

Research progress of traditional Chinese medicine in the treatment of benign thyroid nodules

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Abstract. Thyroid nodules are common diseases of the endocrine system, which belong to the category of "goiter" in Traditional Chinese Medicine (TCM). The TCM treatment of benign thyroid nodules takes syndrome differentiation and treatment as the core, forming a multi-therapy system including oral administration of Chinese herbal medicine and external treatment, with continuous deepening of relevant research and application. This paper systematically sorts out the clinical application status of various characteristic TCM therapies in the treatment of benign thyroid nodules, and looks forward to the prospects around the optimization of clinical diagnosis and treatment and the explanation of mechanisms of action, aiming to provide ideas for the TCM treatment of benign thyroid nodules.

Keywords: benign thyroid nodules, goiter, Traditional Chinese Medicine (TCM)

1. Introduction

Thyroid nodules are discrete lesions caused by abnormal proliferation of thyroid follicular epithelial cells, clinically manifested as solitary or multiple lesions. In recent years, the detection rate of thyroid nodules has been on the rise [1]. Although most thyroid nodules are benign, some nodules may grow progressively and compress surrounding tissues such as the trachea and esophagus, and a few may have a risk of malignant transformation. Therefore, a scientific and systematic diagnosis and treatment management system for thyroid nodules is still needed. Modern medical treatments for thyroid nodules, including regular follow-up, iodine-131 therapy, surgical resection, and levothyroxine suppression therapy, still have certain limitations. For example, surgical resection may lead to complications such as hypothyroidism, and levothyroxine suppression therapy may cause side effects on the heart and bones. TCM has a long history of treating benign thyroid nodules, including various therapies such as oral administration of Chinese herbal medicine, plaster application, and acupuncture, and has unique advantages in clinical efficacy and safety. Based on this, systematically sorting out the clinical research evidence of TCM in the treatment of benign thyroid nodules and exploring its mechanisms of action can provide evidence-based basis for the clinical promotion of safe and effective TCM intervention programs, which has important clinical value.

2. Etiology and pathogenesis of thyroid nodules

Thyroid nodules belong to the category of "goiter" in TCM. Shi Ming (Explaining Names) states: "Ying (goiter) means embracing, as it embraces the larynx in the neck" [2], indicating that goiter is a type of disease characterized by swelling on both sides of the laryngeal prominence in the front of the neck. Four factors—emotion, diet, geographical environment, and physical constitution—are closely related to its occurrence. Among the various pathogenic factors of thyroid nodules, emotional disorders are one of the most common inducing factors in clinical practice. Yan Shi Ji Sheng Fang (Yan's Prescriptions for Benefiting Life) records: "Most goiters and tumors are caused by immoderate joy and anger, and excessive worry and anxiety" [3]. Long-term emotional distress can lead to stagnation of liver qi; stagnant liver qi invades the spleen, affecting the transportation and distribution function of the spleen and stomach, resulting in internal accumulation of phlegm-dampness; the combination of phlegm-dampness and qi stagnation leads to blood stasis over time, which is the main pathogenesis of nodule formation. Improper diet can directly damage the spleen and stomach, leading to endogenous phlegm-dampness. Unfavorable geographical environment is an important external factor for the occurrence of goiter, which is closely related to the onset of this disease. Zhu Bing Yuan Hou Lun (Treatise on the Etiology and Symptoms of Diseases) clearly records: "Those who drink more sandy water will have sand combining with qi, binding under the neck, and also forming goiter" [4]. Residents in mountainous areas, due to the high sand content in water quality, the qi of sand and gravel combines with qi and blood in the human body, accumulating in the neck, which can also form goiter. In addition, internal factors such as overwork and physical weakness cannot be ignored. Jin Kui Yao Lue (Synopsis of the Golden Chamber) states: "Suffering from borborygmus, madao (scrofula of the axilla) and xiaying (scrofula beside the neck) are all caused by overwork" [5], directly pointing out that excessive fatigue can lead to insufficient healthy qi of the body and induce this disease.

