for large-scale and systematic clinical studies. The objective of this paper is to collect the latest randomized controlled trial data on TCM treatment for BTNs, providing high-level evidence support and laying the foundation for future clinical research.


According to the guidelines from the American Thyroid Association and the National Comprehensive Cancer

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Network [1], the diagnosis of the thyroid relies on medical history, physical examination, laboratory tests, and ultrasound examination. Ultrasound examination allows for a detailed assessment of the size and shape of the thyroid and neck structures. In asymptomatic individuals, the proportion of diagnosed nodules through ultrasound examination ranges from 19% to 67% [4]. For patients with TNs, nodular goiter, or incidentally discovered nodules, regardless of the number of nodules, ultrasound examination is recommended, as the risk of developing malignant tumors is the same [5,6]. Ultrasound evaluation of each nodule’s characteristics, particularly those associated with an increased risk of thyroid cancer, such as echogenicity, microcalcifications, irregular or infiltrative borders, tissue structure, shape, and size [7-9], is used to determine the need for fine-needle aspiration (FNA) biopsy [Figure 1].

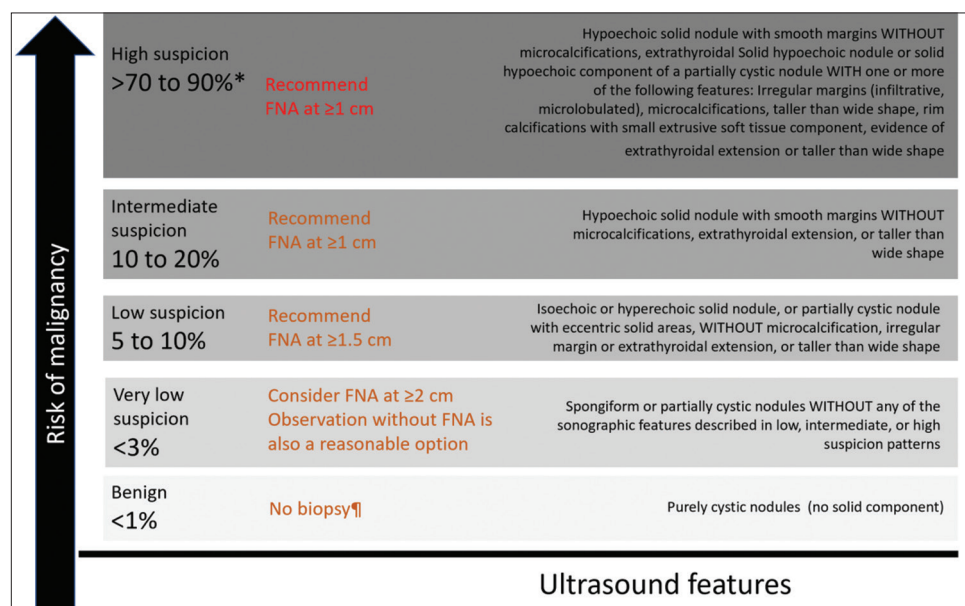
Additional conventional imaging studies such as magnetic resonance imaging or computed tomography may be necessary for tumors with extensive invasion or involvement of adjacent tissues. For patients with decreased serum thyroid-stimulating hormone (TSH) levels, evaluation by a nuclear medicine physician is required, and thyroid radioactive testing may be recommended. Cystic nodules appear as areas of decreased thyroid function (“cold spots”) on radionuclide scans. Typically, FNA

is not necessary for nodules presenting with hyperfunctioning thyroid, as autonomous nodules are rarely malignant [10].

FNA is currently the most accurate and cost-effective test method, particularly for TNs with suspicious ultrasound features, as it can more accurately predict the likelihood of malignant tumors, not solely relying on nodule size [11,12]. According to research findings, for cystic or predominantly cystic nodules without suspicious features, FNA biopsy is recommended if the nodule size is  $\geq 2$  cm. For mixed nodules with suspicious ultrasound features, FNA biopsy is recommended if the nodule size is  $\geq 1.5$ –2 cm, or if the solid component is larger than 1–1.5 cm (0.5 cm in high-risk patients). However, purely cystic nodules usually do not require diagnostic FNA biopsy. FNA provides six broad result categories, each representing different subsequent management approaches [Table 1].

### MANAGEMENT

Treatment options for benign cystic TNs include aspiration, surgery, thyroid hormone therapy, radioactive iodine treatment, percutaneous ultrasound-guided interventions (such as ethanol ablation and radiofrequency ablation), interstitial laser photocoagulation, and polidocanol sclerotherapy.



**Figure 1:** ATA (2015): FNA guidance for thyroid nodules. ATA: American Thyroid Association; FNA: fine-needle aspiration. Aspiration of the cyst may be considered for symptomatic or cosmetic drainage

**Table 1: The Bethesda System for Reporting Thyroid Cytopathology provides an assessment of the potential risk of malignancy and corresponding clinical management recommendations**

Bethesda class	Cytological results of FNA	Cancer risk (%)	Management
I	Nondiagnostic or unsatisfactory	5–10	Repeat FNA with ultrasound guidance
II	Benign	0–3	Clinical and sonographic follow-up
III	AUS or FLUS	10–30	Repeat FNA, molecular testing, or lobectomy
IV	Follicular neoplasm (or suspicious for follicular neoplasm)	25–40	Molecular testing, lobectomy
V	Suspicious for malignancy	50–75	Near-total thyroidectomy or lobectomy
VI	Malignant	97–99	Near-total thyroidectomy or lobectomy

AUS: Atypia of undetermined significance, FLUS: Follicular lesion of undetermined significance, FNA: Fine-needle aspiration

Generally, benign cystic nodules without compressive symptoms do not require aspiration. Following aspiration, 25% to 50% of nodules may disappear, but most nodules may reappear, possibly due to recurrent bleeding or leakage [13,14]. If a cystic nodule recurs, continues to grow, or causes pain after aspiration, many patients may choose surgical removal. A cystic nodule size exceeding 4 cm can be an indication for surgery.

