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T2/T3 Converter

Clinical Applications

- Improves regulation of thyroid hormones
- Helps convert T4 into T3
- Helps convert T3 into T2
- Helps break down rT3 into T2

Indications

T2/T3 Converter is designed to improve the proportion of thyroid hormones including T4, T3, T2, and rT3. It can help lower excess rT3, raise T3 when it is too low, and form T2 out of rT3.

Thyronamines - Overview

The thyroid gland secretes a variable amount of the hormones T4, T3, and T2. The body converts these primary hormones into over a dozen active compounds, collectively known as thyronamines.[1] These compounds are tyrosine peptides organified with iodine.

The difference between thyronamines is the number of iodine atoms and their location on the molecule. T4 and T3 are the best known of the thyronamines but the next most studied include T2 (3,5- diiodo-L-thyronine) and Reverse T3 (3,3',5'-triiodothyronine or rT3).

Thyroid hormones control the body's capacity to burn fuel, repair connective tissues, and regulate nerve conduction rate. These three processes play a role in every cell and can cause nearly any possible symptom.

Thyroid hormones act on these processes by their total amount in circulation, the amount in local tissues, and the proportion between the various hormones.

Clinicians and researchers recognize that the individual levels and ratios of the hormones T4, T3, rT3, and T2 can have marked clinical significance.

Patients can suffer from thyroid symptoms related to the wrong ratio of these hormones independent of the total quantity of thyroid hormones.

Conversion

The thyroid gland can change the ratios of T4 and T3 that It secretes. Yet the proportion of thyronamines in circulation, including T4, T3, T2, and rT3, is primarily by mechanisms outside the thyroid.

Once thyroid hormones enter peripheral circulation, they undergo numerous conversion steps systemically and within target tissues.

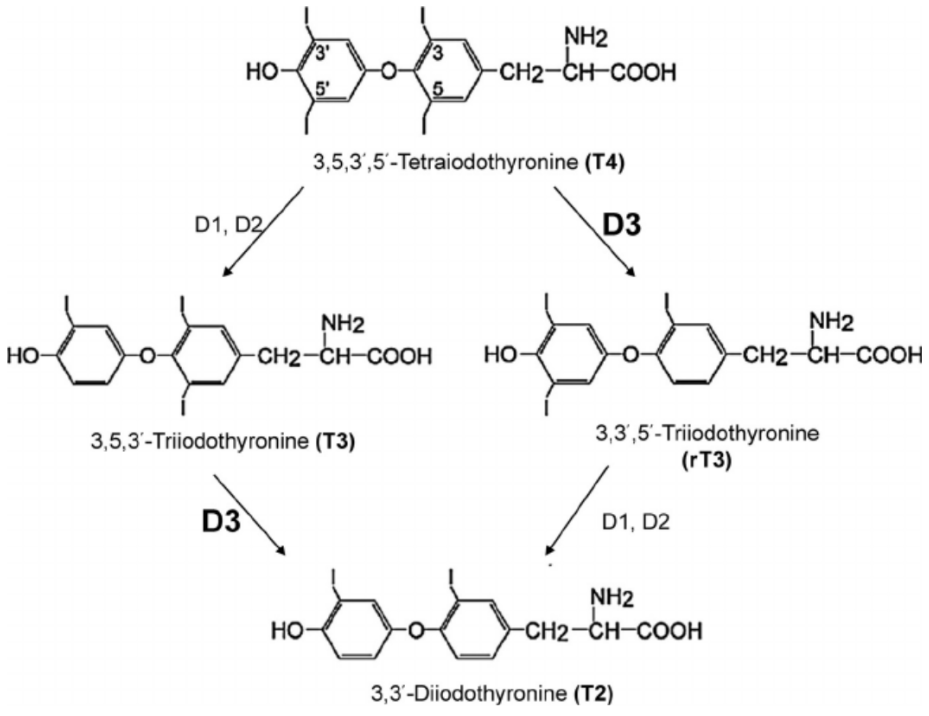
The process of conversion can be thought of as classic and alternate pathways. The alternate pathways involving thyronamines are regulated by numerous overlapping mechanisms. These regulatory systems can be thought of as central and peripheral.

