An complete study of thyroid disease and it's control in India

Vyas Gitesh Vinod[1], Sushma Sanap[2], Phoke S.V[3], Hatkar A.D[4],Laghane P.M [5]
[1,,3,4, 5]*I Assistant Professor in Institute of Pharmacy Badnapur*
[2] *B pharmacy student in Institute of Pharmacy Badnapur*

Abstract: Thyroid disease are major problem as modern society and are classified as disease of civilization unhealthy lifestyle, stress, exposure to chemical, others factor like ageing, smoking status, iodine deficiency, genetic susceptibility, endocrine disruption, immune checkpoint inhibitor also influence thyroid disease it was unfortunate that there had not yet to be any potential care for hypothyroidism, treatment in form of synthetic thyroid hormone cause patient to suffer from symptom of hypothyroid limitations of surgery might need to be rely on synthetic hormone for lifetime, In this report we review key factor responsible for iodine deficiency in India progress made to cour those deficiency herbal drug showing promising result in all age group and pilot plot study recent intiationIodine Bindi by Indian govt. to prevent, treat thyroid disease

Keywords: Thyroid disease; causative factor, treatment, herbal drug, disorder, mechanism of action National Iodine deficiency disorder control programme (Iodine Bindi)

1. INTRODUCTION

The endocrine system is the network of gland that regulate several vital functions of human body. Ranging from regulation of heart beat, normal development of many tissue, metabolism It consist of 10 gland out of which Thyroid gland is considered as one gland even slight hiccup can alter the delicate balance of these gland leading to endocrine disorder, deficiency that manifests in various form.[1]

Usually these disorder have been characterized depending upon amount of hormone, development of lesions/tumor, infection, failure of gland to stimulate another, autoimmune cells, deficiency of micronutrients like Iodine, Iron, Folic acid, Vit A, Zinc[2].

In our country the two endemic disease are Diabetes &thyroid. Which have reported there presence tremendously in last few decades, both these disease are metabolic disorder arise due to improper life style. Thyroid disease is triggered by immune system initiating an attack on own molecules due to deterioration of immunologic tolerance to auto reactivate immune cells.[3,4]

Thyroid gland is commonly targeted by autoimmune disease where most common dysfunction of thyroid gland are hypothyroidism, lymphocytic thyroditis(Hashimoto's thyroiditis) & hyperthyroidism (Grave disease). Grave disease is dominant and account for 50-80% of care of thyroid disease in different region of the world.

Thyroid disease as per age group	
Older age	Greater prevalence
Adult	Age 45 to 65 yrs can also Affect children.
Women	Prone to thyroid disease
Male	less Prone to thyroid.[5,6]

Thyroid disease

Thyroid disease are caused by an abnormal immune response to auto antigen present in thyroid gland.

Three main type of autoimmune thyroid disease.

- Hypothyroidism
- Lymphocytic thyroditis (Hashimoto's thyroditis)
- Hypothyroidism dysfunction of thyroid gland are hypothyroidism, lymphocytic thyroiditis (Hashimoto's thyroiditis) & hyperthyroidism (Grave disease). Grave disease is dominant and account for 50-80% of care of thyroid disease in different region of the world[4,5,6]

Symptoms of thyroid disease:

Typical symptoms of gland disease include: cacophonic voice; slowed speech; puffy face; drooping eyelids; intolerance of cold conditions; constipation; weight gain; dry hair; dry skin; and depression. Patient with gland disease have a larger risk of disorder, pathology, overweight, celiac disease and polygenic disorder [12].