Radioactive iodine therapy is suitable for nontoxic benign thyroid enlargement, particularly for patients who are not suitable for surgery or choose to avoid surgery [15]. However, within 1–8 years after treatment, 22% to 58% of patients may experience thyroid function decline [16].

Most studies indicate that thyroid hormone therapy has limited effectiveness in reducing TNs. Suppressive therapy may interfere with the enlargement of nodules and reduce the risk of thyroid cancer. However, the efficacy of thyroid hormone suppressive therapy is controversial for patients with isolated BTNs or nontoxic multinodular goiter with normal thyroid function [17].

Ultrasound-guided tissue intervention therapies include ethanol or sclerosing agent injection, as well as physical energy therapies guided by ultrasound [18].

Ethanol ablation and radiofrequency ablation are effective in reducing the size of benign cystic TNs [19–22]. Additionally, ultrasound-guided percutaneous laser ablation can also be used for the treatment of cystic nodules.

In China, the sclerosing agent polidocanol is used as an alternative to ethanol for treatment [23].

## THE CONCEPT OF TRADITIONAL CHINESE MEDICINE IN THE TREATMENT OF THYROID NODULES

Clinical studies have shown that herbal decoctions, either alone or in combination with Western medicine, are effective in reducing the maximum diameter of TNs. Treatment methods include standalone TCM therapy, TCM combined with Western medicine, TCM topical treatment, and TCM internal and external application therapy. The clinical efficacy of TCM and Western medicine in the treatment of TNs is evaluated based on treatment response rate, nodule diameter, thyroid volume, FT3, FT4, TSH, TCM syndrome score, transforming growth factor- $\beta$  (TGF- $\beta$ ), vascular endothelial growth factor (VEGF), interferon-gamma, insulin-like growth factor- $\gamma$  (IGF- $\gamma$ ), malignant transformation, and interleukin-4.

According to the “Guidelines for Clinical Research of New TCM (Trial)” [24], the TCM syndrome score includes symptoms such as anterior neck swelling, swallowing movement, neck fullness, difficulty breathing, swallowing impairment, low mood, phlegm sensation in the throat, unfavorable sensation in the throat, and discomfort in the chest and abdomen. The symptoms are scored from 0 to 3, with 0 indicating no symptoms, 1 indicating mild symptoms, 2 indicating moderate symptoms, and 3 indicating severe symptoms.

## Treatment with Chinese medicine alone

According to Xu’s study (2019) [25], TCM treatment has been found to effectively increase the overall efficacy and reduce the maximum diameter of nodules. Zhang *et al.*’s study [26] demonstrated that TCM can improve the overall efficacy, effectively reducing nodule diameter and cross-sectional area. Peng observed that the San Jie Xiao Ying Tang formula (散結消癭湯) could effectively increase the overall efficacy and reduce the maximum diameter of nodules [27]. Chen and Li proposed a modified version of the Ban Xia Hou Pu Tang formula (半夏厚朴湯), which was found to effectively treat nodules, increase the overall efficacy, and improve TCM syndrome scores [28]. Feng *et al.* observed that Xia Gu Xiao Ying powder (夏菇消癭散) could effectively improve nodule size and reduce the maximum diameter [29]. Liu proposed a modified version of the Yi Qi Hua Yu Fang formula (益氣化痰方), which effectively treated nodules, increased the overall efficacy, and reduced the maximum average diameter and volume [30]. Yao (2017) proposed the Hua Tan Qu Yu San Jie Fang formula (化痰祛瘀散結方), which effectively treated nodules, increased the overall efficacy, and reduced the maximum average diameter and volume [31] [Table 2].

## Traditional Chinese medicine combined with Western medicine treatment

According to Wang and Li (2014) [32], combining low-dose thyroid hormone with San Jie Ping Ying Fang (散結平癭方) significantly improved overall efficacy and reduced the number and volume of nodules.

In Wang’s study (2020) [33], combining San Jie Ping Ying Fang (散結平癭方) with levothyroxine sodium tablets effectively improved hormone levels, reduced TNs, and enhanced treatment outcomes.

Wang (2017) [34] demonstrated that combining thyroid hormone with San Zhong San Jie Tang (消腫散結湯) treatment effectively improved TSH levels, reduced TN size, improved clinical symptoms, and increased treatment efficacy.

Han *et al.* [35] observed that combining Yi Qi San Jie Tang (益氣散結湯) with levothyroxine sodium tablets for the treatment of BTNs led to a significant reduction in nodule area after 6 weeks of treatment. After 12 weeks, the reduction in nodule area was significantly greater in the combination group compared to the Western medicine and TCM groups. Additionally, the combination group exhibited a significant decrease in TCM syndrome scores before and after treatment.