Classic Pathways

The classic pathways are primarily mediated through the deiodinase enzymes and involve the removal of target iodine atoms. These include Deiodinase types 1, 2, and 3. These work in different body parts, each having distinct effects.[2]

Type	D1	D2	D3
Tissues	Liver, kidney, thyroid	Brain, pituitary gland, skeletal muscle	Brain, placenta, fetal tissues

Image 1: Pathways of Thyroid Hormone Conversion



Alternate Pathways

The alternate pathways of thyroid hormone regulation are primarily related to the deactivation and elimination of hormones.

They include:

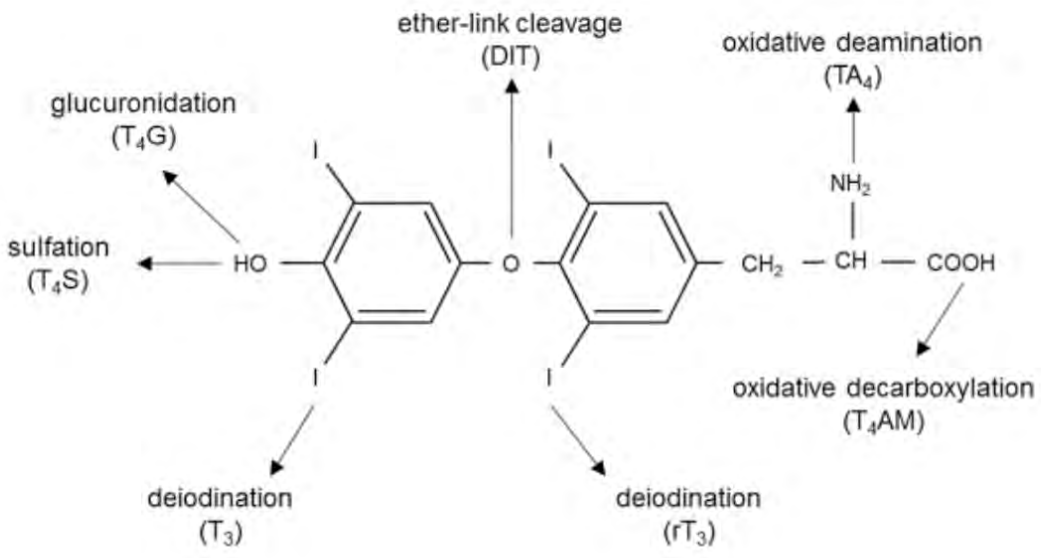
- Glucuronidation
- Sulfation
- Ether bond cleavage
- Oxidative deamination

Clinical Relevance of Conversion

The classical and alternative conversion pathways together create a balance of thyronamines dictated by the needs of local tissues.

During thyroid disease, conversion pathways do not always yield the optimal balance of thyronamines.

Image 2: Alternate Pathways of Thyroid Hormone Conversion[3]



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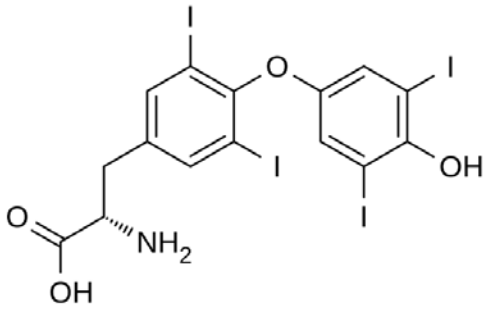
T4

Image 3: Thyroxine (T4)[4]



Thyroxine is the main hormone released by the gland. It is an active hormone by itself and serves as a precursor to T3 and rT3. T4 acts on cells independent from T3, as evidenced by distinct cell receptors.[5]

Low T4

Thyroxine may be lacking in untreated overt hypothyroidism or in suppressive doses of T3-containing medication.