Modern TCM physicians have diverse understandings of the pathogenesis of thyroid nodules, but most focus on treatment based on the liver and spleen. Some scholars have proposed that the occurrence of thyroid nodules is caused by the imbalance of spleen transportation and distribution based on the theory of "spleen transportation balance" [6]. Dysfunction of the transportation function of the spleen in the middle jiao can affect the liver wood; stagnant earth (spleen) leads to stagnant wood (liver), resulting in endogenous qi stagnation, phlegm coagulation, and blood stasis, which accumulate on the side of the neck to form goiter. Song Yujiao et al. [7], under the guidance of the theory of "liver governing dispersion and discharge", believe that the dysfunction of liver dispersion and discharge leading to the production of various pathological products is the core pathogenesis of thyroid nodules, and the production of pathological products can hinder the dispersion and discharge of the liver, forming an interactive relationship between the two. Lan Tian et al. [8], based on the three-layer dynamic syndrome differentiation and treatment theory of "qi movement - zang-fu organs - pathogenic factors", propose that the onset of thyroid nodules starts with unsmooth qi movement, takes insufficiency of the liver, spleen, and kidney as the root, and phlegm-blood stasis as the branch; the combined effect of the three promotes the formation of goiter nodules. The research team of Zhou Zhongying [9], from the perspective of combining pathological factors and syndrome classification, believes that the main pathological factors leading to thyroid nodules are deficiency, stagnation, phlegm, blood stasis, and fire, and classifies the syndromes into yang deficiency type, qi stagnation type, phlegm-dampness type, blood stasis type, and damp-heat type according to the differences in pathological mechanisms and clinical syndromes.

3. TCM treatment of benign thyroid nodules

TCM has various and distinctive treatment methods for benign thyroid nodules, which can be flexibly selected according to the patient's condition, physical constitution, and treatment needs. It mainly includes internal treatment methods, such as the dialectical use of classic prescriptions, empirical prescriptions, and Chinese patent medicines, as well as external treatment methods, such as acupuncture, auricular point pressing with beans, plaster application, and iontophoresis.

3.1. Internal TCM treatments

3.1.1. Classic prescriptions

Classic TCM prescriptions for the treatment of thyroid nodules have been respected by TCM physicians of all dynasties due to their long clinical application history and definite curative effect. Currently, commonly used classic prescriptions include Haizao Yuhu Decoction, Prunella Vulgaris Decoction, Banxia Houpo Decoction, Sihai Shuyu Pill, Chaihu Shugan Powder, and Xiaoluo Pill [10-12]. Haizao Yuhu Decoction, derived from Wai Ke Zheng Zong (Orthodox External Medicine), is famous for its effect of resolving phlegm and dispersing nodules [13]. A randomized controlled trial by Yu Longlong et al. [14] using modified Haizao Yuhu Decoction for the treatment of thyroid nodules showed that patients in the TCM group had reduced diameter and volume of thyroid nodules, improved clinical symptoms, and good results. Clinical practice by Wang Qiyou et al. [15] showed that for patients with benign thyroid nodules, dialectical addition and subtraction treatment with Prunella Vulgaris Decoction combined with Haizao Yuhu Decoction achieved significant clinical efficacy by synergistically soothing the liver and regulating qi, resolving phlegm and dispersing nodules. Banxia Houpo Decoction, from Jin Kui Yao Lue (Synopsis of the Golden Chamber), has the effects of soothing qi movement and resolving phlegm and dispersing nodules according to its pharmacology, so it has a certain curative effect on patients with goiter of qi stagnation and phlegm coagulation type. Shan Changfei et al. [10] found that modified Banxia Houpo Decoction in the treatment of thyroid nodules can reduce the diameter of nodules, and the incidence of adverse reactions is lower than that in the levothyroxine treatment group. Li Lan [16] treated patients with thyroid nodules with Banxia Houpo Decoction, and observed an effective rate of 86.67% after six months; most patients had reduced nodule diameter and improved uncomfortable symptoms.

