Review Article

Study on Antithyroid Property of Some Herbal Plants

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ABSTRACT

The aim of the current study was to evaluate property of antithyroid on herbal plants as well as natural products by using previous events. Isoflavonoids have profound effects on thyroid hormones and on the hypothalamus–pituitary axis. Genistein and daidzein from soy (*Glycine max*) inhibit thyroperoxidase that catalyses iodination and thyroid hormone biosynthesis. Hypothyroid effects include pearl millet (*Pennisetumglaucum*) and fonio millet (*Digitariaexilis*); thiocyanate is found in Brassicae plants. It has been postulated that the fermentation of soybeans commonly used in China and the Orient could decrease some of its antithyroid effects. However, kojic acid, a fungal metabolite produced by *Aspergillusflavus*, used traditionally in the production of miso (soybean paste), shoyu (soy sauce) and sake, also has antithyroid effects including iodine uptake inhibition, decrease in T3 and T4, increase in TSH and induction of goitre. N-propyl disulphide, the major volatile constituent of common onion (*Allium cepa*), inhibited thyroid activity in the rat. It is evident that, at the higher levels used, allyl alcohol and methyl disulphide (constituents of *Allium cepa*) inhibited thyroid function.Sea plants; Bladder wrack, a form of kelp, is used in both western and Chinese herbal medicine. It can be taken as a supplement or as an infusion. This remedy is useful if there is a deficiency of iodine in the diet. Bitters are helpful for mild cases of hypothyroidism. Gum guggle is *commiphoramukul*, the active compound in guggle is called guggulsterone and has the power to influence thyroid function and improve the condition of hypothyroidism. These results suggest that alternative thyroid treatments place more importance on improving lifestyles and nutritional diet, providing spiritual support along with natural thyroid medication.

Keywords: Antithyroid, herbal plants, isoflavonoids, T3, T4, TSH, goitre.

INTRODUCTION

Thyroid disease is common, and disease is more prevalent with increasing age. 5%–9% of adults have subclinical thyroid disease and 0.8%–7.5% have clinical thyroid disease [1–3] in the general population.

Thyroid hormones, the only known iodine-containing compounds with biological activity, have two important functions. In developing animals and human beings, they are crucial determinants of normal development, especially in the central nervous system (CNS). In the adult, thyroid hormones act to maintain metabolic homeostasis, affecting the function of virtually all organ systems. To meet these requirements, the thyroid gland contains large stores of preformed hormone. Metabolism of the thyroid hormones occurs primarily in the liver, although local metabolism also occurs in target tissues such as the brain. Serum concentrations of thyroid hormones are precisely regulated by the pituitary hormone, thyrotropin, in a classic negative-feedback system. The predominant actions of thyroid hormones are mediated *via* binding to nuclear thyroid hormone receptors (TRs) and modulating transcription of specific genes. In this regard, thyroid hormones share a common mechanism of action with steroid hormones, vitamin D, and retinoid, whose receptors make up a superfamily of nuclear receptors[4].

The thyroid gland secretes 3 hormones- thyroxin (T4), triiodothyronine (T3) and calcitonin. Subclinical thyroid disease is defined by abnormal serum thyroid-stimulating hormone (TSH) but normal T4 and T3 levels and does not always require treatment, whereas persons with clinical thyroid disease have abnormal serum TSH, T4, and T3 levels and require treatment. Known risk factors for thyroid disease include autoimmunity, external irradiation of the head and neck, a biosynthetic defect in iodine organification, replacement of the thyroid gland by tumour, and use of certain drugs[5]. Other factors associated with an increased risk of thyroid disease include female sex, increasing age, and iodine deficiency[6,7].

