BOTANICAL MEDICINES FOR THYROID DISEASE

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Conflicts of Interest

I am a Pharma and Natural Products Industry Consultant

Nothing to Declare
Mind Map of Lecture

- Introduction
- Herbal Medicine
- Clinical Tips On Formulation
- Hypo-Thyroidism
- Hyper-Thyroidism
- Adrenal Herbs
Botanical Medicines?

- 88% of the world’s population relies predominantly on herbal medicines for some aspect of primary care.
- 25% of all dispensed prescription drugs in North America are derived from plants.

Plants as Medicine?

Of the ~500 new chemical entities approved by regulatory authorities around the world in the past decade, nearly half are from natural sources.

Learning from Nature

Of the 119 pure chemical compounds extracted from higher plants used in medicine throughout the world, 74% of these compounds have the same or related use as the plants from which they were derived.

Plant Medicine Safety?

History of uses is acceptable as proof of safety

World Health Organization
BROADER APPLICATIONS FOR THYROID HORMONE THERAPY

- Conditions where thyroid hormones may be therapeutic include:
  - Obesity
  - Cardiovascular disease
  - Osteoporosis
  - Depression
ENVIRONMENTAL TOXINS AND CONTRIBUTORS TO THYROID DISEASE

- **POPs!**
- **HALIDES:** Bromine, Chlorine, Flourine
  May interfere with iodine uptake
- **CHEMICALS:** Organochlorides, PCBs. PBDEs
  May agonize, antagonize TH receptors, and other with other endocrine disruption
- **HEAVY METALS:** Cadmium, Lead, Mercury
  May Interfere with T3-T4 Conversion, and ultimately lower T3 levels
- **LOW ANTIOXIDANT LEVELS:** Vitamins E, C, Selenium
  May reduce protective mechanisms against the above heavy metals and chemicals
CLINICAL TOOLS FOR HYPOTHRYOIDISM
Hypothyroidism

• Hypothyroidism affects a significant % of the population, and may occur in tandem with metabolic syndrome, both being associated with:
  – Hyperlipidemia
  – Dysglycemia
  – Reproductive Issues
SEAWEED FOR HYPOTHYROIDISM
Fucus
Traditional Uses

• Used as a food
  – burned to ash for a salty flavor

• Used as a medicine
  – topically for skin and in body wraps to support weight loss
  – orally for cancer, inflammation, goiter, and thyroid disease
Seaweeds are high in numerous minerals and halides including iodine.

The bioavailability of the iodine in seaweed has been shown to be quite good, though slightly less than direct KI supplementation.

Not only do seaweeds such as *Fucus* provide iodine, seaweeds are reported to contain di-iodotyrosine or DIT. Seaweeds, containing DIT may promote thyroid function by making it easier for the thyroid gland to make active thyroid hormones.

Free diiodotyrosine when present at a very low concentration, 50 nM, exerts a stimulatory effect on thyroid hormone synthesis.

The presence of DIT within the colloid of the thyroid gland may stimulate the gland to produce thyroxine.

diiodination occurred as a minor degradation pathway. However, no monoiodo[\(^{131}\)C]tyrosine or [\(^{14}\)C]tyrosine were observed. Exchange reaction between free diiodotyrosine and iodide is therefore
Fucus vesiculosus contains the flavonoid flucoxanthin reported to have the greatest antioxidant activity of all the edible seaweeds tested. This may contribute to stabilizing effects in thyroiditis.
There is no officially approved or standardized dosage, however most providers recommend 4-6 grams of the crude dried seaweed to treat metabolic function.

At 0.01%, this is approximately equivalent to 400 – 500 µg iodine.
Doses from 3-6 mg per day significantly benefited women with cyclic mastalgia as compared to placebo, without notable toxicity, thyroid suppression, or side effects.

No safety data is available, but based on the use of the bladderwrack as a traditional food, moderate consumption of seaweeds is generally considered safe if from a clean and reliable source.