In recent years, the mechanisms of action of classic prescriptions have been further verified and clarified in modern experiments. Lü Yanmin et al. [17] found that both Haizao Yuhu Decoction and the modified Haizao-Gancao combination can increase the expression level of Bax mRNA and promote cell apoptosis. Based on network pharmacology research, Huang Tafa et al. [18] found that various active components of Chinese herbs in Xiaoluo Pill synergistically regulate the thyroid hormone pathway, cancer malignant transformation pathway, and PI3K-Akt pathway, playing an important role in the treatment of thyroid nodules. The combination of Prunella Vulgaris Decoction and Xiaoluo Pill in the treatment of benign thyroid nodules can effectively reduce the number and volume of nodules, and its mechanism of action may be related to regulating the body's AMPK/mTOR signaling pathway, improving cellular energy metabolism, and proliferative imbalance [19]. In addition, studies have shown that the main active components of Banxia Houpo Decoction include luteolin, baicalein, and β -sitosterol, and its mechanisms of action involve multiple signaling pathways such as PI3K-Akt, interleukin-17, and cancer-related pathways [20], reflecting the multi-target and multi-pathway therapeutic characteristics of TCM.

3.1.2. Empirical prescriptions

While inheriting the treatment experience of ancient physicians, modern TCM physicians have continuously improved the treatment prescriptions for thyroid nodules combined with modern medical research, and

innovated many effective self-formulated empirical prescriptions.

Professor Xie Qin, according to the characteristics of liver stagnation and phlegm coagulation in thyroid nodules, formulated the self-formulated Shugan Huatan Xiaoying Decoction based on modified Erchen Decoction. In the prescription, *Fritillaria thunbergii*, *Prunella vulgaris*, and *Scrophularia ningpoensis* are tumor-resolving drugs, which jointly exert the effects of resolving phlegm and softening hard masses; *Cyperus rotundus* and *Aucklandia lappa* regulate qi movement and relieve liver stagnation; *Citrus reticulata*, *Poria cocos*, *Pinellia ternata*, and *Atractylodes macrocephala* strengthen the spleen and dispel dampness, eliminating the source of endogenous phlegm-dampness; in addition, other drugs dredge collaterals and disperse nodules, astringe yin and soften the liver. Studies have found that after 8 weeks of treatment, it can effectively reduce nodules, improve TCM syndrome scores, and alleviate patients' uncomfortable symptoms [21]. There is also the self-formulated Ziyin Huatan Decoction guided by the treatment principle of taking yin deficiency as the root and nourishing yin as the priority, targeting patients with thyroid nodules of yin deficiency and phlegm-blood stasis type. *Prunella vulgaris*, *Concha Ostreae*, and *Carapax Testudinis* are used as monarch drugs together, assisted by *Scrophularia ningpoensis* and other drugs, to exert the effects of softening hard masses and dispersing nodules, nourishing yin and resolving phlegm. It has also been proven in clinical studies to effectively reduce nodule volume and improve uncomfortable symptoms with definite effects [22]. In addition, many physicians, based on the theoretical framework and practical experience of classic prescriptions, combined with the pathogenic characteristics, physical differences, and syndrome evolution rules of patients with thyroid nodules, have formulated targeted self-formulated prescriptions for goiter, forming individualized treatment plans covering different syndromes such as qi stagnation and phlegm coagulation, phlegm-blood stasis intermingling, hyperactivity of liver fire, and hyperactivity of deficient fire. Relevant clinical applications have achieved definite curative effects, providing rich practical basis for the TCM treatment of this disease [23, 24].