In the Agricultural Health Study, Thyroid disease is also evidence of an association between organochlorines exposure and thyroid disease is increasing. In this examined the cross-sectional association between ever use of organochlorines and risk of hypothyroidism and hyperthyroidism among female spouses (n = 16,529) in Iowa and North Carolina enrolled in the Agricultural Health Study in 1993–1997. They also assessed risk of thyroid disease in relation to ever use of herbicides, insecticides, fungicides, and fumigants. Prevalence of self-reported clinically diagnosed thyroid disease was 12.5%, and prevalence of hypothyroidism and hyperthyroidism was 6.9% and 2.1%, respectively. There was an increased odds of hypothyroidism with ever use of organochlorines insecticides (adjusted odds ratio (ORadj) = 1.2 (95% confidence interval (CI): 1.0, 1.6) and fungicides (ORadj = 1.4 (95% CI: 1.1, 1.8) but no association with ever use of herbicides, fumigants, organophosphates, pyrethroids, or carbamates. Specifically, ever use of the organochlorines

chlordane (ORadj = 1.3 (95% CI: 0.99, 1.7), the fungicides benomyl (ORadj = 3.1 (95% CI: 1.9, 5.1) and maneb/mancozeb (ORadj = 2.2 (95% CI: 1.5, 3.3), and the herbicide parquat (ORadj = 1.8(95% CI: 1.1, 2.8) was significantly associated with hypothyroidism. Maneb/mancozeb was the only pesticide associated with both hyperthyroidism (ORadj = 2.3 (95% CI: 1.2, 4.4) and hypothyroidism. These data support a role of organochlorines, in addition to fungicides, in the etiology of thyroid disease among female spouses enrolled in the Agricultural Health Study[8].

There is increasing evidence that environmental exposures, specifically to pesticides, should also be considered potential risk factors for thyroid disease. Certain insecticides, herbicides, and fungicides, should also be considered potential risk factors for thyroid disease, reported to be endocrine disruptors and, more specifically, thyroid disruptors acting through diverse mechanisms[9– 11] such as inhibition of thyroidal iodine uptake, interference at the thyroid hormone receptor, binding to transport proteins, interference with iodothyronine deiodinases, increased clearance of thyroid hormones, interference with cellular uptake of thyroid hormones, and interference with thyroid hormone gene expression[9, 11].

Thyroid hormone receptors (TRs) belong to a superfamily of nuclear hormone receptors that act as ligand-regulatable transcription factors[12, 13]. There are two major TR isoforms, TRα and TRβ, encoded on separate genes. TRs bind to thyroid hormone response elements in the promoters of target genes to regulate their transcription.

The size and function of the thyroid are controlled by a physiological negative feedback mechanism. The thyroid cell secretes thyroid hormones that inhibit the secretion of thyrotropin (TSH) by the pituitary. Whenever thyroid hormone secretion decreases, as it does in iodine metabolism defects, in iodine deficiency, or after goitrogenic or antithyroiddrugs administration, TSH secretion increases, causing an activation of thyroid function and growth[14]. Methylthiouracil (MTU) and other substances derived from thiouracil hinder thyroid peroxidase, blocking iodine oxidation, the attachment of thyroglobulin tyrosyl residues, and iodotyrosine coupling[15]. Thus, deficiency of thyroid hormones induced by these drugs causes an increase in thyrotrophic hormone (TSH) secretion[16, 15].The TSH has a trophic effect on the thyroid and may produce hyperplasia and hypertrophy of follicular cells, causing an increase in glandular volume[17].

TSH is a heterodimer composed of two subunits: TSHα and TSHβ. TSHα, known as glycoprotein hormone α common sub- unit, also is a subunit for several other glycoprotein hormones such as LH, FSH, and human choriogonadotropic hormone, whereas TSHβ is unique to TSH. T3 negatively regulates TSH by decreasing both TSHα and TSHβ gene as well as TRH gene transcription[18-20]. These genes have been studied as models of negatively regulated gene transcription by T3. From a physiological perspective, their negative regulation is critical for feedback control of the hypothalamic/pituitary/thyroid axis. Deficiency of thyroid hormones during critical periods of brain development, both in utero and in the early postpartum period, is a well-recognized cause of brain damage leading to mental retardation, decreased intellectual capacity, psychomotor delay, and deafness[21]. Iodine is essential for the production of thyroid hormones. Lack of iodine in the diet is the most important worldwide cause of hypothyroidism, goitre and other iodine deficiency disorders (IDD) [22].