Hashimoto's thyroiditis (HT) is Associate in Nursing disease within which the body system attacks the thyroid [13]. His can cause decrease in thyroid operate and eventually cause the clinical disorder known as hypothyroid. Untreated hypothyroid will cause patients gentle to severe symptoms starting from hair loss, cold

sensitivity, sleep disturbances, weight gain, depression, constipation, brain fog, fatigue, goiters (enlargement of the thyroid gland) and thyroid cancer [12]. Women are ten to twenty times additional seemingly to be affected by HT sickness than man [14]. Hyperthyroidism conjointly famous could be a condition within which the thyroid gland is hyperactive and produces an excessive amount of internal secretion [3]. Typical symptoms of adenosis include: high blood pressure; fast heartbeat; damp skin; increased sweating; tremor; nervousness; increased appetence with weight loss; intestines |symptom} and/or frequent bowel movements; weakness; eyeballs seem to be protruding; and sensitivity of the eyes to lightweight [15]. adenosis happens in close to a pair of to 3% of the adult population [16]. Hyperthyroidism happens concerning 10 times additional often in ladies than men [3]. Th average age at diagnosis of adenosis is forty eight years [6,17]

Hypothyroidism	Too little thyroid hormone (More in age old person)	Hoarse voice, slow speech, puffy face, droop eyelids, Intolerance of cold conditions, constipation, weight gain, dry hair, dry skin, depression, cardiovascular disease, osteoporosis, overweight, celiac disease, diabetes.[7,8]
Hashimoto's thyroditis	Autoimmune disorder body immune attack the thyroid. (More in women than men)	Hair loss, cold sensitivity, sleep disturbance, weight gain, depression, constipation, brain fog, fatigue, goiter, thyroid Cancer [7,8,9]
Hyperthyroidism	Thyroid gland is our active & produce too much thyroid hormone. (10 times more frequent in women than men)	High blood pressure, fast heartbeat, moist skin, increase sweating, tremor, nervousness, increased appetite with weight loss, diarrhea, frequent bowel movement, weakness, eyeball appear protruding.[7,8,9,10]
Thyroid nodules(benign) & cancer (malignant)	Also called as colloid nodule, cysts, nodular thyrodistoiled fluid fill lump in thyroid.	Does not present symptom but occasionally fat at base of neck & cause shortness of breath, difficulty in swallow[.7,8,9,10]
Reduced sensitivity to thyroid hormone	Impairment of sensitivity to thyroid hormone due to decrease tissue sensitivity to thyroid hormone Thyroid hormone receptor beta gene.	Goiter, hyperactive bhevaiour, learning disability and sinus tachycardia.[7,8,9,10]

Fig1:-table showing an condition of release of thyroid hormone along with its symptoms

Mechansim/pathophysiology

Thyroid hormone production &release are regulated by sensitive feedback loop the hypothalamus- pituitary thyroid axis thyrotropin releasing hormone produce in hypothalamus control production of TSH by anterior pituitary gland.[18]

TSH is turn regulate the production & secretion of two form of thyroid hormone by thyroid gland. T4 and more bioactive hormone triiodothyronine(T3) serum TSH level follow a circadian rhythm level are highest between 9 pm & 5 Am & lowest between 4 Pm and 7 Pm the thyroid gland secret predominantly T4 and to lesser extent T3.which account for up to only-20% of circulating T3. The remaining T3 is produced by peripheral tissue such as liver[18,19] , & skeletal muscle by activating enzyme type 1 & type 2 iodo thyronin deiodoinase which cleave an iodine atom from T4. [20,21]

Most circulating T4 & T3 is bound to transport proteins such as thyroxin binding globulintrasnthyrotin and albumin only ~0.02%of T4 and ~0.2% of T3 are present in an inbound form & this free T4 and free T3 can be measured for diagnostic purpose most biological activities of thyroid hormone are mediated by binding of T3 to nuclear T3 receptor which bind to thyroid response element in thyroid hormone responsive gene and modulate their expression[22,23,24]

