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MEDICINAL PLANTS AS ADJUNCTIVE THERAPIES FOR HYPOTHYROIDISM: A COMPREHENSIVE REVIEW OF CLINICAL AND PRECLINICAL EVIDENCE

B. A. Patel[1], B. K. Makwana[1*]

[1]Department of Pharmaceutical Science, Sardar Patel University, Vallabh Vidyanagar - 388 120, Gujarat, India.

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***Corresponding Author**

B. K. Makwana

Department of Pharmaceutical Science, Sardar Patel University, Vallabh Vidyanagar - 388 120, Gujarat, India.

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ABSTRACT

Hypothyroidism is a widespread endocrine disorder where insufficient hormone secretion causes metabolic and cognitive disturbances. While levothyroxine remains the standard treatment, persistent symptoms like fatigue and weight gain drive interest in traditional phytotherapies. This review synthesizes data from peer-reviewed databases and classical Ayurvedic texts to evaluate the efficacy of medicinal plants. Clinical evidence highlights Ashwagandha's ability to significantly increase T3 and T4 levels while reducing Thyroid Stimulating Hormone. Similarly, Guggulu stimulates hormone production and iodine uptake, and Nigella sativa improves thyroid status in Hashimoto's patients by reducing anti-TPO antibodies. Preclinical studies further support the thyrotropic roles of Brahmi and Shigru. These herbs function through antioxidant, adaptogenic, and immunomodulatory mechanisms to modulate the hypothalamic–pituitary–thyroid axis. Although these plants offer promising adjunctive benefits for metabolic and stress-related imbalances, the lack of large-scale clinical trials necessitates further rigorous research to ensure long-term safety and standardization in clinical practice.

KEYWORDS: Hypothyroidism, Phytotherapy, Hypothalamus Pituitary Thyroid axis, Ashwagandha, Guggulu, Brahmi, Thyroid Stimulating Hormone, Ayurveda.

Thyroid disorders are among the most common endocrine diseases globally, affecting millions of individuals each year. Hypothyroidism, a condition characterized by insufficient secretion of thyroid hormone,[1] leads to symptoms such as fatigue, weight gain, cold intolerance, depression, and metabolic disturbances. The prevalence of hypothyroidism has increased significantly due to factors such as autoimmune diseases, iodine deficiency, environmental toxins, and lifestyle stress. It affects metabolic processes, cognitive function, and overall quality of life.[2] In addition, hypothyroidism is 6 times more common in women than in men.[3] Animal thyroid or its extract was used to control the symptoms of hypothyroidism from the 6th century to the early 20th century.[4] Currently, physicians commonly prescribe levothyroxine for patients with hypothyroidism. However, this treatment fails to bring satisfactory results for some patients because it cannot properly control some symptoms such as weight gain, lethargy, mood disorders, and memory impairment.[4-12] Since the use of traditional and complementary medicine has considerably expanded around the world, the World Health Organization (WHO) has emphasized the revival of traditional medicine in different regions of the world over the last 3 decades.[13]

The current standard treatment for hypothyroidism involves the use of synthetic thyroid hormones, such as levothyroxine. While effective, these treatments can have side effects and are dependent on a stable supply chain. This has led to an interest in exploring alternative treatments, including herbal medicines, which may offer a more natural and potentially safer approach to managing hypothyroidism. Herbal medicines have shown promise in improving thyroid function and normalizing thyroid hormone levels. Despite the promising potential of these herbal medicines, there are limitations to their current use. The lack of large-scale, high-quality clinical trials and concerns regarding long-term safety and efficacy need to be addressed through rigorous research. Future studies should focus on validating the benefits and safety of these herbal medicines and exploring their mechanisms of action in greater detail. By addressing these gaps in knowledge, we can better incorporate herbal medicines into treatment protocols, offering patients a natural and potentially safer alternative for managing hypothyroidism.

This review aims to provide a thorough overview of the current state of research on herbal medicines for treating hypothyroidism, discussing their potential benefits, limitations, and future directions. By examining the evidence and identifying areas for further research, we

hope to contribute to the development of more effective and safer treatment options for patients with hypothyroidism.