In 2005, nearly two billion individuals or almost one-third of the population of the world suffered from insufficient iodine intake and were at risk for IDD[23]. Women of reproductive age are at highest risk for IDD due to the effects of the thyroid on ovulation, fertility, and pregnancy outcome[22].

The main thyroid hormone active in the brain is 3, 5, 3′-triiodothyronine (T3) derived in large part from 5′ deiodination of maternal thyroxin (T4) by local brain deiodinases D2 and D3. Maternal T4 and T3 are transported to the fetal brain from maternal blood across the blood–brain barrier[24, 25]. Prior to the formation of the fetal thyroid around mid- gestation the fetus is unable to produce thyroxin and is therefore completely dependent on maternal thyroxin[25].

In another review of recent articles, there is increasing evidence that triiodothyronine (Ts) plays an important role in normal thyroid physiology. It has even been speculated that thyroxine (T4) exerts little metabolic effect unless it is deiodinated to T8 in the peripheral tissues[26]. Although thyrotoxicosis is most commonly associated with increases in circulating levels of both To and Ts, review of the available studies indicates that the concentration of the latter is generally elevated to a greater extent[27]. The mechanism of this disproportionate increase in Ts and its metabolic implications are not clearly understood. Since serum Ts elevations appear to be consistently present in hyperthyroid patients and since T3 may be the active form of thyroid hormone, it was of interest to document the changes in its concentration during therapy with commonly used antithyroid agents. In addition, the half-life of Ts is short so that inhibition of Ts production should be rapidly reflected in decreases in serum hormone concentrations[28].

Hypothyroidism, known as myxedema when severe, is the most common disorder of thyroid function. Worldwide, hypothyroidism results most often from iodine deficiency. In nonendemic areas where iodine is sufficient, chronic autoimmune thyroiditis (Hashimoto's thyroiditis) accounts for the majority of cases. This disorder is characterized by high levels of circulating antibodies directed against thyroid peroxidase, and less commonly, thyroglobulin. In addition, blocking antibodies directed at the TSH receptor may be present, exacerbating the hypothyroidism. Finally, thyroid destruction may result

from apoptotic cell death due to the interaction of Fas with the Fas ligand in the thyrocytes. Failure of the thyroid to produce sufficient thyroid hormone is the most common cause of hypothyroidism and is referred to as *primary hypothyroidism. Central hypothyroidism* occurs much less often and results from diminished stimulation of the thyroid by TSH because of pituitary failure (*secondary hypothyroidism*) or hypothalamic failure (*tertiary hypothyroidism*). Hypothyroidism present at birth (*congenital hypothyroidism*) is the most common preventable cause of mental retardation in the world. Diagnosis and early intervention with thyroid hormone replacement prevent the development of cretinism[4].

Endemic cretinism is the most severe degree of in utero brain damage from maternal hypothyroxinemia ensuing from dietary iodine deficiency[29,30]. Clinical features include profound mental retardation, deaf–mutism, and squint of eyes, signs of bulbar damage, spastic diplegia, pyramidal and extrapyramidal signs, and typical gait with laxity and deformities of the joints[29]. Endemic cretinism is different from congenital hypothyroidism, which occurs in about 1 in 3500 new-borns as a result of morphological or functional deficiencies of thyroid function in the fetus and the new-born unrelated to dietary iodine deficiency[31].

Insufficient dietary iodine intake and a number of environmental antithyroid and goitrogenic agents can affect maternal thyroid function during pregnancy. The most common causes could include inhibition of deiodinases D2 or D3 from maternal ingestion of dietary flavonoids or from antithyroid environmental contaminants[32].