Xiong and Han [36] compared the combination of levothyroxine sodium tablets and Chai Bei Er Chen Tang (柴貝二陳湯) to the use of levothyroxine sodium tablets alone for treating TNs. The combination therapy significantly improved overall efficacy, significantly reduced the maximum nodule diameter, and lowered the risk factor score for malignant transformation.

Yang [37] found that combining Yi Qi Hua Yu Fang (益氣化痰方) with levothyroxine sodium tablets for treating BTNs resulted in a higher overall efficacy rate compared to

**Table 2: Treatment with Chinese medicine alone**

Author/year	Intervention/medication		Study design	Number of patients	Duration (months)	Results of the experimental group compared to the control group
	Experimental group	Control group				
Xu and Land, 2019 [25]	(Ingredients: <i>Bupleuri radix</i> , <i>Paeoniae radix alba</i> , <i>Chuanxiong rhizoma</i> , <i>Salviae Miltiorrhizae radix</i> , <i>Angelicae Sinensis radix</i> , <i>Pinelliae rhizoma</i> , <i>M. pentadactyla</i> , <i>Curcumae rhizoma</i> , <i>Sparganii rhizoma</i> , <i>Prunellae spica</i> , <i>Gleditsiae spina</i> , <i>Glycyrrhizae radix et rhizoma</i> )	Low-iodine diet	Control treatment and observation	40	3	(1) ↑ ( $P<0.05$ ) (2) ↓ (experimental group: 1.70±0.74→1.15±0.59 cm)
Zhang et al., 2015 [26]	(Ingredients: <i>Aurantii fructus immaturus</i> , <i>Bupleuri radix</i> , <i>Poria</i> , <i>Pinelliae rhizoma</i> , <i>Paeoniae radix alba</i> , <i>Cyperii rhizoma</i> , <i>Sinapis semen</i> , <i>Asarum sagittarioides</i> , <i>Fritillariae thunbergii bulbus</i> , <i>G. scabra</i> , <i>Prunellae spica</i> , <i>Curcumae radix</i> , <i>A. julibrissin</i> , <i>Glycyrrhizae radix et rhizoma</i> )	Not	Controlled	52	3	(1) ↑ (2) ↓ (experimental group: 1.13±0.56→0.78±0.42 cm)
Peng, 2015 [27]	San Jie Xiao, Ying Tang (Ingredients: <i>Coptis rhizome</i> , <i>Rehmannia root</i> , <i>Ophiopogon tuber</i> , <i>Schisandra fruit</i> , <i>Sparganium rhizome</i> , <i>Curcuma rhizome</i> , fossilized bones of <i>Stegodon</i> , <i>Oyster shell</i> , <i>P. vulgaris</i> , <i>Astragalus root</i> )	Thyroxine	RCT	60	2	(1) ↑ ( $P<0.05$ ) (2) ↓ ( $P<0.05$ ) (3) ↓ ( $P<0.05$ )
Chen and Li, 2022 [28]	Modified Ban Xia Hou Pu Tang (Ingredients: <i>P. ternata</i> , <i>M. officinalis</i> , <i>P. frutescens</i> leaf, <i>Poria cocos</i> , <i>Z. officinale</i> , <i>P. vulgaris</i> , <i>Ostrea gigas</i> , <i>B. chinense</i> , <i>C. reticulata</i> peel, <i>Ligusticum chuanxiong</i> , <i>S. ningpoensis</i> , <i>G. uralensis</i> )	Not	RCT	68	2	(1) ↑ ( $P<0.01$ ) (7) ↑ ( $P<0.01$ )
Feng et al., 2019 [29]	Basic treatment: Health education, low-iodine diet, personal peace of mind + Xia Gu Xiao Ying powder (ingredients: <i>Bupleuri radix</i> , <i>Angelicae sinensis radix</i> , <i>Paeoniae radix alba</i> , <i>Atractylodes macrocephalae rhizoma</i> , <i>Poria cocos</i> , <i>Prunellae spica</i> , <i>W. extensa</i> , <i>Ostrea concha</i> , <i>Herba seu radix Ophiopogonis</i> , <i>Scutellariae radix</i> , <i>Glycyrrhizae radix</i> )	Basic treatment	RCT	80	2	(3) ↓ ( $P<0.05$ )
Liu, 2019 [30]	Yi Qi Hua Yu Fang (ingredients: <i>A. membranaceus</i> , <i>C. pilosula</i> , <i>Poria cocos</i> , <i>A. macrocephala</i> , <i>G. littoralis</i> , <i>M. alba</i> , <i>Lablab semen album</i> , <i>T. kirilowii</i> , <i>L. lucidum</i> , <i>O. japonicus</i> , <i>P. sibiricum</i> , <i>B. striata</i> , <i>W. extensa</i> , <i>Platycodon grandiflorus</i> , <i>G. glabra</i> )	Thyroxine	RCT	117	6	(1) ↑ ( $P<0.01$ ) (2) ↓ ( $P<0.05$ ) (3) ↓ ( $P<0.05$ )
Yao, 2017 [31]	Hua Tan Qu Yu San Jie Fang (ingredients: <i>L. japonica</i> , <i>S. ningpoensis</i> , <i>F. cirrhosa</i> , <i>F. vesiculosus</i> , <i>O. edulis</i> , <i>P. ternata</i> , <i>C. reticulata</i> , <i>S. miltiorrhiza</i> )	Thyroxine	RCT	100	39	(1) ↑ ( $P<0.01$ ) (2) ↓ ( $P<0.05$ ) (3) ↓ ( $P<0.05$ )