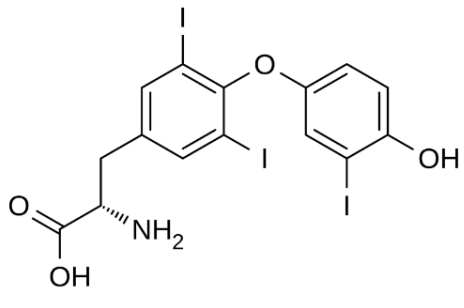
High T4

Thyroxine may be elevated in untreated hyperthyroidism or in excessive amounts of T4-containing medication.

Common clinical scenario: T4 relative to T3 and T2 may be excessive in patients on T4-only medication.

T3

Image 4: Triiodothyronine (T3)



Triiodothyronine is the second most predominant hormone released by the gland. Most, but not all thyroid hormone receptors are T3 responsive. T3 also serves as a precursor for T2.

Low T3

A known subset of hypothyroid patients who receive T4-only replacement has lower levels of T3 relative to T4 than healthy controls.[6] These low T3 issues may not correspond to serum levels. Because of this, patients may manifest hypothyroid symptoms such as fatigue or weight gain even if serum T3 or free T3 levels are normal.[7]

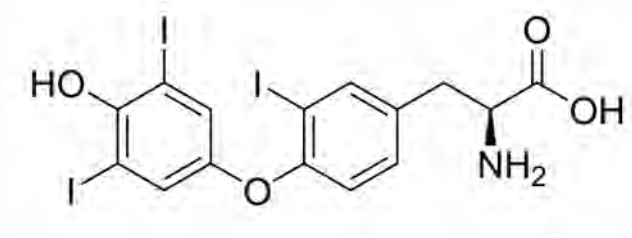
High T3

Triiodothyronine may be elevated in untreated hyperthyroidism or in excessive amounts of T3-containing medication such as Cytomel, Natural Desiccated Thyroid, or compounded T3. Triiodothyronine can be elevated or high normal in states of obesity or pre-diabetes.[8]

Common clinical scenario: T3 relative to T4 and T2 may be lacking in patients on T4-only medication.

rT3

Image 5: Reverse Triiodothyronine (rT3)[9]



Most T4 secreted from the thyroid is converted into Reverse T3 (rt3). rT3 is a deactivated intermediary of T4, but it also has activity on its own.

Low rT3

Low rT3 is not a well-explored clinical condition. The only known scenario in which it might arise would be prolonged T3 monotherapy. Since this has not been

the subject of adequately powered human trials, little is known about its implications. Some local tissues, such as the brain, depend on rT3 for normal metabolism.[10]

High rT3

States of high systemic rT3 can correlate with chronic inflammation, fasting, abnormal cortisol production, and ongoing disease processes. Patients with high rT3 often present with unresolved hypothyroid symptoms. It often remains unclear whether high rT3 is a beneficial adaptation in such states.[11]

Resolving the causes of high rT3 may correlate with numerous clinical benefits including:

- Improved energy
- Weight Loss
- Hair regrowth
- Benefits to cognitive function
- Reduced inflammation

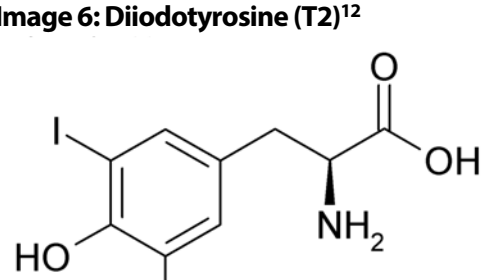
High rT3 can also be present as a beneficial adaptation to thyrotoxicosis. Patients with excess thyroid medication or unresolved hyperthyroidism will form higher amounts of rT3 as a healthy way to clear excess thyroid hormones.

If high rT3 is present, the most effective approaches are managing hyperthyroidism and helping to improve the body's ability to regulate it, and other thyronamines.

Common clinical scenario: High rT3 can come from poor hormone conversion or excessive amounts of T4-containing thyroid medication.