Deficiencies of iodine are the main problems in most developing countries[33]. More than 1 billion persons are at risk of iodine deficiency worldwide and 200 million have goiter. In Africa, goiter is endemic in many countries, notably Congo, Uganda, Kenya, and Sudan; the prevalence of goiter is as high as 81% in some parts of these countries[34]. Although iodine deficiency is the main factor in the etiology of endemic goiter[35], the additional role of goitrogens has been shown or suspected in areas such as Congo[36] and Sudan[37], in which goiter is endemic. As a whole, however, the role of goitrogens is often disregarded. In Sudan, endemic goiter and iodine deficiency disorders are serious health problems in many areas. The prevalence of goiter among schoolchildren was estimated to be 85% in the Darfur region in western Sudan, 74% in the Kosti area in the centre of Sudan, 13.5% in Portsudan in eastern Sudan, and 17% in the capital, Khartoum[38]. Little is known about the prevalence of goiter in other areas of Sudan. In the areas studied so far, iodine deficiency was identified as the principal etiologic factor. However, consumption of pearl millet another most common seen in thyroid incidentalomas, they were commonly found on cross-sectional imaging of the neck and they are equally likely to be malignant as palpable thyroid nodules. The term incidentalomas refers to an unexpected, asymptomatic tumour discovered by chance during the investigation of an un-related condition[39]. The increasing use of high quality imaging of the neck has uncovered a large number of incidental thyroid nodules referred to as thyroid incidentalomas. This has created a clinical management dilemma for several reasons. The incidence of thyroid incidentalomas is high e they are present in up to half of all normal thyroid glands at autopsy[40] and 10-67% of neck ultrasounds (US)[41-46]. US cannot reliably differentiate benign from malignant thyroid nodules and fine needle aspiration cytology (FNAC) is not always indicated.

Although the malignancy rate of impalpable thyroid incidentalomas is the same as that of palpable nodules (4-12%)[44, 47, 49] the natural history of small subclinical thyroid cancers discovered incidentally is considered to be indolent[50]. Identifying a small subclinical thyroid cancer may therefore not have any clinical benefit. The disparity between the incidence of clinically apparent thyroid cancer, which is uncommon accounting for only 1% of all malignancies, and the incidence of subclinical thyroid cancer found at autopsy of 6-11%[51-56] in macroscopically normal thyroid glands, suggests that the majority of subclinical thyroid cancers do not progress to clinical disease. Guidelines on their management are conflicting. Ultrasonography cannot accurately differentiate benign from malignant thyroid nodules and fine needle aspiration biopsy should be used selectively to avoid over-diagnosis and over-treatment [57].

Treatment of the hypothyroid patient is straight forward and consists of hormone replacement. There are more options for treatment of the hyperthyroid patient, including the use of antithyroid drugs to decrease hormone synthesis and secretion and destruction of the gland by the administration of radioactive iodine or by surgical removal. Treatment of thyroid disorders in general is extremely satisfying, as most patients can be either cured or have their diseases controlled.

The main mechanism of action of ATDs is the blockade of thyroid hormone synthesis through inhibition of thyroid peroxidase. This enzyme catalyses iodide oxidation, iodination of tyrosine residues onto thyroglobulin, and coupling of iodotyrosine (monoiodotyrosine, MIT, and diiodotyrosine, DIT) to form thyronines, tetraiodothyronine or thyroxine (T4) and triiodothyronine (T3)[58]. An additional effect of PTU is to inhibit deiodination of T4 to the metabolically active hormone T3. ATDs may also have immunosuppressive actions which might be part of their therapeutic effect in Graves' hyperthyroidism[59]. ATD treatment is associated with a progressive decrease in serum TRAb[60], intracellularadhesion molecule[61, 62] soluble interleukin-2 and interleukin- 6 receptors levels[63, 64], as well as with other in vitro immunomodulatory effects, such a decrease in the expression of HLA class II antigens[65]. Whether these effects are direct or indirect, i.e., related to restoration of euthyroidism still is a matter of argument.

Hyperthyroidism is the hyper metabolic state due to excessive thyroid hormone synthesis and secretion. The

term thyrotoxicosis also includes also conditions not associated with thyroid hyper function, but rather with thyroid-destructive processes or exogenous intake of thyroid hormones. The three most frequent forms of hyperthyroidism are Graves' disease, toxic adenoma, and toxic multinodular goiter. Among them, Graves' disease, an autoimmune disorder ultimately caused by autoantibodies stimulating thyroid growth and function through their interaction with the TSH receptor on thyroid follicular cells (TSH receptor antibodies, TRAbs), is the most common cause of hyperthyroidism in iodine-replete geographical areas[61].