↑: Efficacy (value) increases, ↓: Value decreases, (1): Treatment response rate, (2): Maximum nodule diameter after treatment, (3): Thyroid volume after treatment, (4): FT3 levels after treatment, (5): FT4 levels after treatment, (6): Posttreatment TSH levels, (7): TCM syndrome score (24), (8): TGF-β1, (9): VEGF, (10): IFN-γ, (11): IGF-γ, (12): Malignant transformation and (13): IL-4. FT: Free thyroxine, TSH: Thyroid-stimulating hormone, TGF-β1: Transforming growth factor-beta 1, VEGF: Vascular endothelial growth factor, IFN-γ: Interferon-gamma, IGF-γ: Insulin-like growth factor-γ, IL-4: Interleukin-4, TCM: Traditional Chinese medicine, RCT: Randomized controlled trial, *M. pentadactyla*: *Manis pentadactyla*, *G. scabra*: *Gentiana scabra*, *A. julibrissin*: *Albizia julibrissin*, *P. ternata*: *Pinellia ternata*, *M. officinalis*: *Magnolia officinalis*, *Z. officinale*: *Zingiber officinale*, *P. frutescens*: *Perilla frutescens*, *P. vulgaris*: *Prunella vulgaris*, *B. chinense*: *Bupleurum chinense*, *C. reticulata*: *Citrus reticulata*, *S. ningpoensis*: *Scrophularia ningpoensis*, *G. uralensis*: *Glycyrrhiza uralensis*, *W. extensa*: *Wolfiporia extensa*, *A. membranaceus*: *Astragalus membranaceus*, *C. pilosula*: *Codonopsis pilosula*, *A. macrocephala*: *Atractylodes macrocephala*, *G. littoralis*: *Glehnia littoralis*, *M. alba*: *Morus alba*, *T. kirilowii*: *Trichosanthes kirilowii*, *L. lucidum*: *Ligustrum lucidum*, *O. japonicus*: *Ophiopogon japonicus*, *P. sibiricum*: *Polygonatum sibiricum*, *B. striata*: *Bletilla striata*, *L. japonica*: *Laminaria japonica*, *F. cirrhosa*: *Fritillaria cirrhosa*, *F. vesiculosus*: *Fucus vesiculosus*, *O. edulis*: *Ostrea edulis*, *P. ternata*: *Pinellia ternata*, *S. miltiorrhiza*: *Salvia miltiorrhiza*

the control group, with significant differences observed in hormone levels and related factors.

Zhao et al. (2017) [38] discovered that combining Xiao Zhong San Jie Fang (消腫散結湯) with external application of Hu Yu San (化瘀散外敷) reduced levels of VEGF, IGF-γ, and TGF-β1, thereby reducing nodular swelling [Table 3].

### Traditional Chinese medicine patch therapy

External treatment in TCM is a method of using herbal medicine topically on the skin to achieve therapeutic effects, which has a long history in TCM.

According to Kong's study [39], the use of herbal medicine patches effectively promotes a reduction in TN

**Table 3: Traditional Chinese medicine combined with Western medicine treatment**

Author/year	Intervention/medication		Study design	Number of patients	Duration	Results of the experimental group compared to the control group
	Experimental group	Control group				
Wang and Li, 2014 [32]	Thyroxine + mSan Jie Ping Ying Fang (ingredients: <i>P. vulgaris</i> , <i>Arisaema cum bile</i> , <i>P. ternata</i> , <i>F. vesiculosus</i> , <i>L. japonica</i> , <i>O. edulis</i> , <i>Sparganium stoloniferum</i> , <i>C. zedoaria</i> , <i>A. sinensis</i> , <i>C. reticulata</i> , <i>F. cirrhosa</i> )	Thyroxine	RCT	185	3 months/ 6 months	(2) ↓ (3) ↓
Wang, 2020 [33]	Thyroxine + Ying Liu Xiao San Tang (ingredients: <i>A. membranaceus</i> , <i>C. pilosula</i> , <i>P. vulgaris</i> , <i>F. thunbergii</i> , <i>G. littoralis</i> , <i>C. rotundus</i> , <i>S. divaricata</i> , Pumice stone, <i>T. kirilowii</i> , <i>A. stricta</i> , <i>S. miltiorrhiza</i> , <i>C. aurantium</i> )	Thyroxine	RCT	72	19 months	(2) ↓ (3) ↓ (4) ↓ (6) ↓
Wang, 2017 [34]	Thyroxine + San Zhong San Jie Tang (ingredients: <i>C. zedoaria</i> , <i>M. pentadactyla</i> , <i>P. vulgaris</i> , <i>C. reticulata</i> , <i>M. officinalis</i> , <i>C. longa</i> , <i>Ligusticum chuanxiong</i> , <i>P. polyphylla</i> , <i>F. thunbergii</i> , <i>G. glabra</i> )	Thyroxine	RCT	42	18 months	(1) ↑ (3) ↓ (6) ↓
Han et al., 2021 [35]	Thyroxine + Yi Qi San Jie Tang (ingredients: <i>A. membranaceus</i> , <i>P. heterophylla</i> , <i>O. japonicus</i> , <i>S. chinensis</i> , <i>B. chinense</i> , <i>C. aurantium</i> , <i>C. yanhusuo</i> , <i>C. longa</i> , <i>C. longa</i> , <i>A. lappa</i> , <i>C. cassia</i> , <i>H. erinaceus</i> , <i>P. vulgaris</i> , <i>F. thunbergii</i> )	Thyroxine	RCT	120	3 months	(3) ↓ (7) ↓
Xiong and Han, 2018 [36]	Thyroxine + Chai Bei Er Chen Tang (Ingredients: <i>B. chinense</i> , <i>F. thunbergii</i> , <i>P. ternata</i> , <i>C. reticulata</i> , <i>Poria cocos</i> , <i>P. vulgaris</i> , <i>C. reticulata</i> , <i>G. sinensis</i> , <i>S. alba</i> , <i>C. aurantium</i> )	Thyroxine	RCT	72	12 months	(1) ↑ (2) ↓ (12) ↓
Yang, 2022 [37]	Thyroxine + Yi Qi Hua Yu Fang	Thyroxine	RCT	104	12 months	(1) ↑ (4) ↑ (5) ↑ (6) ↓ (9) ↓ (10) ↑ (13) ↓
Zhao et al., 2017 [38]	Xiao Zhong San Jie Tang + Hua Yu powder for external application (Hua Yu powder for external application) (ingredients: <i>Borneolum Syntheticum</i> , <i>P. vulgaris</i> , <i>P. ternata</i> , <i>Ostrea gigas</i> , <i>C. longa</i> , <i>R. palmatum</i> )	Not	RCT	128	1.5 months	(8) ↑ (9) ↓ (11) ↓