T2

Image 6: Diiodotyrosine (T2)[12]



T2 is one of the most significant of the thyronamines, yet it remains underappreciated by clinicians. It has three types: 3,5 T2 and 3,3' T2 and 3',5' T2. The first, 3,5 T2, is the one I will refer to as T2.[13]

The thyroid may directly secrete T2, but most of it is from T3 and rT3 in circulation. T2 plays many of the same roles as T3 but acts on different receptors. Since there are no commercially available assays for T2, and T2 does not suppress TSH, its absence can contribute to hypothyroidism without being measurable.

Low T2

T2 levels are known to be lower than healthy controls in:

- Pregnancy
- Those on full thyroid replacement
- Elderly patients

The lack of T2 is significant. It can be present in those not on thyroid medication or those taking T4-only medication like Synthroid. It may also be present in patients who take T3 as in Cytomel or Natural Desiccated Thyroid.

Studies have shown that healthy levels of T2 can improve:

- Oxygen utilization (more than T3)[14]
- Detoxification enzymes[15]
- Mitochondrial ATP synthesis[16]
- Activation of brown fat[17]

- Beta oxidation (fat burning)[18]
- Body composition[19]
- Cholesterol levels[20]
- Blood sugar regulation[21]
- Renal function[22]

T2 supplementation?

There are many examples where synthetic hormones taken as pills do not work the same as hormones the body makes naturally.

T2 supplementation is currently unregulated as a nonprescription product. No forms of prescription T2 exist. The drawback to supplementing with T2 is that it is impossible to track blood levels. The other problem is that T2 supplementation can bioaccumulate to dangerous levels within the liver.[23] Preclinical studies have shown that supplementing with T2 supplements can lead to cardiac damage in as little as four weeks.[24]

If low T2 is suspected, the most effective approach is improving the body's ability to regulate it and other thyronamines. T2/T3 Converter can safely help the body regulate its thyroid hormones.

High T2

Excess Diiodotyrosine is present in unmanaged hyperthyroidism and excessive dosing of T2-containing medication such as Natural Desiccated Thyroid or non-prescription T2 supplements.

Common clinical scenario: Hypothyroid patients may fail to achieve symptom resolution due to a lack of T2. This deficit can be corrected by managing hypothyroidism and assuming optimal thyroid hormone conversion with nutraceutical support.

Nutraceuticals for Conversion

Comprehensive literature analysis has been done on using nutraceuticals for hypothyroidism. Criteria employed include efficacy in human studies, safety, availability, and compatibility with thyroid medications when taken at least an hour apart.

Given those criteria, nutraceuticals are safe and beneficial for thyroid hormone conversion.

Selenocysteine

Selenium is an essential trace mineral. All aspects of thyroid function require an adequate supply of selenium. Selenium is also necessary for deiodinase enzymes that regulate peripheral thyroid hormone metabolism.[25]

How it Improves Peripheral Metabolism

Selenium helps the thyroid make glutathione, the antioxidant that protects the thyroid against oxidative damage from iodine. Thyroid antibodies elevate when the damage to the cells escalates, impairing optimal secretion of hormones.[26]