TH receptor/ TH action the major action of TH is exerted through nuclear TH receptors (TRs), that area unit ligand-inducible transcription factors. supported body localization and amino alkanoic acid similarity, 2 categories of TRs, a and β, are known. because of differential splice of those 2 genes, multiple TRs area unit generated as α1, α2, α3, β1, β2, and β3, still as 3 truncated forms, Δa1, Δa2, Δβ (17,18). The α2 and α3 isoforms and every one of the truncated receptors area unit non-T3 binding proteins that operate as antagonists of TH communication (18–20).[25,26] TRa1 and TRβ1 area unit expressed in just about all tissues, however their abundance and roles dissent, looking

on the organic process stage of the organism and on the actual tissue sort (21). TRa1 is a lot of profusely expressed in heart, brain, and bone, whereas whereas is a lot of extremely expressed in liver and pituitary (21). in contrast, expression of TRβ2 is restricted to the neural structure and pituitary wherever it mediates inhibition of thyrotropin-releasing factor and TSH expression and also the tube and tissue layer wherever it regulates sensory organ development (21,22) and TRβ3 is expressed in excretory organ, liver, and respiratory organ (22). Thus, TH action in target tissues is decided partly by the kinds and abundance of TH receptors gift. In the nucleus, TRs kind homodimers with another TR or heterodimers with retinoid X receptors (RXR) and bind to specific TH response component sequences (TREs) settled in promoter regions of T3-target genes and regulate their expression during a ligand-dependent manner. Unliganded TRs bind TREs in T3 target genes and mediate transcriptional repression. Co-repressor proteins like nuclear receptor corepressor protein/silencing intercessor of retinoid and TH receptors area unit recruited to the RXR-TR heterodimer within the absence of T3 and inhibit target organic phenomenon. T3 binding displaces the co-repressor, permitting co-activator proteins like CBP/p300, pCAF, and SRC-1 to act with the RXR-TR heterodimer and activate sequence transcription during a hormone-dependent manner (24–27). Besides the genomic actions of T3, nongenomic mechanism of TH analogues area unit progressively recognized to own downstream consequences at the extent of specific sequence transcription (28,29). The nongenomic mechanisms of TH area unit better-known to be initiated at the cell membrane, within the living substance or within the intracellular organelles, like mitochondria. At the membrane level, TH could act with integrin aV/β3 to activate ERK1/2 that culminates in regulation of particle transport systems or cell proliferation (28). The relative contribution of nongenomic mechanisms in mediating TH effects on skeletal development is nonetheless to be determined.

