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Phytochemical Warriors: Investigating Medicinal Plants for Anticancer Effects

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A B S T R A C T

Thyroid problems include a significant portion of the prevalent endocrine illnesses in India. The frequency of thyroid dysfunction is concerningly on the rise in the Indian population. In India, the two most common thyroid illnesses are hyperthyroidism and hypothyroidism. Thyroid dysfunction has traditionally been treated with hormone replacement medication. However, the use of herbal remedies to treat thyroid dysfunction is becoming more and more common since they are claimed to be as safe, effective, and free of adverse effects. Both hypothyroidism and hyperthyroidism can be effectively maintained and treated with the help of the Ayurvedic medical system. The goal of this review is to give a thorough understanding of the several herbal remedies utilized in Ayurveda to treat thyroid disease. The current study's objective was to assess the antithyroid properties of natural products and herbal plants by drawing on past experiences. Isoflavonoids have a significant impact on the hypothalamus-pituitary axis and thyroid hormones. Iodination and thyroid hormone production are catalyzed by thyroperoxidase, which is inhibited by genistein and daidzein from soy (Glycine max). Pearl millet (Pennisetumglaucum) and fonio millet (Digitariaexilis) are hypothyroid plants; Brassicae plants contain thiocyanate. Some of the antithyroid effects of soybeans, which are widely used in China and the Orient, may be mitigated by fermentation, according to a theory. Bitters are beneficial for hypothyroidism in moderate situations. Gum guggle, also known as commiphoramukul, contains guggulsterone, an active ingredient that can affect thyroid function and treat hypothyroidism. These findings indicate that, in addition to natural thyroid medicine, alternative thyroid therapies emphasize better diets and lifestyle modifications as well as spiritual assistance.

Keywords: Thyroid, Anti-thyroid drugs, Herbal drugs, Hypothyroidism, Hyperthyroidism,T3, T4, TSH

INTRODUCTION

The thyroid plays a significant role in the human endocrine system, which controls growth and development, basal metabolic rate, oxygen consumption, and cellular metabolism. [1] Thyroxine (T4) and triiodothyronine (T3), which are essential for healthy growth and development and are largely in charge of establishing the baseline metabolic rate, are secreted by the thyroid gland. The thyroid hormones function at the cellular level and are carried by the blood. Thyroid hormones raise the BMR via stimulating protein synthesis, maturing the neurological system, and speeding up tissue cell respiration through gene activation[2].Variations in these hormone levels cause altered bone mineral metabolism (BMR), which manifests as systemic signs and symptoms. One of the most prevalent endocrine conditions in the world is thyroid illness. A recent estimate based on several research indicates that 42 million Indians are thought to be affected by thyroid disorders. It is estimated that between 1% and 2% of adults have thyroid issues. [3] Because this dysfunction is becoming more common, there is a greater need than ever to address it. The chosen course of treatment has been hormone replacement. However, because of their effectiveness and few side effects, alternative medical techniques are becoming more and more popular. This article clarifies a number of medications derived from plants that have been shown to affect the thyroid and how it functions, as well as a number of variables linked to thyroid malfunction.

There's growing evidence that exposure to the environment, especially to pesticides, may potentially pose a risk for thyroid illness. A number of insecticides, herbicides, and fungicides have been identified as potential risk factors for thyroid disease. These substances have been shown to be endocrine disruptors, and more specifically, thyroid disruptors, operating through a variety of mechanisms, including binding to transport proteins, inhibiting the uptake of thyroidal iodine, interfering with the thyroid hormone receptor, increasing the clearance of thyroid hormones, interfering with the uptake of thyroid hormones by cells, and interfering with the expression of thyroid hormone genes. [4] If they appear at all, the signs and symptoms of hyperthyroidism and hypothyroidism are frequently ambiguous. Serum TSH, T3, and T4 levels should be measured in order to diagnose both overt and subclinical thyroid disorders. [5] Hypothyroidism results from low thyroid hormone levels. Symptoms of hypothyroidism include dry skin, decreased sweating, myxedema, puffy face with edematous eyelids, pallor, non-pitting pretibial edema, constipation, weight gain, dry, brittle hair, decreased libido, and menstrual disturbances, including menorrhagia in common and oligomenorrhoea or amenorrhea in long-term cases. [6]

Excessive thyroid function results in hyperthyroidism. Thyrotoxicosis, a condition characterized by an excess of thyroid hormone, is sometimes confused with hyperthyroidism. On the other hand, toxic multinodular goitre, toxic adenomas, and graves' disease are typically secondary causes of thyrotoxicosis.