3.1.3. Chinese patent medicines

Chinese patent medicines are widely used in the TCM treatment of thyroid nodules due to their advantages of small dosage form, portability, and ease of use, with high patient compliance. With the gradual deepening of research on the material basis and mechanisms of action of TCM efficacy, the development of Chinese patent medicines based on the screening of core active components and compatibility optimization has become an important development direction in the field of TCM treatment of thyroid nodules. At present, commonly used Chinese patent medicines for the clinical treatment of thyroid nodules include Xiaojin Capsules (Pills), Pingxiao Capsules, Chaixiang Sanjie Granules, Neixiao Luoli Pills, Honghua Xiaoyao Tablets, and *Prunella Vulgaris* Capsules, whose efficacy and mechanisms of action have been confirmed by multiple clinical studies and basic experiments.

The results of a Meta-analysis by Liu Ping et al. [25] showed that Xiaojin Capsules combined with Euthyrox in the treatment of thyroid nodules is superior to the control group in improving the total clinical effective rate and reducing the maximum diameter of nodules. Its mechanism of action may be related to blood circulation-promoting and stasis-resolving drugs such as *Aconiti Kusnezoffii Radix Cocta* improving the body's microcirculation and inhibiting the abnormal proliferation of nodule tissue [26]. Another study found that Pingxiao Capsules in the treatment of thyroid nodules can also effectively reduce the diameter of nodules and downregulate the level of serum Thyroid-Stimulating Hormone (TSH) [27]. In addition, the dialectical application of Chinese patent medicines for thyroid nodules of different syndromes has also achieved definite curative effects. For example, Neixiao Luoli Pills are suitable for thyroid nodules of qi stagnation and phlegm obstruction type, and Honghua Xiaoyao Tablets have shown good clinical effects in the treatment of thyroid nodules of qi stagnation and blood stasis type [28, 29].

Studies by Xu Yulin et al. [30] showed that *Prunella Vulgaris* Capsules can improve the blood circulation of thyroid tissue, promote the operation of qi and blood, and at the same time clear the liver and relieve depression, regulate emotions, thereby inhibiting the formation and development of nodules. Studies by Teng Tao et al. [31] showed that *Chaixiang Sanjie Granules* can inhibit the progression of nodules by downregulating the expression of fibroblast growth factor and reducing the body's oxidative stress response, and its mechanism is related to improving metabolic disorders and inflammatory reactions caused by liver qi stagnation.

3.1.4. Chinese herbal medicines

In the TCM treatment of thyroid nodules, commonly used clinical medicines include *Prunella vulgaris*, *Bupleurum chinense*, *Concha Ostreae*, *Fritillaria thunbergii*, *Cyperus rotundus*, and *Angelica sinensis*. Most of these medicines are bitter, pungent, and sweet in nature, with meridian tropism mainly in the liver, lung, and stomach meridians. Their core effects focus on dispersing nodules and resolving masses, regulating qi and activating blood circulation, resolving phlegm and softening hard masses, which are consistent with the core pathogenesis of "phlegm, qi, and blood stasis" intermingling in thyroid nodules. Specifically, *Prunella vulgaris* is pungent, bitter, and cold in nature, acting on the liver and gallbladder meridians, with core effects of clearing liver fire, dispersing nodules, and reducing swelling. It is an essential medicine for TCM in the treatment of goiter and tumors. *Shen Nong Ben Cao Jing* (Shennong's Classic of Materia Medica) clearly records that it "governs cold-heat, scrofula, mouse fistula, head sores, breaks masses, and disperses goiter and stagnant qi" [32]; *Angelica sinensis* is sweet, pungent, and warm in nature, acting on the liver, heart, and spleen meridians, with effects of nourishing blood and activating blood circulation, and can play a role in resolving stasis and dispersing nodules for thyroid nodules of blood stasis obstruction type; *Fritillaria thunbergii* is bitter and cold in nature, acting on the lung and heart meridians, good at clearing heat and resolving phlegm, dispersing nodules and reducing carbuncles, especially suitable for thyroid nodules caused by phlegm-heat stagnation. In clinical practice, it is necessary to dialectically select TCM medicines with different natures and effects according to the nature of nodules, the patient's physical constitution, and syndrome characteristics to achieve the treatment principle of "treating the root cause of the disease and treating based on syndrome differentiation".