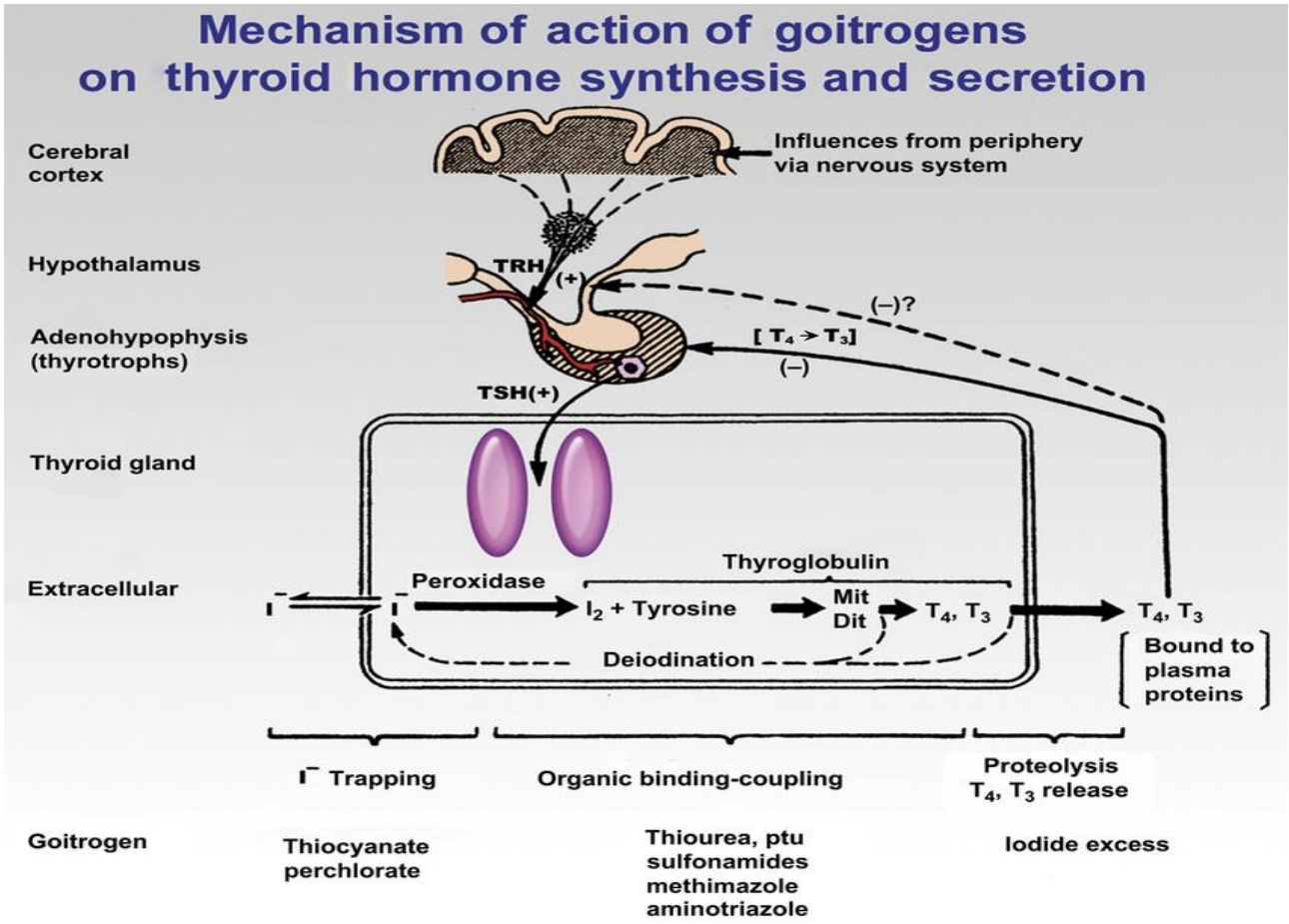


Fig2: Release and mechanism of action of thyroid gland

Pathophysiology;-

Hashimoto's thyroiditis (HT) is Associate in Nursing autoimmune disease during which the body system attacks the thyroid [13]. this can cause decrease in thyroid operate and eventually cause the clinical disorder known as hypothyroid. Untreated hypothyroid will cause patients gentle to severe symptoms starting from hair loss, cold sensitivity, sleep disturbances, weight gain, depression, constipation, brain fog, fatigue, goiters (enlargement of the thyroid gland) and thyroid cancer [29]. Women square measure ten to twenty times additional seemingly to be affected by HT sickness than man [30]. Hyperthyroidism conjointly famed could be a condition during which the thyroid gland is hyperactive and produces an excessive amount of hormone [11]. Typical symptoms of thyrotoxicosis include: high blood pressure; fast heartbeat; wet skin; exaggerated sweating; tremor; nervousness; increased appetency with weight loss; diarrhoeas symptom} and/or frequent bowel movements; weakness; eyeballs seem to be protruding; and sensitivity of the eyes to lightweight [31]. thyrotoxicosis happens in or so a pair of to 3% of the adult population [32]. Hyperthyroidism happens concerning 10 times additional oftentimes in girls than men [3]. He average age at diagnosis of thyrotoxicosis is forty eight years [33,34]