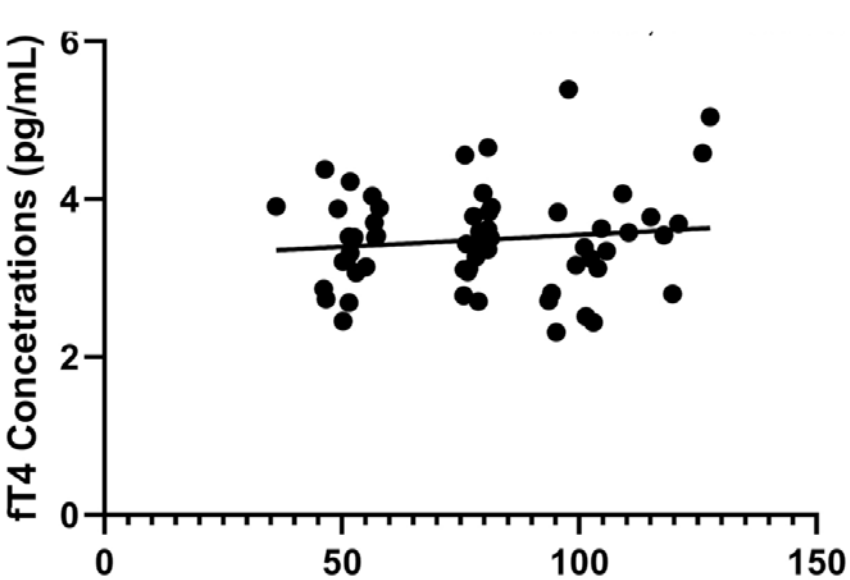
Mechanisms of Action

All deiodinase enzymes (D1, D2, D3) are selenoproteins that contain selenocysteine as their active center.[27] Even in cases of selenium sufficiency, when selenoproteins are not adequately synthesized into selenocysteine, the deiodinase enzyme activity is impaired. This impairment of deiodinase enzymes can impair the conversion of thyroid hormones and inhibit the optimal balance of thyronamines.[28]

Clinical Trials

In a study of hypothyroid pregnant women, selenium status was directly shown to correlate with better thyroid function and more optimal free T4 levels.[29]

Image 7: Serum Selenium and fT4



Vitamin E

Vitamin E is a family of lipid-soluble antioxidants, including multiple isomers and sub-compounds. D-Alpha Tocopheryl Succinate is a representative Vitamin E isomer that has been shown to have beneficial effects on the balance of thyronamines.

How it Improves Peripheral Metabolism

D1 peripheral metabolism can be disrupted by free radical stress such as lipid peroxidation. Exposure to numerous environmental toxicants, including cadmium and lead, is known to cause lipid peroxidation and disrupt deiodinase activity.

Preclinical trials have shown that the administration of vitamin E isomers can prevent lipid peroxidation from leading to disruptions in thyroid metabolism.[30]

Zinc

Next to iodine and selenium, zinc is arguably the next most critical mineral for thyroid hormone production and regulation.

How it Improves Peripheral Metabolism

Zinc regulates all deiodinase enzymes and can improve the balance of T3, T2, and rT3. It is essential for the hypothalamic activity of thyrotropin-releasing hormone and the pituitary production of TSH.

Zinc also plays a role in the action of transcription factors used in thyroid hormone synthesis. Circulating levels of zinc can directly affect levels of TSH, T4, and T3.[31,32]

D-Limonene and Calcium-D-Glucarate

VD-limonene is a naturally occurring monocyclic monoterpene. It is found in a wide variety of citrus fruits and other plants.

Humans metabolize d-limonene into various compounds, including perillic acid, dihydroperillic acid, limonene-8,9-diol, and monohydroxylated limonene. All of these metabolites are known to act as glucuronides.[33] Oral usage of glucuronides lower beta-glucuronidase, an enzyme produced in the large intestine.[34]

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Why Glucuronidation Matters

In The colon contains a reservoir of thyroid hormones, especially T4. As much as 20% of a given day's thyroid hormones may be bound by glucaric acid in the colon. This reservoir of hormones is loosely bound to gluconic acid and can be assimilated via entero-hepatic recirculation. Healthy euthyroid controls can draw on this source against times of lower hormone availability and add to it during times of hormone excess.

Studies have shown that when glucuronidation is impaired, TSH levels can increase, and medication changes may be necessary.[35] Glucuronidation is also a critical pathway in humans for clearance of rT3.[36]

Improving glucuronidation restores the critical connection between the thyroid-gut axis allowing the body to maintain ideal proportions of circulating thyroid hormones.

Ellagic Acid

Ellagic acid is a polyphenol found in many fruits and vegetables. Pomegranates are a particularly rich source of it. The FDA lists it with other culinary herbs and spices in its Generally Recognized as Safe ingredients.