Traditional Approach for Hypothyroidism

Modern endocrinology recognizes hypothyroidism as a dysfunction of the hypothalamic–pituitary–thyroid (HPT) axis involving impaired thyroid hormone synthesis, altered thyroid-stimulating hormone (TSH) receptor signaling, autoimmune-mediated thyroid destruction, oxidative stress, and inflammatory dysregulation. Several medicinal plants used in Ayurveda, Siddha, Unani, and Traditional Chinese Medicine may influence these molecular pathways through antioxidant, adaptogenic, immunomodulatory, and thyrotropic mechanisms. Phytoconstituents such as withanolides, guggulsterones, bacosides, and thymoquinone have demonstrated the ability to modulate oxidative stress markers, inflammatory cytokines, cortisol signaling, peripheral conversion of T4 to T3, and thyroid hormone biosynthesis.[14-20] Therefore, bridging traditional concepts with molecular endocrinology may provide a scientifically relevant framework for understanding the therapeutic potential of herbal medicines in hypothyroidism. Traditional systems of medicine describe hypothyroidism through functional disturbances in metabolism, energy regulation, and systemic homeostasis. In Ayurveda, the concept of *Agni* represents metabolic transformation and energy utilization, which can be mechanistically correlated with thyroid hormone–mediated regulation of basal metabolic rate, mitochondrial respiration, thermogenesis, and lipid-carbohydrate metabolism. Similarly, the Ayurvedic condition *Galaganda* may be interpreted in the context of thyroid enlargement or goitrous disorders associated with impaired thyroid hormone synthesis.[21-22]

Overview of the HPT Axis

Disruption in this axis leads to thyroid dysfunction, including hypothyroidism.[23] The **figure 1** illustrates the physiological role and systemic effects of thyroid hormones in maintaining normal body homeostasis. Thyroid hormones, primarily triiodothyronine (T3) and thyroxine (T4), synthesized by the thyroid gland under the regulation of the hypothalamic–pituitary–thyroid (HPT) axis, exert widespread metabolic and developmental effects throughout the body. As shown in the figure, these hormones play a crucial role in regulating basal metabolic rate and energy metabolism by influencing carbohydrate, lipid, and protein metabolism. In addition, thyroid hormones are essential for normal growth and development, particularly in neural maturation and skeletal growth.

The diagram further highlights the supportive role of thyroid hormones in maintaining cardiovascular function by regulating heart rate, cardiac output, and vascular resistance. Moreover, thyroid hormones contribute significantly to cognitive performance, mood stabilization, and neurological function through modulation of neurotransmitter activity and cerebral metabolism. Impairment in thyroid hormone production, as observed in hypothyroidism, may therefore result in fatigue, weight gain, depression, cognitive dysfunction, reduced metabolic activity, and cardiovascular abnormalities. Overall, the figure summarizes the broad physiological importance of thyroid hormones and their role in sustaining metabolic, cardiovascular, developmental, and neuropsychological health.

The HPT axis is a regulatory system involving:

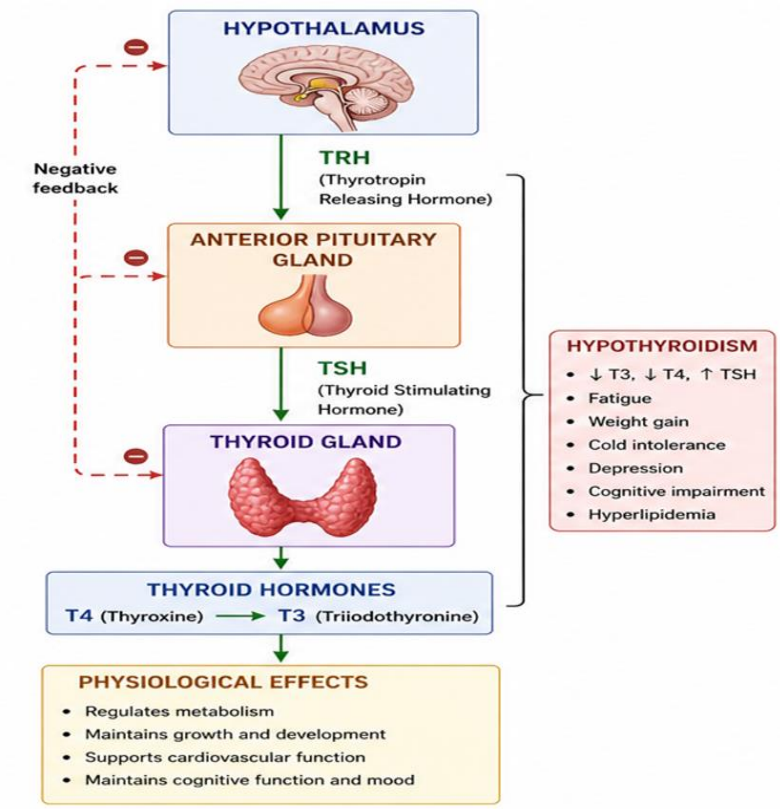

Fig. 1: The Hypothalamic-Pituitary-Thyroid (HPT) Axis.

Biomarkers for Diagnosing Hypothyroidism

Hypothyroidism is primarily diagnosed through the measurement of thyroid hormones and thyroid-stimulating hormone (TSH). The most common biomarkers include serum levels of T3, T4, and TSH. In primary hypothyroidism, there is a reduction in T4 and T3 with a corresponding increase in serum TSH. These biomarkers are essential for confirming the diagnosis and guiding treatment. The measurement of serum TSH levels is the most common

method for determining thyroid hormone status. Elevated TSH levels indicate hypothyroidism, while low levels suggest hyperthyroidism. Direct tests include measuring T3, T4, free-T4, free-T3, T4 resin uptake, free T4 index, T4 binding globulin, and anti-TPO.[24] These tests provide a thorough assessment of thyroid function and help in diagnosing hypothyroidism accurately. This review, for the sake of brevity, focuses on interventions which have been tested for their impact on TSH.

SYSTEMATIC REVIEW METHODOLOGY

A systematic literature review was conducted to collect and analyse published scientific evidence related to the role of medicinal plants and Phyto therapeutic agents in the management of hypothyroidism. Electronic databases including PubMed, Scopus, Web of Science, Google Scholar, and Science Direct were systematically searched for relevant articles published between 2000 and 2026. Classical Ayurvedic literature, including the Charaka Samhita and Sushruta Samhita, was additionally reviewed to correlate traditional concepts with modern endocrine mechanisms.

Search Keywords

The literature search was performed using combinations of Medical Subject Headings (MeSH) terms and keywords including: Hypothyroidism, Thyroid disorders, Phytotherapy, Medicinal plants, Ayurveda and hypothyroidism, Herbal treatment for hypothyroidism, Hypothalamic–pituitary–thyroid axis, Ashwagandha, Withania somnifera, Commiphora muku, Bacopa monnieri, Moringa oleifera, Nigella sativa, Oxidative stress and thyroid, Autoimmune thyroiditis, TSH, T3 and T4 regulation.

Boolean operators such as “AND” and “OR” were applied to refine and optimize the search strategy.

REVIEW RESULTS

Therapy for hypothyroidism involves medication that eventually increases serum T3, serum T4, and decreases the serum thyrotropin (serum TSH). As discussed earlier, a large number of previous studies had reported the efficacy of Ayurvedic and herbal remedies against hypothyroidism.

1. Ashwagandha (*Withania somnifera*)

Ashwagandha (Withania somnifera) is an adaptogenic herb known for its potential role in modulating thyroid function through various physiological mechanisms. Its bioactive

compounds, including Withanolides, alkaloids, and saponins, contribute to its therapeutic effects. Withanolides exhibit anti-inflammatory and antioxidant properties, alkaloids provide neuroprotective effects, and saponins enhance Ashwagandha's adaptogenic properties, helping the body cope with physiological stress.[25] Given these properties, Ashwagandha has been increasingly studied for its ability to support thyroid regulation.