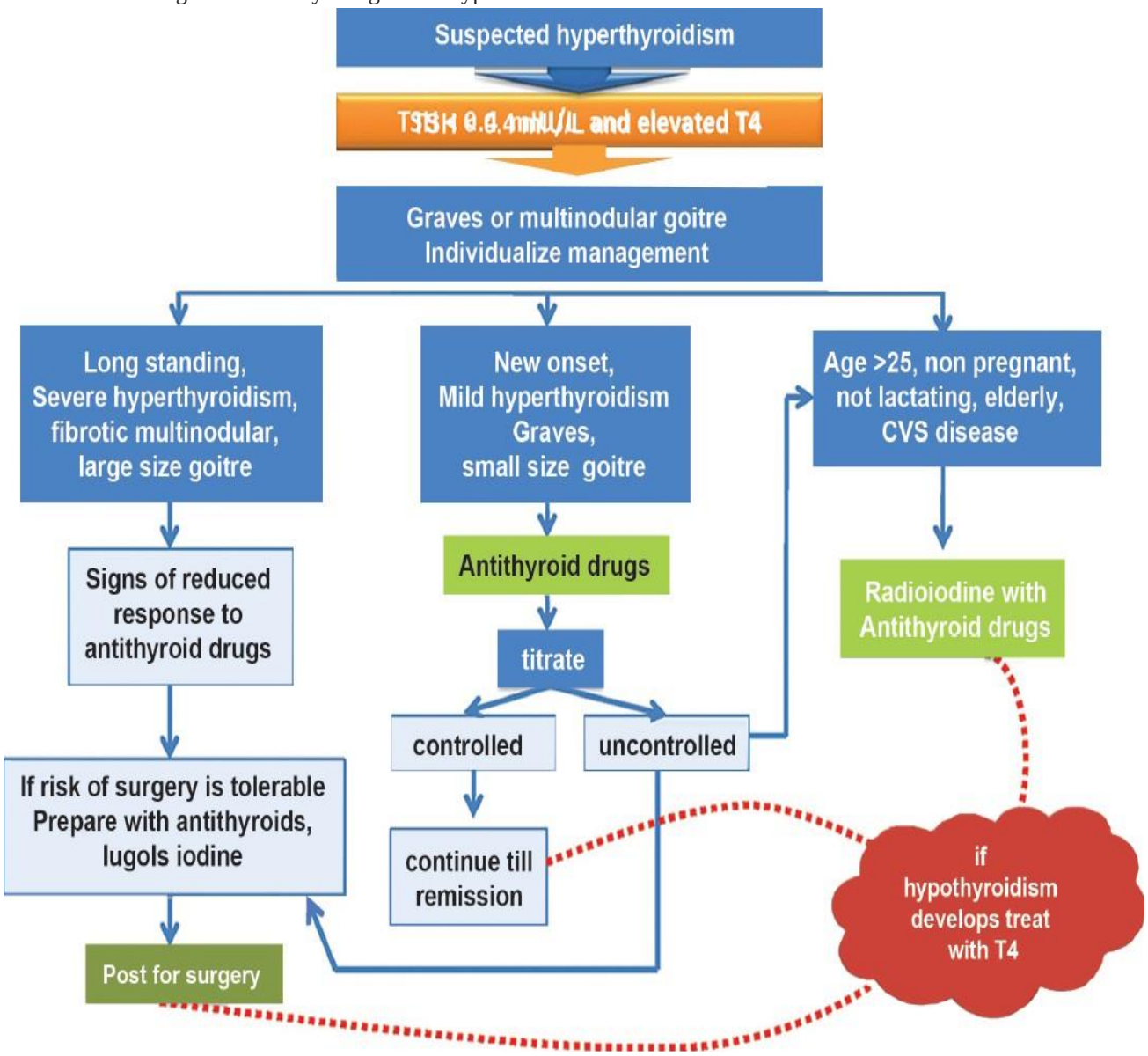
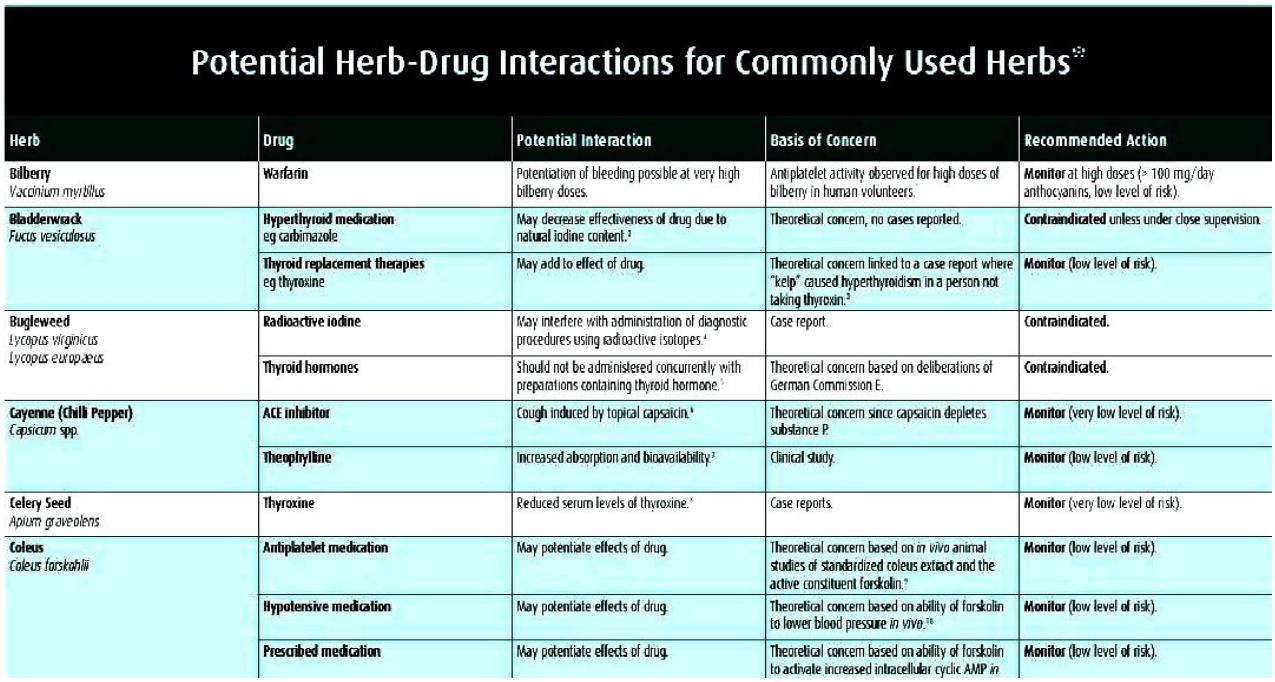