↑: Efficacy (value) increases, ↓: Value decreases, (1): Treatment response rate, (2): Maximum nodule diameter after treatment, (3): Thyroid volume after treatment, (4): FT3 levels after treatment, (5): FT4 levels after treatment, (6): Posttreatment TSH levels, (7): TCM syndrome score (24), (8): TGF-β1, (9): VEGF, (10): IFN-γ, (11): IGF-γ, (12): Malignant transformation and (13): IL-4. FT: Free thyroxine, TSH: Thyroid-stimulating hormone, TGF-β1: Transforming growth factor-beta 1, VEGF: Vascular endothelial growth factor, IFN-γ: Interferon-gamma, IGF-γ: Insulin-like growth factor-γ, IL-4: Interleukin-4, TCM: Traditional Chinese medicine, RCT: Randomized controlled trial, *P. vulgaris*: *Prunella vulgaris*, *P. ternata*: *Pinellia ternata*, *F. vesiculosus*: *Fucus vesiculosus*, *O. edulis*: *Ostrea edulis*, *C. zedoaria*: *Curcuma zedoaria*, *A. sinensis*: *Angelica sinensis*, *C. reticulata*: *Citrus reticulata*, *F. cirrhosa*: *Fritillaria cirrhosa*, *A. membranaceus*: *Astragalus membranaceus*, *C. pilosula*: *Codonopsis pilosula*, *G. littoralis*: *Glehnia littoralis*, *C. rotundus*: *Cyperus rotundus*, *S. divaricata*: *Saposhnikovia divaricata*, *T. kirilowii*: *Trichosanthes kirilowii*, *A. stricta*: *Adenophora stricta*, *S. miltiorrhiza*: *Salvia miltiorrhiza*, *C. aurantium*: *Citrus aurantium*, *M. pentadactyla*: *Manis pentadactyla*, *M. officinalis*: *Magnolia officinalis*, *P. polyphylla*: *Paris polyphylla*, *G. glabra*: *Glycyrrhiza glabra*, *P. heterophylla*: *Pseudostellaria heterophylla*, *O. japonicus*: *Ophiopogon japonicus*, *S. chinensis*: *Schisandra chinensis*, *C. yanhusuo*: *Corydalis yanhusuo*, *A. lappa*: *Arctium lappa*, *C. cassia*: *Cinnamomum cassia*, *H. erinaceus*: *Hericium erinaceus*, *B. chinense*: *Bupleurum chinense*, *G. sinensis*: *Gleditsia sinensis*, *S. alba*: *Sinapis alba*, *R. palmatum*: *Rheum palmatum*, *L. japonica*: *Laminaria japonica*, *F. thunbergii*: *Fritillaria thunbergii*, *C. longa*: *Curcuma longa*, *P. ternata*: *Pinellia ternata*

volume, alleviates clinical symptoms, and has a high level of safety.

Jiang et al. [40] found significant differences in clinical efficacy and changes in the maximum transverse diameter of TNs after

3 months of treatment with herbal medicine patches. The efficacy was significantly improved, and the nodule volume was noticeably reduced. The application method of herbal medicine patches involves applying an appropriate amount of ointment to the center of a medical adhesive patch, which is then placed on both sides of the patient's thyroid gland in the neck. Substances such as alcohol, honey, and sesame oil can be used as excipients [Table 4].

### Chinese medicine is taken internally and treated with external patch therapy

Through TCM pattern differentiation, the combination of oral herbal medicine and external application of herbal medicine can achieve a synergistic effect, shortening the course of the disease and alleviating patients' suffering and anxiety.