Ashwagandha influences thyroid function through multiple pathways. Research suggests that it can stimulate the secretion of thyroid hormones, increasing T3 and T4 levels. Additionally, its adaptogenic effect reduces cortisol, mitigating stress-induced suppression of thyroid function. Its strong antioxidant profile also helps protect thyroid cells from oxidative damage. A randomized, double-blind, placebo-controlled trial found that daily supplementation of 600 mg of Ashwagandha for eight weeks resulted in a 41.5% increase in T3, a 16% increase in T4, and a significant reduction in TSH ($p<0.001$), with minimal transient adverse effects.[2] Another 60-day clinical study by Lopresti et al. demonstrated a 23% reduction in morning cortisol levels, improved stress markers, and indirect support for thyroid function.[25,26]

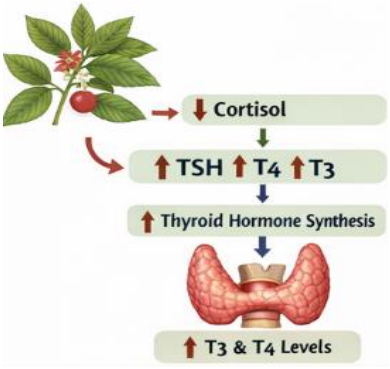

Fig. 2: Mechanism of action of Ashwagandha.

2. Guggulu (*Commiphora mukul*)

Commonly known as guggulu and guggul, is one of the ancient and the most used medicinal plant in Ayurveda. Commiphora (C.) mukul belongs to the family Burscraccae. It is among the fundamental folk resin medicine. Resin means volatile oil which is a usual metabolite or secretion of plant tissues, cells, resin channels or ducts. The resin of this plant is rich in biologically active compounds and is responsible for therapeutic effects. This plant usually grows in dry areas of India, Pakistan, Bangladesh and less commonly in Eastern Africa and Arab regions. Guggulu has been mentioned in Vedas (Sacred scripture of India) for more than 3000 years for its medicinal properties. C. mukul has antioxidant, antiinflammatory, nervous system protection, anti-bacterial, hypolipidemic, bone resorption, myocardial

protection, antiobesity, hepatoprotective, anti-arthritic, cytotoxic, antiatherosclerotic, anti-psoriatic, anti-hemorrhoid, anti-fertility, anti-acne, anti-urolithic and thyroid stimulating potential.[27,28] Biological active compounds of guggul consist of alkaloids, saponins, carbohydrates, terpenoids (mono-, di- & tri-terpenoids), lignans, lipids, steroids (Z-guggulsterone and E-guggulsterone) and flavonoids.[29,30] Scientific studies have been conducted to understand the benefits of Guggulu in induced hypothyroidism patients. It was shown that C. mukul has the potential to initiate the production of thyroid hormones T3 and T4 and in turn, ameliorate the symptoms of hypothyroidism.

There are various preclinical studies that demonstrated the efficacy of other known Ayurvedic remedies. Studies showed that the Commiphora mukul extract at a dose of 200 mg/kg administered for 15 days in mice significantly increased the T3 concentration ($p < 0.001$) and also the food consumption ($p < 0.001$).[31,32] A dose of 200 mg of its petroleum ether extract was also earlier reported to enhance thyroidal weight and I131 uptake ($p < 0.001$) in melatonin-induced (250 mg/kg) hypothyroid rats.

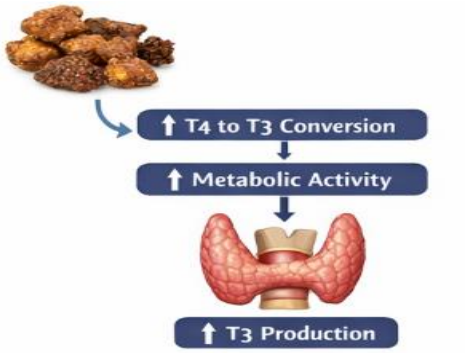

Fig. 3: Mechanism of action of Guggulu.