Classification of different forms of thyrotoxicosis[61]

With hyperthyroidism

Common forms:

Graves' disease,

Toxic adenoma,

Toxic multinodular goiter,

Iodine-induced thyrotoxicosis.

Uncommon forms:

Congenital hyperthyroidism,

Hashitoxicosis,

TSH-secreting pituitary adenoma,

Trophoblastic tumours,

Metastatic thyroid carcinoma,

Struma ovarii.

Without hyperthyroidism

Common forms:

Sub-acute (De Quervain's thyroiditis),

Painless thyroiditis,

Post-partum thyroiditis,

Iodine-induced thyrotoxicosis,

Uncommon forms:

Thyrotoxicosis factitia,

Iatrogenic thyrotoxicosis.

SYMPTOMS OF HYPERTHYROIDISM AND HYPOTHYRODISM

It sometimes seems that the symptoms of a thyroid problem whether underactive (hypothyroidism) or overactive (hyperthyroidism) can be as hard to pin down as the diagnosis itself. Hypothyroidism as something can make you tired and gain weight. While problematic, these were understandable symptoms. Among reputable medical sources, it seems that there is some medical agreement that the following are the basic symptoms of hypothyroidism and hyperthyroidism[66].

Key Symptoms of Hypothyroidism (An underactive thyroid)

Fatigue; exhaustion feeling run down and sluggish depression, moodiness difficulty concentrating; brain fog; unexplained or excessive weight gain; dry, coarse and/or itchy skin; dry, coarse and/or thinning hair; feeling cold, especially in the extremities; constipation; muscle cramps; increased menstrual flow; more frequent periods; infertility/miscarriage; low blood pressure; frequent infections; bloating/puffiness in hands, feet, eye area, face, etc.

Key Symptoms of Hyperthyroidism (An overactive thyroid)

Nervousness; irritability; increased perspiration; thinning of your skin; fine brittle hair; muscular weakness especially involving the upper arms and thighs; shaky hands; panic disorder; insomnia; racing heart; more frequent bowel movements; weight loss despite a good appetite; lighter flow, less frequent menstrual periods, etc.

ADVERSE EFFECTS OF ANTITHYROID DRUGS

Thyroid hormone, especially thyroxine, are widely used either at replacement doses to correct hypothyroidism or at suppressive doses to abolish thyrotropin (thyroid-stimulating hormone) secretion in patients with differentiated thyroid carcinoma after total thyroidectomy or with diffuse/ nodular nontoxic goitre. In order to suppress thyrotropin secretion, it is necessary to administer slightly supraphysiological doses of thyroxine. Possible adverse effects of this therapy include cardiovascular changes (shortening of systolic time intervals, increased frequency of atrial premature beats and, possibly, left ventricular hypertrophy) and bone changes (reduced bone density and bone mass), but the risk of these adverse effects can be minimised by carefully monitoring serum free thyroxine and free liothyronine (triiodothyronine) measurements and adjusting the dosage accordingly. Thionamides [thiamazole (methimazole), carbimazole, propylthiouracil] are the most widely used antithyroid drugs. They are given for long periods of time and cause adverse effects in 3 to 5% of patients. In most cases, adverse effects are minor and transient (e.g. skin rash, itching, mild leukopenia). The most dangerous effect is agranulocytosis, which occurs in 0.1 to 0.5% of patients. This life-threatening condition can now be effectively treated by granulocyte colony-stimulating factor administration. Other major adverse effects (aplastic anaemia, thrombocytopenia, lupus erythematous-like syndrome, and vasculitis) are exceedingly rare[67].

MANAGEMENT

Hyperthyroidism can be managed either by a conservative treatment (antithyroid drugs, ATDs) or by reduction/ ablation of the thyroid tissue (radioactive iodine [RAI], thyroidectomy)[68]. However, in the case of toxic adenoma and toxic multinodular goiter, ATDs should

be merely regarded, with few exceptions, as a tool to prepare the patient to the definitive treatment, because drug withdrawal is inevitably followed by a relapse of hyperthyroidism[69].