Fig3:- diagram representing different condition of thyroid abnormalities and precautionary measure for the same



Potential Herb-Drug Interactions for Commonly Used Herbs*

Herb	Drug	Potential Interaction	Basis of Concern	Recommended Action
Bilberry *Vaccinium myrtillus*	**Warfarin**	Potentiation of bleeding possible at very high bilberry doses.	Antiplatelet activity observed for high doses of bilberry in human volunteers.	**Monitor** at high doses (> 100 mg/day anthocyanins, low level of risk).
Bladderwrack *Fucus vesiculosus*	**Hyperthyroid medication** eg carbimazole	May decrease effectiveness of drug due to natural iodine content.[2]	Theoretical concern, no cases reported.	**Contraindicated** unless under close supervision.
	Thyroid replacement therapies eg thyroxine	May add to effect of drug.	Theoretical concern linked to a case report where "kelp" caused hyperthyroidism in a person not taking thyroxin.[3]	**Monitor** (low level of risk).
Bugleweed *Lycopus virginicus* *Lycopus europaeus*	**Radioactive iodine**	May interfere with administration of diagnostic procedures using radioactive isotopes.[4]	Case report.	**Contraindicated.**
	Thyroid hormones	Should not be administered concurrently with preparations containing thyroid hormone.[5]	Theoretical concern based on deliberations of German Commission E.	**Contraindicated.**
Cayenne (Chili Pepper) *Capsicum* spp.	**ACE inhibitor**	Cough induced by topical capsaicin.[6]	Theoretical concern since capsaicin depletes substance P.	**Monitor** (very low level of risk).
	Theophylline	Increased absorption and bioavailability.[7]	Clinical study.	**Monitor** (low level of risk).
Celery Seed *Apium graveolens*	**Thyroxine**	Reduced serum levels of thyroxine.[8]	Case reports.	**Monitor** (very low level of risk).
Coleus *Coleus forskohlii*	**Antiplatelet medication**	May potentiate effects of drug.	Theoretical concern based on *in vivo* animal studies of standardized coleus extract and the active constituent forskolin.[9]	**Monitor** (low level of risk).
	Hypotensive medication	May potentiate effects of drug.	Theoretical concern based on ability of forskolin to lower blood pressure *in vivo*.[10]	**Monitor** (low level of risk).
	Prescribed medication	May potentiate effects of drug.	Theoretical concern based on ability of forskolin to activate increased intracellular cyclic AMP *in*	**Monitor** (low level of risk).