Exophthalmos, elevated BMR, hyperactivity, dysphoria, irritability, weakened muscles, anxiety, palpitations, exhaustion, weight loss with increased hunger, diarrhea, polyuria, warm, moist skin, and tremor are some of the symptoms of hyperthyroidism. [7]. The majority of thyroid diseases are associated with the Ayurvedic ailments gandamala and galanganda. Nonetheless, the two conditions are mostly associated with thyroid gland nodules, which are comparable to different forms of goiter. The thyroid gland may swell and become palpably enlarged, however conspicuous growths in the gland are not a characteristic of thyroid dysfunction. Thyroid dysfunction and the conditions of sthoulya and karshya, as described in the Charaka Samhita's Ashtou Nidinitiya Adhyaya, appear to be comparable in their aetiology and symptomatology. [8].

In the realm of medicine, we are currently exploring new frontiers, particularly with regard to phytocontituents and secondary metabolites. Ten years prior, the world had completely forgotten about the use of herbal remedies and phytomedicines since at that time, western science relied blindly on alleopathic medications, which had the exclusive right to cure illnesses. [9] However, during the past several years, herbal medications have once again demonstrated their effectiveness in treating a range of metabolic disorders, including diabetes and hormone imbalances. The purpose of this review is to address the applicability of herbal remedies for the treatment of "Thyroid," a condition that progresses slowly. Low levels of T4 and T3 are the consequence of hypothyroidism in the systemic circulation. When there is insufficient T4 and T3 in the systemic circulation, the body's metabolism slows down. The following are typical symptoms: Having trouble focusing due to mood swings,

- Weary
- Prolonged weight increase
- Cognitive disorientation Hair becomes thin, coarse, and dry. I'm feeling chilly.
- Dry, rough, and itchy skin
- Puffiness and swelling in the hands, feet, face, and eye region Infertility or miscarriage.[9][11]
- Constipation, muscular cramps, increased menstrual flow, low blood pressure Depression brought on by fatigue results in a lethargic and fatigued sensation.

ADVERSE REACTION TO ANTITHYROID MEDICATION

Particularly thyroxine, thyroid hormone is commonly used in patients with diffuse/nodular nontoxic goitre, differentiated thyroid carcinoma following total thyroidectomy, or at suppressive doses to eliminate thyrotropin (thyroid-stimulating hormone) secretion. Thyroxine at dosages that are marginally supraphysiological is required to inhibit thyrotropin secretion. The therapy may cause cardiovascular changes (shortening of systolic time intervals, increased frequency of atrial premature beats and possibly left ventricular hypertrophy) and bone changes (reduction of bone mass and density). However, the risk of these side effects can be minimized by closely monitoring measurements of serum free thyroxine and free liothyronine (triiodothyronine) and modifying the dosage as necessary. The most popular antithyroid medications are thionamides, which include carbimazole, propylthiouracil, and thiamazole (methimazole). They are administered over extended periods of time and affect 3–5% of individuals adversely. Adverse effects are often modest and temporary (e.g., skin rash, itching, mild leukopenia). Agranulocytosis is the most serious side effect, affecting 0.1 to 0.5% of individuals. Granulocyte colony-stimulating factor therapy is now an effective treatment for this potentially fatal illness. Very uncommon side effects include thrombocytopenia, vasculitis, lupus erythematous-like syndrome, and aplastic anemia [10].