3. Brahmi (*Bacopa monnieri*)

Brahmi has long been associated with Indian traditional medicinal studies and utility. Therapeutic potential of Bacopa monnieri (200 mg/kg) leaf extracts in the regulation of hypothyroidism in mice was studied, in which T4 concentration was increased by B. monnieri extract suggesting its thyroid-stimulating role without enhancing hepatic lipid peroxidation (LPO) suggesting it as a thyroid-stimulating drug.[33] However, only T4 and not T3 level was reported to be raised by the Brahmi extract, indicating its direct conversion or releasing efficacy of T4 rather than a peripheral conversion, associated with T3. Moreover, the notable part of this study is that the thyroid stimulatory role was studied independent of

any induced hypothyroidism model, suggesting heavy potentials of Brahmi as a thyroid stimulator, comparable to the allopathic medications available today.

Fig. 4: Mechanism of action of Brahmi.

4. Shigru (*Moringa oliefera Lam.*)

The ameliorative effect of Moringa leaf aqueous extract in the regulation of hypothyroidism in the rat model has already been studied. Male albino rats of 120–150 g were treated orally with doses of 500 mg/kg body weight (bw) and 250 mg/kg of the aqueous extract of the Moringa oleifera leaf. The group that received maximum test dose (500 mg/kg, 14 days) showed maximum percentage increase in hormone concentration of T3, T4, and maximum percentage decrease in TSH levels when compared to the other dose levels, which showed M. oleifera leaf extracts can be used in hypothyroidism condition.[34]

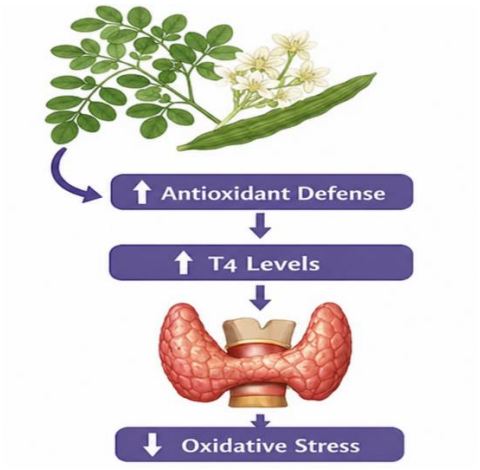

Fig. 5: Mechanism of action of Shigru.

5. Upakunjika (*Nigella sativa L.*)

Hashimoto's Thyroiditis (HT) is an autoimmune thyroid disorder primarily managed with levothyroxine, but novel adjunct therapies are under investigation. This 8-week randomized,

double-blind, placebo-controlled trial evaluated the effects of Nigella sativa (2 g/day) in 40 patients with HT. Twenty participants per group completed the study. Nigella sativa was generally well tolerated, with mild itching and nausea in three cases. Compared with placebo, supplementation significantly reduced body weight, BMI, waist, and hip circumference ($p<0.05$). Thyroid function improved with lower serum TSH and anti-TPO antibody levels and higher T3 concentrations ($p<0.05$). Serum VEGF decreased significantly ($p=0.02$), while Nesfatin-1 levels did not change. However, regression analysis showed that changes in waist-to-hip ratio, TSH, and T3 were significant predictors of Nesfatin-1 variation. These findings demonstrate beneficial effects of Nigella sativa in improving thyroid status, reducing VEGF, and aiding weight control in HT patients, supporting its potential role as an adjunctive therapy.[35]

Fig. 6: Mechanism of action of Upakunjika.

Table 1: Summary of key evidence and mechanism of herbs.

Herb	Key Evidence & Mechanism
Ashwagandha	Significant clinical evidence showing a 41.5% increase in T3 and 16% increase in T4 with a reduction in TSH.
Guggulu	Known to enhance thyroidal weight and $I^{[131]}$ uptake; contains guggulsterones that initiate thyroid hormone production.
Brahmi	Acts as a thyroid stimulator specifically by raising T4 levels, suggesting a direct release or conversion efficacy.
Shigru / Drumstick	Improves T3 and T4 levels, decreases TSH, antioxidant support
Black Seed	Clinical evidence in Hashimoto's patients showing reduced anti-TPO antibodies and improved T3 concentrations.