Antithyroid drugs (ATDs) can effectively control hyperthyroidism. While in toxic adenoma and toxic multinodular goiter, ATD treatment is only preparatory to radioactive iodine (RAI) therapy or thyroidectomy, in Graves' hyperthyroidism it is a valid alternative to thelatter methods. Side effects are generally minor. However, major and even life-threatening untowardeffects may rarely occur, such as agranulocytosis, severe hepatoxicity, and vasculitis. Major side effects are more frequent (and dose-unrelated) using propylthiouracil (PTU) than using methimazole (MMI) [70].

The recent observation that PTU can be associated, although rarely, with very severe liver damage which may be lethal or require liver transplant, prompted recommendation that MMI rather than PTU be prescribed as first-line ATD both in adults and children[71, 72]. It should be mentioned that hepatic abnormalities, with cholestasis features (but occasionally also with necrotic features also), may rarely occur also in patients treated with MMI[73], these are usually less severe than in PTU-treated patients and usually reversible after MMI withdrawal[73]. Another major, although rare, complication of ATD treatment is vasculitis, more common in PTU-treated than in MMI treated patients[73].

The major drawback of ATD treatment is the high rate of recurrences after drug withdrawal. As many 30–70% of patients experience a relapse of hyperthyroidism[74] in the majority of cases within one year after ATD discontinuation[74]. Hyperthyroidism may however relapse even years after ATD withdrawal[74].

ATDs represent the treatment of choice in pregnant and lactating women, and the first line treatment in children and adolescents. The dilemma of whether ATDs or a definitive treatment (RAI or thyroidectomy) is the best treatment in patients with Graves' orbitopathy is still unsolved.

ANTITHYROID ACTIVITY OF HERBAL PLANTS

Some plants isoflavonoids have profound effects on thyroid hormones and on the hypothalamus–pituitary axis. Genistein and daidzein from soy (*Glycine max*) inhibit thyroperoxidase that catalyses iodination and thyroid hormone biosynthesis.

Other plants with hypothyroid effects include pearl millet (*Pennisetum glaucum*) and fonio millet (*Digitaria exilis*); thiocyanate is found in Brassicae plants including cabbage, cauliflower, kale, rutabaga, and kohlrabi, as well as in tropical plants such as cassava, lima beans, linseed, bamboo shoots, and sweet potatoes. Tobacco smoke is also a source of thiocyanate[32].

The antithyroid and goitrogenic effects of Brassicae plants (Family *Cruciferae*) have long been known[75] including cabbage (*Brassica oleracea*), broccoli, cauliflower, kale, kohlrabi, Brussels sprouts, and rutabaga (swede or yellow turnip, *Brassica napobrassica*), rapeseed and mustard. SCN interferes with active uptake and concentration of inorganic iodide by the thyroid and inhibits the enzyme thyroperoxidase thereby preventing the incorporation of iodine into thyroglobulin.

Rutabaga and turnips contain a thiourea like product (progoitrin), a precursor of goitrin that also interferes with thyroperoxidase[75].

A number of staple foods in the tropics contain large amounts of cyanogenic glycosides that are detoxified as SCN[21]. These plants include cassava (*Manihot esculenta Crantz*), millet, yam, sweet potato, corn, bamboo shoots, and lima beans (*Phaseolus vulgaris*). Tobacco smoke (*Nicotianatabacum)* also contains considerable amounts of cyanide (150–300µg per cigarette) in addition to other goitrogenic products such as resorcinol derivatives, flavonoids, and hydroxypyridines[76].

Natural flavonoids are usually conjugated to sugars or carbohydrates (glycosides) and polymerized to other flavonoids and non-flavonoids (acyl derivatives); non-conjugated forms are called aglycones. Flavonoid aglycones resulting from intestinal digestion are rapidly and readily absorbed[77] increasing the likelihood of development of antithyroid effects and goitre in infants receiving soy based formulas as milk substitute[78-84]. It has been postulated that the fermentation of soybeans commonly used in China and the Orient could decrease some of its antithyroid effects[84]. However,kojic acid, a fungal metabolite produced by *Aspergillusflavus*, used traditionally in the production of miso (soybean paste), shoyu (soy sauce) and sake, also has antithyroid effects including iodine uptake inhibition, decrease in T3 and T4, increase in TSH and induction of goitre[86].