MEDICINAL HERBS FOR ANTITHYROIDISM

Many plants have anti-thyroid properties, affecting thyroid disorders such as hyperthyroidism and hypothyroidism. We have attempted to condense a few anti-thyroid herbs in our review, which are explained below. distinct authors have investigated under each medicinal plant or herb, and they have shown that distinct phytoconstituents primarily have different mechanisms of action and usefulness against both thyroid illnesses. The following section discusses several significant plants that are used to treat thyroid disease:

Withania somnifera (Ashwagandha) :

The purpose of the study was to assess ashwagandha methanolic extract's (AME) potential as an anti-hypothyroidism treatment. Propylthiouracil was used to induce hypothyroidism in an animal model in order to achieve this goal. After a month of therapy, thyroid gland, liver, and kidney were removed for histological analysis, blood samples were taken for biochemical analysis, and oxidative stress indicators were determined. Additionally, the extract's total phenolic components and its capacity to scavenge radicals in vitro were ascertained. The findings showed that, in comparison to the control values, the induction of hypothyroidism by propylthiouracil resulted in a considerable drop in the levels of total T4, free T4, and free T3 hormones but a large increase in the serum TSH level. Additionally, there was a large decline in blood hemoglobin and IL-10 levels, but a significant rise in body weight growth, serum glucose, and IL-6 levels. The induction of hypothyroidism also resulted in a substantial drop in the values of GSH, GPx, and Na+/K+-ATPase, as well as an increase in the levels of MDA and NO in the liver and kidney. Although to varying degrees, AME and the anti-hypothyroidism medication both markedly reduced the alterations that had occurred in the levels of the aforementioned parameters and enhanced the thyroid gland's histological appearance; ashwagandha methanolic extract shown the greatest improvement. By reducing oxidative stress and enhancing thyroid hormones, ashwagandha methanolic extract administration enhances thyroid function, it may be concluded. [10]

Commiphora mukul (Guggle)

Commiphora mukul is the botanical name of gum guggle, a natural thyroid stimulant. The Mukul myrrh tree's stem yields a yellow, resinous extract that is rich in volatile oils and resins. Guggulsterone, the active ingredient in Guggle, is capable of influencing thyroid function and treating hypothyroidism. One further benefit of the herb is that it lowers dangerous cholesterol, which is one of the signs of hypothyroidism. Although they are rare, adverse effects might include skin rashes, headaches, upset stomachs, and hiccups. [11]

Camellia sinensis (Green Tea)

Tea's main ingredient is polyphenolic flavonoids, particularly catechins. It has been documented that flavonoids have goitrogenic and antithyroidal properties. The tea leaves of Camellia sinensis are used to make green tea, which is enjoyed all over the world. Male rats were given green tea extracts (GTE) orally for 30 days at three different concentrations: 1.25g% equals five cups of tea per day; 2.5g% equals ten cups of tea per day; and 5.0g% equals twenty cups of tea per day. In a similar vein, male albino rats were given oral doses of pure catechin for 30 days at rates of 25, 50, and 100 mg/kg body weight. These amounts correspond to the above-mentioned doses of green tea extract in terms of total catechin content, and the effects on thyroid morphology and function have been studied.

The overall findings show that oral administration of green tea extract at 2.5g% and 5.0g% concentrations for 30 days altered the morphology and histology resembling hypertrophy of thyroid follicles with differential colloid sizes as found in hypothyroid due to environmental influences associated with significant inhibited activities of thyroid peroxidase (TPO) and 5' monodeiodinase (5' DI1) with elevated Na+,K+ ATPase and concurrent decrease in serum levels of thyroxine (T4), triiodothyronine (T3), and increase in serum levels of thyrotropin (TSH), resulting in an absolute biochemical hypothyroidism. All of these indicate that the catechin found in green tea may have goitrogenic and antithyroidal effects, and that frequent use of relatively large amounts of it may be harmful to thyroid function. [12].

Scutellaria baicalensis

The purpose of this study was to assess the anti-hyperthyroidal effects and mode of action of the medicinal plant Scutellaria baicalensis Georgi (SB) in rats that had been given levothyroxine (LT4)-induced hyperthyroidism. The SB and PTU groups showed substantially lower pulse rate, serum T3, T4, triglyceride, thyroid follicle size, and deiodinase 1 (Dio1) gene expression when compared to the Control group. The thyroxine-binding globulin (Tbg) gene expression and serum TSH levels were notably elevated in the SB and PTU groups. These findings imply that SB may modulate Dio1 and Tbg expression to inhibit T3, T4, and adrenergic activity; as a result, SB may offer an alternate treatment option for hyperthyroidism [13].