Nagataki S. The average of dietary iodine intake due to the ingestion of seaweeds is 1.2 mg/day in Japan. Thyroid. 2008 Jun;18(6):667-8
Zava TT, Zava DT. Assessment of Japanese iodine intake based on seaweed consumption in Japan. Thyroid Res. 2011 Oct 5;4:14
Fucus
Safety

Source is crucial

There have been case reports of nephrotoxicity from bladderwrack, possibly due to arsenic contamination

Iodine may suppress thyroid function when consumed in large amounts


S. Garbardi, C. Cormeir, J, Cina et al. *Renal Dysfunction Associated with Herbal Remedies and Dietary Supplements*.

Nephrology, June/July 2003, Vol I, Issue 2

Nagataki S. *The average of dietary iodine intake due to the ingestion of seaweeds is 1.2 mg/day in Japan*. Thyroid. 2008 Jun;18(6):667-8

Zava TT, Zava DT. *Assessment of Japanese iodine intake based on seaweed consumption in Japan*. Thyroid Res. 2011 Oct 5;4:14

Fucus
Pregnancy

• There is no research suggesting *Fucus* is not safe during pregnancy

• A human study of iodine content of breast milk in Korean women consuming an average of 2.7 mg of iodine per day, reported that the colostrum contained 2.2 mg per liter and mature milk 0.9 mg/L
  – 0.00022% I for colostrum
  – 0.00009% I for breast milk
COMMIPHORA MUKUL FOR HYPOTHYROIDISM
Commiphora mukul
Traditional Use

- arthritis, gout, promotes appetite
- rheumatism, lumbago,
- nervous disorders, obesity
- chronic indigestion, hepatitis
- leucorrhea, debility, diabetes, tumors
- cystitis, skin diseases, hemorrhoids
Commiphora mukul
Constituents

*Commiphora mukul* contains sterols referred to as guggulsterones

\[ Z\text{-guggulsterone} \]
\[ E\text{-guggulsterone} \]
*Commiphora mukul* has a thyroid stimulating effect and is useful for high cholesterol, obesity, and sluggish metabolic functioning.

Ketosteroid found in *Commiphora* increases the uptake of iodine by the thyroid gland and enhances the activity of thyroid peroxidase enzymes.
Animal studies have shown Commiphora mukul to reduce the effects of thyroid suppressive drugs, indicating a thyroid hormone-enhancing effect and possible utility for hypothyroidism.
Commiphora mukul has been shown to promote T3 along with healthy alterations in the ratio of T3 to T4, indicating a thyroid-supportive effect.
Resin from the mukul myrrh tree, guggul, can it be used for treating hypercholesterolemia? A randomized, controlled study

Lise Anett Nohrª, Lars Bjørn Rasmussenª, Jørund Straand©

A randomized, double-blinded placebo controlled study reported guggul supplementation significantly reduced total cholesterol after 12 weeks.

Research has shown guggulsterones to inhibit nuclear receptors involved with basic metabolic functions and cholesterol metabolism, contributing to the plant's hypolipidemic effect.

This use is increasing in the US and Western Europe. Guggulsterones, the presumed bioactive compounds of guggul, may antagonise two nuclear hormone receptors
Commiphora mukul
Dosing

Physiological: 250 – 500 mg up to TID

Pharmacological: up to 2000 mg up to TID
**Commiphora mukul**

Safety/Adverse Events

While few side effects are commonly reported among users or prescribers, guggul may cause stomach discomfort or allergic rash.

Concentrated guggulipid may cause a dermatologic hypersensitivity reaction in some patients.

No studies on long term use have been conducted as yet.


Commiphora mukul

Pregnancy

There has not been extensive reviews, but a comprehensive search of published literature recommends that guggul be avoided during pregnancy.

IRIS VERSICOLOR

FOR THYROID SUPPORT

AND

MOVING STAGNANT FLUIDS
*Iris versicolor* is small wild Iris used medicinally by native Americans and early American pioneers.
Iris versicolor
Traditional Use

• *Iris* bulbs have been used traditionally for:
  – goiter, both topically and internally, to improve sluggish metabolic function

• To move bodily fluids
  – including saliva, lymph, bile, and digestive secretions
Iris veriscolor

Iris is used for moving stagnant fluids and secretions in the body and to stimulate thyroid function.
One respected early American practitioner, HW Felter said that Iris "impresses the thyroid function"
Iris versicolor for Hypothyroid Conditions

Iris was used as an adjuvant for decongesting and detoxifying tissues including the thyroid, so that normal functioning could be restored.
Iris versicolor

Dosing

• Physiological: 20 – 50 mg; 2-5 gtts. tincture
• Pharmacological: up to 200 mg; up to 20 gtts.tincture
• Often diluted or mixed with other plants to prevent oral or digestive irritation
Iris versicolor

SAFETY AND PREGNANCY

No published data suggest contraindications in the proper use of Iris versicolor
In summary, safe, natural remedies for hypothyroidism include:

- Selenium 200 μg, BID
- Tyrosine
- Fucus
- Commiphora mukul
- Iris versicolor
- Adaptogens and adrenal supportive herbs
- Immunomodulating herbs, antimicrobials
ROSMARINIC ACID FOR HYPERTHYROIDISM
Rosmarinic Acid for Hyperthyroidism