Deiodinase I is also affected by other plant flavonoids[87] including catechin from tea (*Camellia sinensis*), quercetin (found in apples, onions, red grapes, citrus fruits, broccoli, cherries, berries, and prickly-pear cactus), kaemp- ferol (from Delphinium, Witch-hazel, and grapefruit), rutin (found in buckwheat), and baicalein, isolated from the roots of baikal or Chinese skullcap (*Scutellaria baicalensis* Georgi). In the presence of iodine deficiency, some antho-cyanins, catechins and tannins from nuts exhibit goitrogenic effects[88]; these include peanuts (*Arachis hypogea*), cashew nuts (*Anacardium* occidentale), almonds (*Prunus amygdalus*), and the areca nut (*Areca catechin*). Other plants with hypothyroid effects include millets such as pearl millet (*Pennisetum glaucum*) and fonio millet *(Digitaria exilis)*[89]; bugleweed (*Lycopus virginicus*), gypsywort (*Lycopus europaeus*), water horehound (*Lycopus lucidus or Lycopus Americana's*), gromwell (*Lithospermum ruderale*), European gromwell (*Lithospermum officinale*), lemonbalm (*Melissa officinalis*), and perhaps rosemary (*Rosmarinus officinalis*) and sage (*Salvia officinalis*)[90].

N-propyl disulphide, the major volatile constituent of common onion (*Allium cepa*), inhibited thyroid activity in the rat[91]. The possible antithyroid activity of four other volatile compounds of Allium: methyl disulphide, allyl disulphide, allyl alcohol, and allyl monosulphide, these 4 compounds constitute the major volatile constituents of common onion; however they are also present in other Allium species. It is evident that, at the higher levels used, allyl alcohol and methyl disulphide inhibited thyroid function significantly, and as is shown by the low values for uptake of iodine-131 in the treated animals; however, allyl monosulphide showed no antithyroid activity even at the highest level used[91].

Klein and Farkass have detected thiourea by micro chemical methods in *Laburnum anagyroides*. In 1938 Hopkins obtained 5, 5-dimethyl-2-thiooxazolidone from seeds of the crucifer *Conringia orientalis*; this compound was approximately one-fifth as active as thiouracil in the rat. On the other hand, the alleged existence of benzyl thiourea in seeds of *Carica papaya* is questionable[92].

The most useful herbal remedies for both under and overactive thyroid are sea plants. Bladder wrack, a form of kelp, is used in both western and Chinese herbal medicine. It can be taken as a supplement or as an infusion. Pour boiling water over 2 to 3 tsp. of the dried herb and steep for 10 minutes. This remedy is useful if there is a deficiency of iodine in the diet. Bitters are helpful for mild cases of hypothyroidism. These can be found in natural foods stores usually as a liquid supplement. Hyperthyroidism can be supported by an herb called bugleweed. This herb should not be taken without a doctor's support. It can interfere with thyroid replacement therapy, should not be taken by pregnant women, and can result in enlargement of the thyroid. Insomnia associated with hyperthyroidism can be helped by valerian and passion flower. To use these herbs, take 15 drops of each tincture in water, one half hour before bed[93].

Many more like botanical name of herbal thyroid stimulant, Gum guggle is *commiphora mukul*. The yellow resinous extract derived from the stem part of Mukul myrrh tree consists of volatile oils and resins in abundance. The pungent smell and acrid taste of this herb. The active compound in Guggle is called guggulsterone and has the power to influence thyroid function and improve the condition of hypothyroidism. A published journal titled 'Phototherapy research 'confirms the role of guggulsterone. An added advantage of having the herb is a decrease in the level of harmful cholesterol, one of the features of hypothyroidism. The incidence of side effect is low, but can range from headache, gastric upset, skin rash and rarely, hiccups[93].