Pennisetum millet

In many semiarid tropical regions, pearl millet, or Pennisetum millet (L.) leeke, is the primary food supply for the impoverished living in rural areas. Sparse experimental data in rats supports the hypothesis that millet may contribute to the formation of endemic goiter in these places, which is supported by epidemiological evidence. This investigation was conducted to ascertain the goitrogenic and antithyroid effects of millet diets, millet extracts, and specific pure chemicals present therein in vivo in rats and in vitro utilizing porcine thyroid slices and a thyroid peroxidase (TPO) test. To be used in these investigations, whole grain millet was gradually dehulled to produce four bran and four flour fractions, each of which had progressively decreasing C-glycosyl flavone contents according to direct analyses. [14]When bran fraction 1, which is highest in C-glycosyl flavones, was fed in vivo, the thyroid weight increased significantly and the antithyroid effects were seen. Similar, albeit less pronounced, effects were seen when bran fraction 2, which is the next highest in C-glycosyl flavones, was fed. Bran fractions 1 and 2 extracts were the most effective in in vitro tests of 125I metabolism using pig thyroid slices, eliciting alterations that were comparable to those brought about by methimazole (MMI). The main C-glycosylflavone found in millet, glucosylvitexin, had effects equivalent to 1 mumol/L MMI at a concentration of 60 mmol/L. Similar to this, bran fraction 1 extracts strongly (85%) inhibited enzyme activity in trials with porcine TPO, but bran fraction 2 and 3 extracts gradually reduced this inhibition.

Digitaria exilis

People who live in semi-arid areas often consume a little form of millet called Digitaria exilis, or fonio. To determine the possible contributions made by vegetable molecules to the goitrogenic processes, phytochemical analyses were performed on a sample of fonio that was taken directly in the center of a highly iodine-depleted goitrous endemic. The edible whole wheat grains contain 500 mg/kg of flavonoids overall. Their extraction and identification reveal the presence of luteolin (L1 = 350 mg/kg) and apigenin (A = 150 mg/kg), but fail to discover the C-glycosylflavones reported in other millet types. 90% of A and 20% of L1 are bonded as O-glycosylflavones, whereas 10% of A and 80% of L1 are present in free form. Strong anti-thyroid peroxidase (TPO) activities are shown by both A and L1 aglycones, which significantly lowers the enzyme's ability to be hormonogenic. Furthermore, L1 dramatically inhibits cyclic AMP phosphodiesterase, suggesting an excess of the thyrotropin-dependent nucleotide at the same time. [15] It is thought that these last, unreported data somewhat mitigate L1's goitrogenic effects mediated by TPO. The absence of other chemicals that might potentially disrupt thyroid function in fonio leads to a direct and causal relationship between the results and the consumption of A and L1 in the typical diet.

Lycopi europaei

During a three-month follow-up phase, the prospective two-armed open trial set out to investigate the impact of Lycopi europaei herb on thyroid function and related symptoms. Patients having symptoms consistent with hyperthyroidism and a basal TSH of less than 1.0 mU/l made up the study population. The T3/T4 excretion in 24-hour urine was assessed as a major objective metric for the first time. Additional hormones, the overall health, and the hyperthyroidism-related symptoms were recorded as secondary criteria. Patients treated with Lycopus europaeus had substantially higher urine T4 excretion ($p=0.032$). It is thought that either a change in the glomeruli or poor reabsorption are the renal processes responsible for the elevated excretion

of T4. There was a decrease in thyroid-specific symptoms, such as the morning heart rate rise. The preparation of Lycopus europaeus shown acceptable tolerance. These results support Lycopus europaeus' beneficial benefits on mild cases of hyperthyroidism. [16]