In recent years, research on the mechanisms of action of Chinese herbal medicines in the treatment of thyroid nodules has continued to deepen. Diosgenin, an active component isolated and purified from *Dioscorea bulbifera* L., can improve thyroid enlargement by regulating the protein and mRNA expression levels of Insulin-like Growth Factor-1 (IGF-1), Nuclear Factor- κ B (NF- κ B), and Proliferating Cell Nuclear Antigen (PCNA) in thyroid tissue, and reducing free thyroxine [33]. Quercetin, an active component extracted from *Laminaria japonica* and *Sargassum fusiforme*, can upregulate the expression level of YAP gene, inhibit the abnormal proliferation of thyroid nodule cells and induce their apoptosis, thereby achieving nodule reduction [34]. *Curcuma zedoaria* and *Sparganium stoloniferum* are commonly used pairs of blood-breaking and qi-regulating medicines in clinical TCM. They can improve the body's microcirculation disorders by increasing red blood cell deformability and reducing whole blood viscosity, realizing the efficacy of "breaking blood and regulating qi, dispersing masses and resolving nodules" [35]. Modern studies have shown that *Sparganium stoloniferum* contains active components such as phenylpropanol and flavonoids, which have various pharmacological activities such as anti-tumor, anti-thrombosis, anti-inflammation, analgesia, anti-oxidation, and anti-organ fibrosis; while *Curcuma zedoaria* extract can regulate the balance of cell proliferation and apoptosis by regulating the expression of cyclooxygenase-2 (Cox-2), myeloid cell leukemia 1-1 (Mcl-1), and Bcl-2-associated X protein (Bax) [36]. The main active components of *Prunella vulgaris* inhibit oxidative stress and ferroptosis through the NRF2/GPX4 pathway [37], and also act on autophagy

through the AMPK/mTOR/ULK1 signaling pathway [38]. The two synergistically participate in the balance regulation of proliferation and apoptosis of nodule cells, thereby achieving therapeutic effects.

3.2. External TCM treatments

3.2.1. *Acupuncture and moxibustion*

Acupuncture and moxibustion are important components of characteristic TCM therapies, and have gradually formed a relatively complete theoretical system and rich diagnosis and treatment experience in clinical practice. Clinical statistical data show that the Stomach Meridian of Foot-Yangming and the Large Intestine Meridian of Hand-Yangming are the main meridians selected in the acupuncture treatment of this disease, and acupoints such as Sanyinjiao (SP6), Zusanli (ST36), and Taichong (LR3) are the most commonly used clinical treatment acupoints [39].