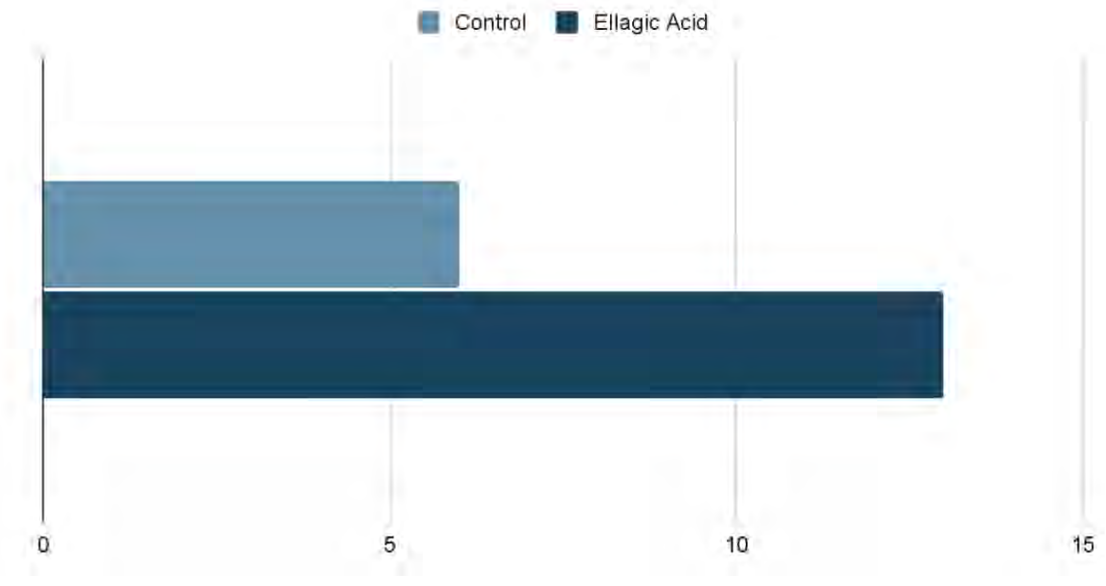
How it Improves Peripheral Metabolism

Ellagic acid and its metabolites, have numerous effects on thyroid hormone metabolism. Some of these effects come from the inhibition of beta-glucuronidase, as in the case of D-limonene and calcium-d-glucarate.[37]

Other effects come from the activity ellagic acid has on thyroid hormone receptors. Ellagic acid and ellagitannins are converted in the gut to urolithins. These urolithins improve the circulating proportion of thyronamines.

In preclinical studies, ellagic acid metabolites have been shown to increase T3 production from brown adipose tissue. This change increased basal metabolic rate and prevented weight gain.[38]

Image 8: T3 in Adipose Tissue (ng/g)



Turmeric Root

Turmeric has thyroprotective effects by improving antioxidant, anti-inflammatory, and anti-apoptotic effects. It can also activate NRF2 pathways that prevent oxidative damage to thyroid tissues.

How it Improves Peripheral Metabolism

Curcumin from turmeric root can improve low levels of T3. This effect was documented when T3 was low, secondary to high levels of pro-inflammatory cytokines.

A study used pharmacologic doses of lithium to induce thyroid dysfunction. The production of cytokines caused elevations of TSH and dramatic reductions in fT3. The usage of curcumin prevented over 75% of the fT3 inhibition. [39]

Grape Seed Extract

Grape seed extract is considered by researchers to be among the most effective plant antioxidants. It has been shown to benefit numerous oxidative, inflammatory, and vascular issues.[40]

It is thought to benefit thyroid disease by improving hypervascular states and lowering chronic tissue inflammation.

Human Clinical Trials

In a clinical trial, a group of adults was given levothyroxine for 30 days. Researchers tracked their free radicals, inflammation, symptoms, and thyroid levels.

Image 9: Protective effects of curcumin against lithium toxicity.

They were then divided into three groups, each of which received an additional pill to take after taking levothyroxine. One pill was a placebo, one was a blend of bioflavonoids, and one was oligomeric proanthocyanidins from grape seed extract.