Melissa officinalis

Numerous substances, both natural and man-made, have been identified as possible thyroid disruptors. To thoroughly evaluate a substance's or complex mixture's possible thyroid-disturbing action, it has been advised to create in-vitro tests. The efficacy of 12 chemicals thought to function as thyroid disruptors to prevent TSH-stimulated cAMP synthesis in vitro was examined in this work. To determine the degree to which those chemicals interfere with this stage of thyroid cell activity, more research was done on those compounds that produced an inhibition. 1,1-bis-(4-chlorphenyl)-2,2,2-trichloroethan (DDT), Aroclor 1254, and Melissa Officinalis were shown to provide a dose-dependent suppression of TSH-stimulated adenylate cyclase activity using Chinese hamster ovary cells (CHO) transfected with the recombinant human TSH receptor. Additionally, the TSH receptor antibody-stimulated cAMP generation was reduced by all three drugs. Aroclor 1254 and DDT did not significantly alter the results of these tests, however Melissa Officinalis significantly inhibited both TSH binding to its receptor and antibody binding to TSH. These findings imply that although DDT and Aroclor 1254 primarily influence cAMP synthesis at the post-receptor stage, principles found in Melissa Officinalis may prevent TSH from attaching to its receptor by acting on the hormone as well as the receptor itself. To sum up, A created a series of in vitro tests that enable research into how thyroid disruptors affect the cAMP cascade's TSH-mediated activation. These tests, in addition to and in support of animal research or epidemiological surveys, may be helpful in determining the mode of action of thyroid disruptors.[17]

Carica papaya

The effects of an extract from Carica papaya seeds on the parathyroid, thyroid, and pituitary glands in rats were studied. Male wistar rats that were sexually mature were given an oral dose of 50 and 200 mg/kg of the ethanolic extract of C. papaya seeds every day over a period of one to eight weeks. Pituitary and thyroid histology was produced. Thyrotrophs (TSH cells) from the anterior pituitary displayed increasing hypertrophy and degranulation over the course of one and eight weeks, respectively, at high dosage levels of 200 mg/kg. When comparing the experimental groups to the control, neither the acidophil somatotrophs (STH cells) nor the lactotrophs or prolactin cells (LTH/PRL cells) displayed any discernible alterations. On the other hand, rats treated with 200 mg/kg extract had considerable hypertrophy, hyperplasia, and degranulation in their thyroid glands, along with a large number of empty follicles devoid of colloid. Parathyroid glands showed no abnormalities. [18].These findings suggested potential negative effects of C. papaya seeds on rats.

Lycopus virginicus

In one study, it was demonstrated that freeze-dried extracts (FDE) of Lactobacillus virginianus and Lactobacillus europaeus, along with a few of its oxidized components, exhibited anti-thyrotropic action by forming adducts with TSH and so preventing it from binding to the TSH receptor. The Graves autoantibody, which is thought to be the pathophysiological mechanism for Graves' illness, has also been shown to exhibit this inhibitory interaction in vitro. It functions similarly to thyroid-stimulating hormone (TSH) in that it may attach to the thyroid plasma membrane and stimulate the gland. The results of this study, which looked at how FDE and its constituents affected Graves'-IgG binding and biological activity, showed a dose-dependent decrease in TSH-binding inhibitory activity. This suggests that the active ingredients in FDE may interact with Graves'-IgG to prevent it from binding to the TSH receptor and activating the thyroid in the same way that they do with TSH. The results, according to the authors, may support the empirical application of FDE in the management of Graves' illness.[19].

Inula racemosa

The ability of extracts from Gymnema sylvestre (leaf) and Inula racemosa (root) to reduce corticosteroid-induced hyperglycemia in mice was assessed, either separately or in combination. To determine whether or not the effects are mediated by thyroid hormones, radio-immunoassay (RIA) was used to assess thyroid hormone levels simultaneously. Although the corticosteroid (dexamethasone) treatment raised the blood glucose level, it also reduced the blood levels of thyroid hormones, triiodothyronine (T3) and thyroxine (T4). In rats with dexamethasone-induced hyperglycemia, the administration of the two plant extracts, either alone or in combination, reduced the blood glucose levels. Nevertheless, it was shown that administering the extracts of Gymnema sylvestre and Inula racemosa together was more beneficial than using them alone. These results were similar to those of ketoconazole, a common medication that inhibits corticosteroids. Given that none of the plant extracts significantly altered the concentrations of thyroid hormones in animals receiving dexamethasone, it is possible that these extracts are more beneficial for steroid-induced type II diabetes than for thyroid hormone-mediated type II diabetes.[20]