Fig4:- herbal drug used in thyroid disease along with contradiction while using it[36-40]

Thyroid issues in india

Goiter and Iodine Deficiency

Immune system thyroid illnessis presumably plebeian than iodine lack as a reason for goiter in regions that are currently iodine adequate. This prompted milestone concentrates on which showed that iodine inadequacy was related with hypothyroidism in children, laying everything out for the now unbelievable salt iodization program upheld by the Government of India [41-44]. Subsequent to this program, it was shown that in chose areas of Uttar Pradesh, the pervasiveness of inborn hypothyroidism had descended from 100/1000 to 18/1000. Around 14,762 kids from everywhere India were read up for the accompanying qualities: goiter pervasiveness, urinary iodine and thiocyanate discharge, practical status of the thyroid, just as serological and cytopathological markers for thyroid autoimmunity. The creators recommended that regardless of iodization, the commonness of goiter has not significantly declined.

Immune system Thyroiditis in India

Among them, 1810 school children had a goiter. Among them 764 subjects went through a fine needle desire cytology, and of these subjects, 58 (7.5%) had proof of adolescent immune system thyroiditis (the term included both Hashimoto's thyroiditis and central lymphocytic thyroiditis).

Thyroid Cancer and India [41-44]

Among these patients, the NCRP noted 5614 instances of thyroid malignant growth, and this included 3617 females and 2007 guys. The six habitats engaged with the examinations were at Mumbai, Delhi, Thiruvananthapuram, Dibrugarh, Chandigarh, and Chennai. Among them, Thiruvananthapuram had the most noteworthy relative recurrence of instances of thyroid disease among all malignant growth cases took on the clinic library, 1.99% among guys and 5.71% among females. The histological kinds of thyroid malignant growth were considered in a Hospital Cancer Registry of 1185 "new cases" of thyroid disease. [41-44]

Recommended Daily Intake of Iodine: (2)

Age or population group a	U.S. Institute of Medicine	Age or population group	World Health Organization
Infants 0–12 months	110-130	Children 0-5 years	90
Children 1-8 years	90	Children 6-12 years	120

Children 9-13 years	120	Adults >12 years	150
Adults ≥14 years	150	Adults >12 years	150
Pregnancy	220	Pregnancy	250
Lactation	290	Lactation	250

Role of Iodine in Thyroid Physiology:

Iodine is a trace element in soil and water that is ingested in several chemical forms. Most forms of iodine are reduced to iodide in the gut. Iodide is nearly completely absorbed in the stomach and duodenum. Iodine is cleared from the circulation primarily by the thyroid and kidney. Under normal circumstances, plasma iodine has a half-life of approximately 10 hours, but this is shortened if the thyroid is overactive, as in iodine deficiency or hyperthyroidism. The mean daily turnover of iodine by the thyroid is approximately 60-95 µg in adults in iodine-sufficient areas. The body of a healthy adult contains from 15 to 20 mg of iodine, 70%-80% of which is in the thyroid. In the basolateral membrane of the thyroid cell, the sodium/iodine symporter (NIS) transfers iodide into the thyroid across a concentration gradient 20-50 times that of plasma by active transport. Degradation of T4 and T3 in the periphery releases iodine that re-enters the plasma iodine pool. Most ingested iodine is eventually excreted in the urine. Only a small amount appears in the feces. The mammary gland concentrates iodine and secretes it into breast milk to provide for the newborn. The salivary glands, gastric mucosa, and choroid plexus also take up small amounts of iodine.