In terms of acupoint compatibility and acupuncture method innovation, many scholars have formed distinctive treatment plans. Professor Jin Rui proposed the "Tusan Zhen" (Three Protruding Points) therapy, which is widely used in the treatment of thyroid nodules. This therapy selects Tiantu (CV22), Futu (LI18), and Shuitu (ST10) in the neck as the core acupoint group, following the compatibility principle of "treating protrusion with protrusion points", and exerts therapeutic effects by regulating the operation of qi and blood in the neck meridians. Shao's formula uses Ashi points and Hegu (LI4) combined with Tusan Zhen (Three Protruding Points) for the treatment of thyroid nodules, with obvious effects, which can effectively reduce nodule volume and improve uncomfortable symptoms [40]. The comprehensive acupuncture plan proposed by Hua Yongqin et al. is also quite distinctive: superficial needling is used to stimulate Tanzhong (CV17) to open the chest and regulate qi, harmonize lung qi; filiform needle acupuncture is used at Huantiao (GB30) to strengthen the spleen and dispel dampness, disperse turbid pathogens; at the same time, intradermal needle surrounding needling is performed around the nodule to activate blood circulation and dissipate stasis, soften hard masses and disperse nodules. The combination of multiple methods achieves the effect of treating both symptoms and root causes, with significant clinical efficacy [41]. Professor Chen Yiguo founded the "Sixiang Tiaoqi Acupuncture" (Four-Phase Qi-Regulating Acupuncture), based on the core TCM theory of "qi movement disorder as the root of disease", by accurately selecting specific acupoints for acupuncture to regulate the qi movement of zang-fu organs, restore the dynamic balance of qi ascending, descending, entering, and exiting in the human body, thereby achieving the effects of dredging meridians, activating blood circulation and dissipating stasis, softening hard masses and disperse nodules, realizing the intervention and treatment of thyroid nodules, and achieving good clinical efficacy in clinical application [42]. Li Zhijuan's team used golden needle therapy along the meridian from Quchi (LI11) to Binao (LI14) to treat multiple patients with thyroid nodules. Re-examination results after 3 months of treatment showed that the patients' nodule volume was significantly reduced and clinical symptoms were significantly improved [43]. In addition, treatment plans such as acupuncture combined with oral administration of TCM and fire needle warming penetration are also widely used in clinical practice and have achieved good therapeutic effects.

3.2.2. *Plaster application*

The thyroid gland is located in the superficial area of the neck, providing an anatomical basis for local external application of TCM. The external application of TCM plaster exerts targeted therapeutic effects by directly acting on the local skin of the thyroid gland or related acupoints with active components of medicines, which reach the affected area directly through skin penetration and meridian conduction.

For patients with benign thyroid nodules of qi stagnation and phlegm obstruction type, treatment with Chaihu Sanjie Decoction combined with acupoint application. After 12 weeks, the patients' nodule volume was significantly reduced, TCM syndrome scores were improved, and serum Thyroid-Stimulating Hormone

(TSH) and thyroid-related antibody levels were significantly lower than before treatment, achieving the dual efficacy of nodule reduction and thyroid function regulation [44]. Chai Shufang et al. [45] applied self-formulated TCM plaster locally on the thyroid gland, combined with a TCM directional drug penetration instrument to enhance drug penetration effect. After treatment, the patients' clinical symptoms such as anterior cervical mass, chest tightness, poor appetite, and distension of the chest and hypochondrium were significantly improved, and the maximum diameter of nodules was significantly reduced. Its comprehensive efficacy was superior to that of the simple oral TCM group. In addition, a study by Wang et al. [46] found that the self-formulated external TCM preparation Jiajie Ointment can regulate thyroid hormones and TSH levels, and at the same time inhibit the abnormal activation of the (IL-6, TNF- α , IL-1 β)/JAK2/STAT3/VEGF signaling pathway in thyroid tissue, exerting effects in regulating thyroid function, inhibiting inflammatory reactions, and angiogenesis, providing modern medical evidence support for the mechanism of action of external TCM preparations.

3.2.3. Other external treatments

In addition to acupuncture and moxibustion and plaster application, other external TCM treatments are also widely used in the clinical treatment of thyroid nodules, including auricular point pressing with beans, Chinese herbal medicine packet, and Chinese herbal medicine iontophoresis.

Auricular point pressing with beans is based on the theory that "the ear is the convergence of all meridians". By stimulating specific reflex areas and tender points corresponding to zang-fu organs in the ear, it plays the roles of dredging meridians, harmonizing qi and blood, and balancing zang-fu organ functions. This therapy has the advantages of simple operation, high safety, and no obvious adverse reactions, and is highly accepted by patients, being widely used in the adjuvant treatment of benign thyroid nodules. Tu Chunlian et al. [47] applied *Vaccaria segetalis* seeds to specific acupoints such as the Thyroid point and Shenmen point (AH6) in the ears of patients with thyroid nodules. After treatment, the patients' TCM syndrome scores were significantly improved, and the volume of thyroid nodules was effectively controlled.