Rosmarinic acid is a phenolic compound derived from caffeic acid and is most common in Lamiaceae and Boraginacea family plants including:

- *Melissa officianalis* (Lemon Balm)
- *Lycopus europaeas* (Gypsywort)
- *Lycopus virginia* (Bugleweed)
- *Lithospermum officianalis* (Stoneseed or Gromwell)

All have been traditionally used for hyperthyroid symptoms

Keyvan Dastmalchi et al. *Chemical composition and in vitro antioxidative activity of a lemon balm (Melissa officinalis L.) extract* Food Science and Technology, Volume 41, Issue 3, April 2008, Pages 391-400

Rosmarinic acid appears to reduce:

- Autoimmune responses
- Auto antibody production
- Autoimmune processes contributing to Graves Disease
• Normally, when TSH binds thyroid cells, a cAMP response is initiated via adenylate cyclase enzymes.

• Based on animal studies, rosmarinic acid is hypothesized to inhibit these enzyme systems and thereby retard the ability of TSH to stimulate thyroid gland.
At concentrations of 20 or 40 \( \mu g \)/ml, the plant extracts did not affect basal cAMP concentration, but inhibited the increase in cAMP concentration induced by TSH from 26-43%.

*Lycopus virginicus* and *L. europaeus*, *Melissa officinalis* and *Lithospermum officinale* each have been shown to inhibit thyroid TSH response.
Inhibition by Certain Plant Extracts of the Binding and Adenylate Cyclase Stimulatory Effect of Bovine Thyrotropin in Human Thyroid Membranes*

MICHAEL AUF'MKOLK, JONATHAN C. INGBAR, SYED M. AMIR, HILKE WINTERHOF, HILDEGARD SOURGENS, ROLF D. HESCH, AND

Lycopus, Lithospermum and Melissa inhibits adenylate cyclase in thyroid cells and thereby reduces output of thyroid hormones.

dried aqueous extracts (FDE) of plants of the species Lycopus virginicus and Lycopus europaeus, Melissa officinalis (Lamiaceae), and Lithospermum officinale (Boraginaceae) have the ability to inhibit at least many of the effects of exogenous and endogenous TSH on the thyroid gland. To this end, we have examined the in vitro effects of FDE from these plants on the ability of bovine TSH (bTSH) to both bind to human thyroid plasma membranes (TPM) and activate adenylate cyclase therein.

FDE of these four species produced a dose-related, ultimately binding of FDE to TPM or damage to the TSH receptor.

When [125I]bTSH was incubated with the active FDE in Tris-BSA and the mixture was chromatographed on Sephadex G-100 using the same buffer, [125I]bTSH was shifted from an apparent mol wt of 30,000 and eluted at the void volume. Direct binding of [125I]bTSH in fractions from the new, large molecular peak was nil. Addition of a large excess of unlabeled bTSH during preincubation prevented the shift in the elution pattern of [125I] bTSH produced by these FDE. When the same experiment was performed in the presence of 50 mM NaCl, only about half of the [125I]bTSH was shifted.
Rosmarinic acid also shows a binding affinity for Graves autoantibodies.

Inhibition by Certain Plant Extracts of the Binding and Adenylyl Cyclase Stimulatory Effect of Bovine Thyrotropin in Human Thyroid Membranes*

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Rosmarinic acid shows a binding affinity for TSH, may form adducts with TSH and has antithyrotropic activity.
Rosmarinic acid inhibits de-iodinase.

Lycopus, and Melissa inhibit deiodinase enzymes outside of the thyroid and thus interfere with activation of thyroid hormones.
The plant extract given p.o. caused a long lasting (24 h +) decrease of T3 levels.

A pronounced reduction of T4 and TSH concentrations was observed 24 h after dosing.

Luteinizing hormone (LH) decreased as well.
Thyroxine-induced hyperthyroidism were treated with either *Lycopus* or atenolol. Both were able to reduce BP, HR, and cardiac hypertrophy over 5 ½ weeks time.

*Lycopus* reduced hyperthermia while atenolol did not. Further study showed the number of $B$-adrenoreceptors (heart muscle) reduced by *Lycopus* “almost equal” to atenolol.

Extracts from the plant *Lycopus europaeus* L. are traditionally used in mild forms of hypothyroidism. High doses caused a reduction of TSH or thyroid hormone levels in animal experiments, whereas in hyperthyroid patients treated with low doses of *Lycopus* an improvement of cardiac symptoms was reported without major changes in TSH or thyroid hormone concentrations.