According to Wang and Wang study [41], the use of Xiao Ying Tang (消癭散) combined with herbal ointment for external application in patients with BTNs can reduce nodule size and restore thyroid function.

In Wang *et al.*'s study [42], it was found that in patients with phlegm-stasis type TNs, the combination of Xia Ling Xiao Ying Tang (夏稜消癭湯) and Huang Yao Zi Gao plaster (黃藥子膏貼) for 3 months significantly improved symptoms, reduced nodule volume and quantity, and decreased TGF- $\beta$ 1 levels.

Qin *et al.*'s study [43] demonstrated that in patients with BTNs, the combination of oral Jia Yi Fang (甲一方) and external application of Jin Huang Gao (外敷金黃膏) could

**Table 4: Traditional Chinese medicine patch therapy**

Author/year	Intervention/medication		Study design	Number of patients	Duration	Results of the experimental group compared to the control group
	Experimental group	Control group				
Kong, 2022 [39]	TCM patches (ingredients: <i>C. reticulata</i> , <i>Ligusticum chuanxiong</i> , <i>P. vulgaris</i> , <i>C. longa</i> , <i>C. longa</i> )	Not	RCT	80	3 months	(1) $\uparrow$ (2) $\downarrow$
Jiang <i>et al.</i> , 2017 [40]	TCM patch (ingredients: <i>C. reticulata</i> , <i>Ligusticum chuanxiong</i> , <i>P. vulgaris</i> , <i>C. longa</i> )	Not	RCT	60	12 months	(1) $\uparrow$ (2) $\downarrow$

$\uparrow$ : Efficacy (value) increases,  $\downarrow$ : Value decreases, (1): Treatment response rate, (2): Maximum nodule diameter after treatment, (3): Thyroid volume after treatment, (4): FT3 levels after treatment, (5): FT4 levels after treatment, (6): Posttreatment TSH levels, (7): TCM syndrome score (24), (8): TGF- $\beta$ 1, (9): VEGF, (10): IFN- $\gamma$ , (11): IGF- $\gamma$ , (12): Malignant transformation and (13): IL-4. FT: Free thyroxine, TSH: Thyroid-stimulating hormone, TGF- $\beta$ 1: Transforming growth factor-beta 1, VEGF: Vascular endothelial growth factor, IFN- $\gamma$ : Interferon-gamma, IGF- $\gamma$ : Insulin-like growth factor- $\gamma$ , IL-4: Interleukin-4, TCM: Traditional Chinese medicine, RCT: Randomized controlled trial, *P. vulgaris*: *Prunella vulgaris*, *C. longa*: *Curcuma longa*, *C. reticulata*: *Citrus reticulata*

**Table 5: Chinese medicine is taken internally and treated with external patch therapy**

Author/year	Intervention/medication		Study design	Number of patients	Duration	Results of the experimental group compared to the control group
	Experimental group	Control group				
Wang and Wang, 2019 [41]	Xiao Ying Tang (ingredients: <i>P. vulgaris</i> , <i>C. longa</i> , <i>Dendrobium officinale</i> , <i>P. ternata</i> , <i>R. ternatus</i> , <i>C. longa</i> , sodium sulfate) + Chinese medicine external gel	Not	Case report	1	15 days	(1) $\uparrow$ (3) $\downarrow$
Wang <i>et al.</i> , 2020 [42]	Thyroxine + Xia Ling Xiao Ying Tang (ingredients: <i>P. vulgaris</i> , <i>C. longa</i> , <i>Sparganium stoloniferum</i> , <i>Ligusticum chuanxiong</i> , <i>A. sinensis</i> , <i>F. thunbergii</i> , <i>P. ternata</i> , <i>F. suspensa</i> , <i>C. reticulata</i> , <i>C. reticulata</i> , <i>G. uralensis</i> ) + Huang Yao Zi ointment (ingredients: <i>D. bulbifera</i> , <i>Borneolum syntheticum</i> , <i>C. longa</i> , <i>L. japonica</i> , <i>Z. officinale</i> , <i>Glycerinum</i> , <i>Mel</i> )	Thyroxine	RCT	90	3 months	(1) $\uparrow$ (2) $\downarrow$ (7) $\downarrow$ (8) $\uparrow$
Qin <i>et al.</i> , 2019 [43]	Jia 1 Fang + Jin Huang Gao	Not	RCT	80	45 days	(1) $\uparrow$ (3) $\downarrow$
Chi, 2019 [44]	TCM patches + Xiao Jie San Ying Tang (ingredients: <i>P. vulgaris</i> , <i>Sparganium stoloniferum</i> , <i>C. longa</i> , <i>B. chinense</i> , <i>Ostrea gigas</i> , <i>Ligusticum chuanxiong</i> , <i>C. reticulata</i> , <i>C. reticulata</i> , <i>F. thunbergii</i> , <i>P. ternata</i> , <i>G. uralensis</i> )	Not	Case-control	42	12 weeks	(2) $\downarrow$ (7) $\downarrow$