DISCUSSION

Natural goods and medicinal plants are among the most often used alternative therapies. A large number of natural compounds have hormonal properties. and have been used for a long time to prevent and cure illnesses, such as thyroid problems, and may be beneficial even if synthetic antithyroid medications are developed. The antithyroid effects of certain medicinal plants were discovered in the current investigation to decrease thyroid hormone or radioactive iodine absorption in a way that is comparable to those of antithyroid chemicals. The most potent of them was daidzein and genistein from soy (Glycine max), which block the enzyme thyroperoxidase, which is responsible for the manufacture of thyroid hormone and iodination. Additionally, thiocyanate is present in Brassicae plants, and hypothyroid effects can be caused by fonio millet (Digitaria exilis) and pearl millet (Pennisetum glaucum). Brassicae plants (Family Cruciferae), which include rutabaga (swede or yellow turnip, Brassica napobrassica), mustard, rapeseed, broccoli, cauliflower, kale, Brussels sprouts, and cabbage (Brassica oleracea), have long been recognized to have antithyroid and goitrogenic properties75. The results of our current

investigation also show that progoitrin, a thiourea-like substance that inhibits thyroperoxidase and is a precursor to goitrin, is present in turnips and rutabagas.[20-23].

Furthermore, a number of noteworthy research have indicated that soy diet can have goitrogenic consequences in both adult and newborn humans. The goitrogenic isoflavonoid components of soy, genistein and daidzein, have recently been found. Additionally, the methods for inhibiting thyroid peroxidase (TPO)-catalyzed thyroid hormone production in vitro have been characterized. Given that the primary autoantibody involved in autoimmune thyroid illness is anti-TPO, the reported suicidal inactivation of TPO by isoflavones through covalent binding to TPO increases the risk of neoantigen development. But there's also a chance of serious, sometimes fatal side effects include vasculitis, severe hepatoxicity, and agranulocytosis. Compared to MMI, PTU causes more frequent major adverse effects that are not dose-related. Experts recommended using MMI instead of PTU in cases of hyperthyroidism as a result of this. PTU continues to play a part in the first trimester of pregnancy due to the possibility of "methimazole embryopathy," which is rare but possible. Furthermore, PTU is better in the early therapy of patients with thyroid storm due to its influence on the peripheral conversion of T4 to T3. Relapses are common following ATD removal, occurring in 50–60% of cases, and usually occur within a year of medication termination. In most cases, a specific treatment plan should be implemented for hyperthyroidism that relapses.

And many more, such as the quick and easy absorption of naturally occurring flavonoids with aglycones from intestinal digestion, which raises the risk of goiter and antithyroid effects developing in newborns fed soy-based formulas in place of milk. Prior research has demonstrated that the main volatile component of common onions (Allium cepa), N-propyl disulphide, suppressed thyroid function in rats91. The low values for iodine-I31 uptake in the treated animals demonstrate that allyl alcohol and methyl disulphide, two constituents of Allium cepa, significantly inhibited thyroid function at the higher levels used. However, allyl monosulphide showed no antithyroid activity even at the highest level used.

CONCLUSION

The use of herbal remedies for thyroid dysfunction is always required in order to prevent the many negative consequences of hormone therapy. The adoption of herbal remedies is expanding globally, and this has highlighted the importance of contemporary scientific investigation and assessment of plant-based ethnomedicine. To confirm that the aforementioned plant is effective in normalizing thyroid dysfunction, clinical study is required. These will result in amazing findings from ethnomedical plant-based medicine. The study's conclusions imply that a component with antithyroid properties comparable to those of herbal plants and natural goods has been extracted from the root, leaf, and seed of those different plants. Alternative thyroid therapies prioritize bettering nutritional diets and lifestyles, offering spiritual support in addition to natural thyroid medicine, and enhancing the activities of other organs that elevate thyroid function. However, there were still a number of doubtful herbal plants that needed more research.

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