*Lycopus* extract was tested in thyroxine treated hyperthyroid rats (0.7 mg/kg BW i.p.). Co-treatment with an hydroethanolic extract from *L. europaeus* L. started one week later than $T_4$-application and lasted 5.5 weeks. As reference substance atenolol was used. The raised body
Hyperthyroid patients were treated with *Lycopus europaeus* for 3 mo. Thyroid hormones and TSH were not noticeably impacted. However, the urinary excretion of T4 was greatly increased.

The proposed mechanisms are either glomerular effects by *Lycopus* or interference with renal resorption of T4.

Elevated heart rate was also reduced in the hyperthyroid patients experiencing this symptom.
Safe and natural remedies for hyperthyroidism include:

- Selenium 200 mcg BID
- Rosmarinic acid 150- 200 mg BID
- Plants containing rosmarinic acid
- Immunomodulating herbs, anti-allergy herbs
- Adaptogens and adrenal supportive herbs
- Herbal specifics for individual presentations
CLINICAL APPLICATIONS: FORMULATION TIPS
USE IN PRACTICE

The herbs and nutrients discussed in this presentation can be used in tinctures, concentrated extracts and encapsulations, and combined with nutrients that support thyroid function such as iodine and selenium.
USE IN PRACTICE

Look for formulations with the desired combinations for user-friendly prescriptions, and complement with any specific herbs or supplements lacking in the desired formula to create personalized prescriptions.
Include adrenal and thyroid herbs as an important part of your clinical tools in treating patients with endocrine imbalances.
USE IN PRACTICE

• The adrenals are synergistic and should always be considered in formulas for thyroid disorders.

• Adrenal herbs include *Panax, Eleutherococcus, Glycyrrhiza, Withania* and *Rhodiola*
thyroid hormones, and gonadotropins can be used as indicators of HPA axis function

thyroid hormones, and gonadotropins can be used to predict the development of adrenal insufficiency
The development of an adrenal crisis due to underlying adrenal insufficiency has been reported after the administration of thyroxine replacement therapy to patients initially thought to have only hypothyroidism.

**Case reports**

**CASE 1**

A 47 year old woman had presented elsewhere three years previously with a history of lethargy. No clinical or biochemical abnormality had been detected. Her symptoms persisted, and two years later a low serum thyroxine concentration and a raised serum thyroid stimulating hormone concentration were recorded. Plasma urea and electrolyte concentrations were normal. She was prescribed thyroxine 50 μg daily, increasing to 100 μg after two weeks, but felt ill and dizzy, lost weight, and stopped taking the

seen by several doctors; low serum thyroxine and raised serum thyroid stimulating hormone concentrations were found each time, and she was advised to resume taking thyroxine. Initially she took it only intermittently because it made her feel unwell within a few days, but eventually, because of repeated medical persuasion, she took it continuously for two months. During this period she became progressively more unwell, lost 10 kg in weight, and was confined to bed, unable to cope with daily activities; menstruation, however, continued. She then stopped taking thyroxine and was referred to this hospital.

On examination she was thin and pale; there was no pigmentation of the cheek or skin. Secondary sexual characteristics were well preserved. Her blood pressure was 110/70 mm Hg both recumbent and standing. Systemic examination did not elicit any abnormality. Investigation showed: plasma urea concentration 8 mmol/l (48 mg/100 ml) (normal range 4-7 mmol/l; 24-42
Common hyperthyroid clinical presentations include:

- Overlap with anxiety and insomnia
- Overlap with adrenal fatigue and imbalance
- Overlap with WBC suppression and allergies
- Overlap with tachycardia and hypertension
- Overlap with nutritional deficits
- Overlap with skin rashes, pretibial myxedema
Common hypothyroid clinical presentations include:
Overlap with metabolic syndrome
Overlap with PCOS and infertility
Overlap with amenorrhea, menstrual disorders
Overlap with obesity and weight issues
Overlap with fatigue, lethargy, and depression
Overlap with chronic infections, fungus
Summary

- Hypothyroidism is not uncommon
- Herbs for hypothyroid based conditions
  - Seaweed (*Fucus* spp.)
  - Guggul (*Commiphora mukul*)
  - Iris (*Iris versicolor*)
  - Nutrients (e.g. Se, Tyr)
Summary

• Hyperthyroidism

• Strategies for hyperthyroidism
  – Rosmarinic acid
    • *Melissa officianalis* (Lemon Balm)
      – *Lycopus europaeas* (Gypsywort)
      – *Lycopus virginia* (Bugleweed)
      – *Lithospermum officianalis* (Stoneseed or Gromwell)
QUESTIONS?