The expectation was that extra T4 relative to T3 would cause symptoms since these patients were euthyroid before the trial. The group that was given grape seed extract saw lower rates of inflammation, free radicals, and negative symptoms than those groups on bioflavonoids or placebo.[41]

Supportive Strategies for Hormone Conversion

T2/T3 Converter is best used as part of a comprehensive protocol aimed to improve thyroid hormone conversion.

Additional therapies should include:

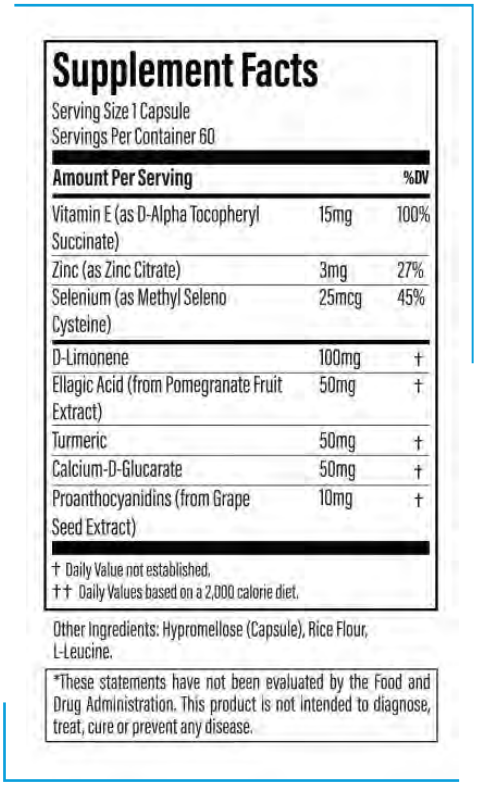
- Thyroid Specific Multivitamin - Thyroid Daily
- Iodine regulation as per the book The Thyroid Reset Diet
- Identification of sources of chronic inflammation such as infections, or toxicants
- Correction of abnormalities of cortisol slope

T2/T3 Converter Dosage

1 capsule once daily with food or as recommended by your health care professional.

Does Not Contain

T2/T3 Converter does not contain Iodine, gluten, corn, yeast, soy, GMOs, dairy products, artificial colors, artificial flavors, or preservatives.



Supplement Facts

Serving Size 1 Capsule
Servings Per Container 60

Amount Per Serving		%DV
Vitamin E (as D-Alpha Tocopheryl Succinate)	15mg	100%
Zinc (as Zinc Citrate)	3mg	27%
Selenium (as Methyl Seleno Cysteine)	25mcg	45%
D-Limonene	100mg	†
Ellagic Acid (from Pomegranate Fruit Extract)	50mg	†
Turmeric	50mg	†
Calcium-D-Glucarate	50mg	†
Proanthocyanidins (from Grape Seed Extract)	10mg	†

† Daily Value not established.
†† Daily Values based on a 2,000 calorie diet.

Other Ingredients: Hypromellose (Capsule), Rice Flour, L-Leucine.

*These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.

Side Effects

The ingredients in T2/T3 Converter are categorized as Generally Recognized as Safe (GRAS) by the FDA.

Common side effects to GRAS ingredients are similar to the rates of side effects to placebo and can include nausea, headache, and fatigue. Inform your doctor or pharmacist about any possible side effects of supplements or medications.

Cautions

Timing

- T2/T3 Converter must be taken at least an hour after thyroid replacement medication.

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Medication Compatibility

- Those on prescription medications are advised to consult their personal doctor or pharmacist about any known interactions between their medications and the ingredients found in T2/T3 Converter.

Dosage Modification

- Those taking T2/T3 Converter while on thyroid replacement medication (hypothyroidism, Hashimoto's) or thyroid suppression therapy (Graves' Disease) are advised to monitor thyroid levels closely. When thyroid antibodies reduce, some need decreases or adjustments to their medication.

Allergy Warning

- This product is contraindicated in an individual with a history of hypersensitivity to any of its ingredients.

Pregnancy Warning

- If pregnant or nursing, do not use unless on the advice of and under the direct supervision of a health professional.

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