$\uparrow$ : Efficacy (value) increases,  $\downarrow$ : Value decreases, (1): Treatment response rate, (2): Maximum nodule diameter after treatment, (3): Thyroid volume after treatment, (4): FT3 levels after treatment, (5): FT4 levels after treatment, (6): Posttreatment TSH levels, (7): TCM syndrome score (24), (8): TGF- $\beta$ 1, (9): VEGF, (10): IFN- $\gamma$ , (11): IGF- $\gamma$ , (12): Malignant transformation and (13): IL-4. FT: Free thyroxine, TSH: Thyroid-stimulating hormone, TGF- $\beta$ 1: Transforming growth factor-beta 1, VEGF: Vascular endothelial growth factor, IFN- $\gamma$ : Interferon-gamma, IGF- $\gamma$ : Insulin-like growth factor- $\gamma$ , IL-4: Interleukin-4, RCT: Randomized controlled trial, TCM: Traditional Chinese medicine, *P. vulgaris*: *Prunella vulgaris*, *C. longa*: *Curcuma longa*, *P. ternata*: *Pinellia ternata*, *R. ternatus*: *Ranunculus ternatus*, *A. sinensis*: *Angelica sinensis*, *F. thunbergii*: *Fritillaria thunbergii*, *F. suspensa*: *Forsythia suspensa*, *C. reticulata*: *Citrus reticulata*, *G. uralensis*: *Glycyrrhiza uralensis*, *Z. officinale*: *Zingiber officinale*, *B. chinense*: *Bupleurum chinense*

significantly reduce nodules, with a higher overall efficacy rate compared to the control group.

Chi [44] observed the clinical efficacy of TCM herbal patches combined with Xiao Jie San Ying Tang (消結散癭湯) in treating TNs, which resulted in a reduction in nodule diameter and improvement in TCM symptoms and signs [Table 5].

According to the research findings, herbal medicine has been shown to reduce TNs without significant adverse reactions [45]. The formation of TNs is primarily influenced by factors such as qi stagnation, phlegm stagnation, and blood stasis, as well as environmental, dietary, and emotional changes. The herbal medicines used in TCM treatment are adjusted based on the patient's

TCM symptoms, with the main goal of clearing phlegm, promoting liver qi circulation, regulating qi and blood, and promoting blood circulation and eliminating stasis. According to clinical trials conducted, the 17 most frequently used herbs include *Pinellia*, *Prunella vulgaris*, *Curcuma zedoaria*, *Bupleurum*, *Atractylodes macrocephala*, *Salvia miltiorrhiza*, *Angelica sinensis*, *Citrus reticulata*, *Panax notoginseng*, *Codonopsis pilosula*, *Dendrobium*, *Ligusticum chuanxiong*, *Seaweed*, *Poria cocos*, *Paeonia lactiflora*, and *Cyperus rotundus*, among others. These herbs possess various pharmacological actions, including anti-inflammatory, anti-tumor, immune-regulating, and blood-activating properties [Table 6].