Table 2: Medicinal Plants Used in Management of Hypothyroidism Across Traditional Systems.

Sr. No.	Herb / Common Name	Botanical Name	Traditional System	Family	Part Used	Major Phytoconstituents	Proposed Role in Hypothyroidism	Evidence Type
1	Ashwagandha	*Withania somnifera*	Ayurveda	Solanaceae	Root	Withanolides, alkaloids, saponins	Enhances T3 and T4 levels, reduces TSH, adaptogenic and antioxidant activity	Clinical + Preclinical
2	Guggulu	*Commiphora mukul*	Ayurveda	Burseraceae	Resin	Guggulsterones, terpenoids, flavonoids	Stimulates thyroid gland activity, increases iodine uptake and T3 production	Preclinical
3	Brahmi	*Bacopa monnieri*	Ayurveda	Plantaginaceae	Whole plant / Leaves	Bacosides	Increases T4 levels, neuroendocrine modulation, antioxidant effect	Preclinical
4	Shigru / Drumstick	*Moringa oleifera*	Siddha	Moringaceae	Leaves	Flavonoids, vitamins, polyphenols	Improves T3 and T4 levels, decreases TSH, antioxidant support	Preclinical
5	Black Seed	*Nigella sativa*	Unani	Ranunculaceae	Seeds	Thymoquinone	Reduces TSH and anti-TPO antibodies, improves thyroid status and body metabolism	Clinical

CONCLUSION

The present review highlights the considerable therapeutic potential of medicinal plants used in traditional systems of medicine, including Ayurveda, Siddha, Unani, and other ethnomedicinal practices, for the management of hypothyroidism. Herbal agents such as *Withania somnifera*, *Commiphora mukul*, *Bacopa monnieri*, *Moringa oleifera*, and *Nigella sativa* demonstrated promising thyroid-regulating, antioxidant, adaptogenic, anti-inflammatory, and immunomodulatory activities through modulation of the hypothalamic–pituitary–thyroid (HPT) axis and associated metabolic pathways. Emerging mechanistic evidence suggests that bioactive phytoconstituents including withanolides, guggulsterones, bacosides, and thymoquinone may influence thyroid hormone synthesis, oxidative stress signaling, cytokine regulation, peripheral conversion of T4 to T3, and autoimmune responses associated with thyroid dysfunction. These findings provide important mechanistic validation supporting the traditional therapeutic claims of these medicinal plants.

The integration of traditional herbal medicine with modern endocrinology presents significant translational potential for the development of complementary and adjunctive therapeutic approaches in hypothyroidism management. Evidence-based integration of phytotherapy into clinical practice may offer supportive benefits for patients experiencing persistent metabolic, neuropsychological, and inflammatory symptoms despite conventional levothyroxine therapy. Furthermore, the multitargeted pharmacological nature of herbal medicines aligns with the growing concept of personalized medicine, where therapeutic interventions can be tailored according to individual metabolic status, immune profile, oxidative stress burden, and disease progression.

However, despite encouraging preclinical and limited clinical evidence, the current literature remains constrained by insufficient large-scale randomized controlled trials, lack of phytochemical standardization, inadequate long-term safety evaluation, and variability in herbal formulations. Therefore, future clinical investigations are critically necessary to establish standardized dosing strategies, pharmacokinetic profiles, safety parameters, and molecular biomarkers associated with therapeutic efficacy. Advanced research approaches including systems biology, network pharmacology, molecular docking, multi-omics analysis, and precision phytomedicine may further strengthen the scientific understanding and clinical applicability of herbal therapeutics in hypothyroidism. Collectively, the present review

supports the future potential of scientifically validated phytotherapeutic interventions as integrative and patient-centered strategies for the management of hypothyroidism.

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