Chinese herbal medicine packet therapy is an external TCM treatment based on thermal effect. It wraps decocted TCM with gauze and directly applies it to the affected area. With the help of thermal stimulation, it promotes local blood circulation, accelerates the penetration and absorption of active components of TCM, thereby exerting the effects of activating blood circulation and dissipating stasis, regulating qi and resolving masses, which is consistent with the pathogenesis of "phlegm-blood stasis intermingling" in thyroid nodules. Clinical studies have shown that for patients with thyroid nodules of phlegm-qi-blood stasis syndrome, the comprehensive therapy of Chinese herbal medicine packet combined with auricular point pressing with beans can regulate thyroid function, improve patients' TCM syndromes, and enhance patients' quality of life [48].

Chinese herbal medicine iontophoresis is an innovative external treatment combining TCM theory and modern pharmaceutical technology. This therapy first extracts the core active components of TCM through modern high-efficiency extraction technology, and then uses the directional guidance of medium-frequency pulse current to directly introduce the medicine into the body through the skin barrier, allowing the medicine to penetrate quickly and accurately into the thyroid target tissue, avoiding the loss of efficacy due to gastrointestinal metabolism, and giving full play to the efficacy of TCM. A clinical study conducted by Lu Jun et al. [49] confirmed that the treatment of thyroid nodules with Chinese herbal medicine iontophoresis combined with oral TCM had a total effective rate of 92.11% in the experimental group, which was significantly higher than that in the control group. The results showed that this combined plan can effectively improve patients' clinical symptoms such as anterior cervical discomfort, promote nodule volume reduction, and can be used as an effective adjuvant treatment for thyroid nodules. Another study used Jiayu No.1 Decoction for external application on the neck through iontophoresis to treat patients with thyroid nodules.

After the course of treatment, it was found that this plan can not only effectively reduce the maximum diameter of thyroid nodules, but also significantly improve patients' clinical uncomfortable symptoms, with definite efficacy [50].

4. Conclusion and prospect

TCM treatment of thyroid nodules has a profound theoretical basis and a long clinical practice. Taking the holistic concept as the core and syndrome differentiation and treatment as the guiding principle, it achieves the goals of regulating physical constitution and improving diseases through multiple therapies such as oral administration and external application of TCM, and acupuncture, showing unique advantages in clinical practice. However, the current clinical application and research of TCM in the treatment of thyroid nodules still face many problems to be solved. Firstly, existing studies lack large-sample and long-term follow-up data, and there is a lack of research on indicators such as nodule recurrence rate, long-term complications, and quality of life more than 2 years after treatment, which affects the level of evidence-based medical evidence for TCM treatment. Secondly, the depth of research on mechanisms of action is insufficient, and the regulatory mechanisms at the molecular level have not been fully clarified. Finally, there is a lack of unified standards for clinical diagnosis and treatment, the syndrome differentiation and classification of the disease have certain subjectivity, and the selection of treatment prescriptions and plans also shows individual differences, leading to insufficient standardization of diagnosis and treatment.

Future research can focus on improving the clinical research system and establishing a multi-center, large-sample, long-term follow-up clinical research platform; formulating standardized diagnosis and treatment guidelines for integrated traditional Chinese and Western medicine, standardizing syndrome diagnosis, treatment plans, and efficacy evaluation standards to make TCM diagnosis and treatment more accurate; deepening the research on mechanisms of action, systematically exploring the core targets and signaling pathways of TCM with the help of modern molecular biology technologies; promoting the innovation of diagnosis and treatment technologies, developing new TCM preparations and intelligent diagnosis and treatment equipment, and improving the accuracy and effectiveness of treatment. It is expected that the standardization, individualization, and intelligence of TCM diagnosis and treatment of thyroid nodules can be realized in the future, providing more high-quality integrated traditional Chinese and Western medicine diagnosis and treatment services for patients.

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