**Table 6: Types, pharmacology, and frequencies of herbal medicine mentioned in the aforementioned studies**

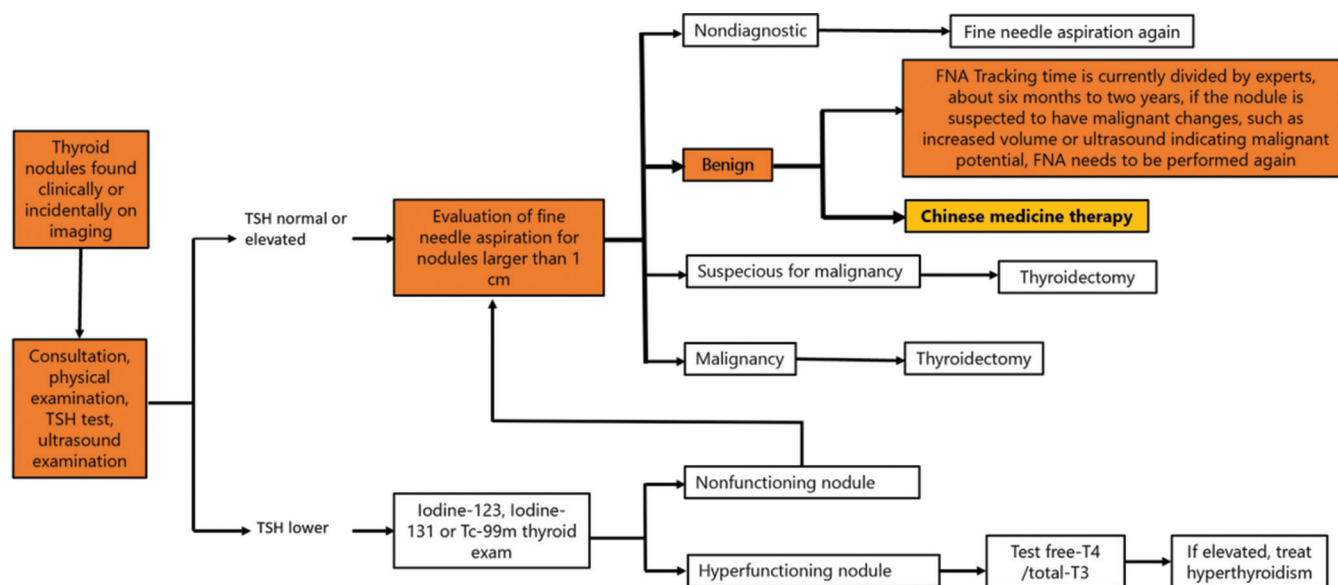
Drug name	Pharmacological action	Frequency (%)
Ban Xia ( <i>Pinelliae rhizoma</i> )	Alleviating inflammation and tumors caused by TNs [46]	6 (8)
Xia Ku Cao ( <i>Prunellae spica</i> )	Regulating blood lipid, anti-inflammatory, and anti-tumor [47]	6 (8)
E Zhu ( <i>Curcuma rhizoma</i> )	Anti-tumor, anti-thrombotic, and anti-inflammatory analgesic [48]	5 (7)
San Qi ( <i>Notoginseng radix et rhizoma</i> )	Anti-inflammatory, antioxidant, and promoting blood circulation [49]	4 (5)
Chai Hu ( <i>Bupleuri radix</i> )	Regulating the immune system and anti-inflammatory [50]	3 (4)
Bai Zhu ( <i>Atractylodes macrocephalae rhizoma</i> )	Anti-inflammatory, analgesic, and immune regulation [51]	3 (4)
Dan Shen ( <i>Salviae Miltiorrhizae radix et rhizoma</i> )	Anti-inflammatory, antioxidant, and promoting blood circulation [49]	3 (4)
Dang Gui ( <i>Angelicae sinensis radix</i> )	Nourishing blood, regulating immunity, and promoting blood circulation [52]	3 (4)
Qing Pi ( <i>Citri reticulatae pericarpium viride</i> )	Relieving meridian blockage, promoting blood circulation, and anti-inflammatory [53]	3 (4)
Dang Shen ( <i>Codonopsis radix</i> )	Tonifying qi and regulating immunity [54]	2 (3)
Shi Hu ( <i>Dendrobii caulis</i> )	Anti-inflammatory, antioxidant, and immune-modulatory effects [55]	2 (3)
Chuan Shan Jia ( <i>Manis squama</i> ) (“Not allowed for use”)	Anti-inflammatory and immune-modulatory effects [56]	2 (3)
Chuan Xiong ( <i>Chuanxiong rhizoma</i> )	Anti-inflammatory, antibacterial, anti-proliferative, and pro-apoptotic activity [57]	2 (3)
Hai Zao ( <i>Sargassum</i> )	Alleviating inflammation and tumors caused by TNs [58]	2 (3)
Fu Ling ( <i>Poria</i> )	Regulating immunity and diuresis [59]	2 (3)
Bai Shao ( <i>Paeoniae radix alba</i> )	Activating the nervous and immune systems [60]	2 (3)
Xiang Fu ( <i>Cyperus rhizoma</i> )	Promoting blood circulation and relieving pain [61]	2 (3)
Hai Dai ( <i>L. japonica</i> )	Anti-thyroid tumor [62]	1 (1)
Bai Hua She She Cao ( <i>H. diffusa</i> )	Anti-tumor and immune-modulatory effects [63]	1 (1)
Huang Yao Zi ( <i>D. bulbifera</i> )	Anti-tumor and immune-modulatory effects [64]	1 (1)
Other		19 (26)
Total		74 (100)

*D. bulbifera*: *Dioscorea bulbifera*, *L. japonica*: *Laminaria japonica*, *H. diffusa*: *Hedyotis diffusa*, TNs: Thyroid nodules

**Table 7: A comparison of advantages and disadvantages of traditional Chinese medicine and Western medicine in the treatment of thyroid nodules**

Western medicine	TCM
<b>Advantages</b>	
1. Emphasizes scientific evidence and clinical trials to ensure the effectiveness and feasibility of treatment methods	1. Has lower side effects and risks
2. Capable of effectively surgically treating nodules with malignant tendencies, reducing the risk of cancer cells	2. Maintains thyroid function balance and health. There is a wide variety of medications available with multiple therapeutic effects
3. Conducts regular examinations and clinical observations to effectively manage benign nodules, avoiding unnecessary surgeries and treatments	3. Provides personalized treatment plans, emphasizing overall health and mind-body balance
<b>Disadvantages</b>	
1. Patient fear and posttreatment side effects, requiring long-term medication for substitution therapy	1. Personal experience takes precedence, and the effectiveness is uncertain
2. Potential for over-treatment, leading to unnecessary surgical procedures and treatment risks	2. It requires a longer treatment duration to observe noticeable effects
3. Risk of thyroid function impairment	3. Lack of large-scale and systematic clinical research

TCM: Traditional Chinese medicine



**Figure 2:** Process algorithm of traditional Chinese medicine and Western medicine for the treatment of thyroid nodules

## ADVANTAGES AND DISADVANTAGES

TCM and Western medicine have different advantages and disadvantages in the treatment of TNs [Table 7].

## CONCLUSION

TCM research offers multiple methods for preventing and treating TNs. Chinese herbal medicine shows potential for clinical application, effectively preventing benign nodules with high compliance and minimal side effects, providing safer and more effective treatment options. Future research can explore the pharmacological effects and treatment mechanisms of commonly used Chinese herbs, such as their anti-inflammatory, anti-tumor, immune modulation, and blood circulation promotion properties. These TCM research methods can help prevent the formation of TNs, offering corresponding treatment measures to alleviate symptoms and improve patients' health.

Based on clinical research data and experience in TCM, it is recommended to incorporate TCM into the treatment guidelines for TNs and establish new treatment algorithms [Figure 2].

### Data availability statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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### Conflicts of interest

There are no conflicts of interest.

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