DISCUSSION

Medicinal plants and natural products represent one of the most popular alternative treatments. Many of the natural products have hormonal activity. And have long been used to prevent and treat diseases including thyroid and might be good whatever the development of the synthetic drugs of antithyroid.

In the present study determined the antithyroid effects of various medicinal plants were found to inhibit uptake of thyroid hormone or radioactive iodine in a manner similar to that of antithyroid compounds. The most effective of these was Genistein and daidzein from soy (*Glycine max*) inhibit thyroperoxidase that catalyses iodination and thyroid hormone biosynthesis. And also hypothyroid effects include pearl millet (*Pennisetum glaucum*) and fonio millet (*Digitaria exilis*); thiocyanate is found in Brassicae plants[32].

The antithyroid and goitrogenic effects of Brassicae plants (Family *Cruciferae*) have long been known[75], including cabbage (*Brassica oleracea*), broccoli, cauliflower, kale, kohlrabi, Brussels sprouts, and rutabaga (swede or yellow turnip, *Brassica napobrassica*), rapeseed and mustard.

Our current study also demonstrates that the Rutabaga and turnips contain a thiourea like product (progoitrin), a precursor of goitrin that also interferes with thyroperoxidase[75].

And many more like natural flavonoids containing aglycones resulting from intestinal digestion are rapidly and readily absorbed[77], increasing the likelihood of development of antithyroid effects and goitre in infants receiving soy based formulas as milk substitute [78-84].

In previous studies shown that N-propyl disulphide, the major volatile constituent of common onion (*Allium cepa*), inhibited thyroid activity in the rat[91]. It is evident that, at the higher levels used, allyl alcohol and methyl disulphide (constituents of *Allium cepa*) inhibited thyroid function significantly, and as is shown by the low values for uptake of iodine-I31 in the treated animals; however, allyl monosulphide showed no antithyroid activity even at the highest level used[91].

Moreover, there are significant reports of goitrogenic effects from soy consumption in human infants and adults. Recently, we have identified genistein and daidzein as the goitrogenic isoflavonoid components of soy and defined the mechanisms for inhibition of thyroid peroxidase (TPO) catalysed thyroid hormone synthesis *in vitro*. The observed suicide inactivation of TPO by isoflavones, through covalent binding to TPO, raises the possibility of neoantigen formation and because anti-TPO is the principal autoantibody present in auto immune thyroid disease.

This hypothetical mechanism is consistent with the reports of Fort et al. (1986, 1990) of a doubling of risk for autoimmune thyroiditis in children who had received soy formulas as infants compared to infants receiving other forms of milk. The serum levels of isoflavones in infants receiving soy formula that is about five times higher than in women receiving soy supplements who show menstrual cycle disturbances, including an increased estradiol level in the follicular phase[94-97].

ATDs represent an effective tool to control hyperthyroidism. While in toxic adenoma and toxic multi-nodular goiter ATD treatment is merely preparatory to the definitive treatment by either RAI or thyroid- ectomy, in Graves' hyperthyroidism it is a valid alternative to the latter methods, particularly for the first episode of hyperthyroidism;

However, major and even life-threatening untoward effects may also occur, such as agranulocytosis, severe hepatoxicity, and vasculitis. Major side effects are more frequent (and dose-unrelated) using PTU than using MMI. This prompted the recommendation from experts that MMI rather than PTU should be used in hyperthyroidism. PTU maintains a role in the first trimester of pregnancy because of the potential (although rare) "methimazole embryopathy". In addition the effect of PTU on the peripheral conversion of T4 to T3 makes it preferable in the initial management of patients with thyroid storm; Relapses are frequent after ATD withdrawal, in the order of 50–60%, mostly within 1 year after treatment discontinuation. Relapsing hyperthyroidism should be generally managed by a definitive treatment[73].

CONCLUSION

The findings of the study suggest that an antithyroid compound, equal in potency to herbal plants and natural products, has been isolated from the root, leaf and seed of that various plants. Alternative thyroid treatments place more importance on improving lifestyles and nutritional diet, providing spiritual support along with natural thyroid medication and also places a priority on improving functions of other organs that increase thyroid performance. Still various herbal plants were questionable need to be further study.

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