Iodine deficiency is a major health problem in India

The soil of the subcontinent has little iodine, so food grown on it shows few traces of the element. As a result, all Indians are prone to iodine deficiency disorders. The most popular method of tackling the problem has been to encourage the consumption of iodised salt, which reaches about 91% of Indian households. Even so, some 350 million people remain at risk of iodine deficiency disorders that can lead to goiter, hypothyroidism and even brain damage. Even mild iodine deficiency in pregnant women can result in children being born with cretinism and mental retardation. (45)

Current India plans to eradicate thyroid disease

Iodine patch as regular bindi:

Most people across the United States and throughout the developed world get their body's requisite dose of iodine by way of their diet (think "iodized salt"). For those whose diets don't provide enough of this hormone-regulating chemical, supplements can help boost the body's iodine levels. In parts of rural India, however, those supplements can be both prohibitively expensive, and hard to come by. (45)

Women in India have been sporting small dots between their eyebrows since the third or fourth century. The mark is called a bindi and is a Hindu tradition. (46,47)

This attempt is being materialized through "daily dose" of iodine incorporation into the traditional Bindis. The wearing of bindis form part of a cultural practice of Indian Women, which are "self-adhesive" in between their eyebrows, have been impregnated with a solution of iodine.

For age immemorial, in Hindu culture, the bindi has been symbolizing a chakra, or the point of energy, among other six, situated in the body. Therefore, the practice of wearing bindi has been quite prevalent across the Indian peninsula. (48)

An Iodine patch, designed like a r"gula' bindi, is expected to help one lakh tribal women in north-west Maharashtra battle iodine deficiency. Since these tribals don't consume iodized salt, they are usually deficiency in this nutrient. (49)

It seems like a brilliantly simply idea. Indian women with iodine deficiencies could be spared severe medical conditions, says an advertising agency, if they use a special version of an everyday beauty accessory: the Jeevan Bindi or the Life-Saving Dot. The firm says it has handed out packets of iodine-coated bindis to women in rural areas, which will provide users with their daily dose of the essential element through the skin on their foreheads. (50)

Created by Grey For Good, the philanthropic arm of the Grey Group Singapore communications firm, in partnership with the Neelvasant Medical Foundation and Research Centre and Talwar Bindi manufacturers, the patches slowly release the recommended amount of iodine over the course the day, while fitting seamlessly into the daily routines

of millions of Indian women who already affix bindis to their foreheads on a regular basis. Grey Group Singapore release, the bindis have already been put into circulation at medical camps in a number of rural villages across India. What's more, according to CEO Ali Shabaz, "This program can easily be extended to reach a larger population of women in India who need this vital mineral for a healthier life."(50)

CONCLUSION

A better understanding of metabolic physiological state in healthy individuals and also the altered metabolic constitution in T2D can likely result in the event of higher treatments for T2D. The role of the system, genetics, hormones concerned in metabolic physiological state (such as hypoglycaemic agent, glucagon, GLP-1 and GIP), glucolipotoxicity diets and feeding behaviours, sedentary lifestyles, altered island design, the immune system, altered islet-cell behaviour, UCP2, altered extrapancreatic behaviour and risk factors (such as psychological stress) have in T2D aetiology and pathological process remains to be mechanistically understood. Only if T2D could be a complex illness involving AN array Of hormones, their receptors and future living thing activity, future therapeutic research must take into consideration however the action of all of these hormones move synergistically in T2D to supply the altered metabolic constitution, and conjointly however treatments such as GLP-1R activation-based therapies in which IODINE BINDI [program of Indian government] will influence this secretion synergism to supply a metabolic constitution additional similar to that of a healthy individual. GLP-1R agonists are an attractive target to come up with simpler therapies for T2D only if they need been reported to possess helpful effects on multiple organs within the body, that are concerned in disease pathology

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