

# Thyroid SAP

Science-based formulation for thyroid support

The thyroid gland produces thyroid hormone (TH) by synthesizing it through the iodination of tyrosine residues in the glycoprotein thyroglobulin. TH regulates metabolic processes necessary for average growth and development and for maintaining adult metabolism. TH level in the body influences body weight and energy expenditure. Low TH levels can reduce cardiac output, increase systemic vascular resistance, and impair immune function, possibly delaying injury repair. Compared to pharmacological options to manage thyroid imbalance that have adverse side effects, nutraceuticals, such as selenium, zinc, myo-inositol, and N-acetyl-L-cysteine are used for treating thyroid complications and have fewer side effects on general health.

**NFH Thyroid SAP** provides a synergistic blend of evidence-based key nutraceuticals that can help promote thyroid gland function, foster immune system, and help manage symptoms of thyroid disorders.

## ACTIVE INGREDIENTS

Each vegetable capsule contains:

L-Tyrosine	250 mg
Inositol	150 mg
Ashwagandha ( <i>Withania somnifera</i> ) root extract, 5% withanolides	125 mg
N-Acetyl-L-cysteine	125 mg
Zinc (from zinc citrate)	2.5 mg
Copper (from copper gluconate)	125 mcg
Iodine (from potassium iodide)	62.5 mcg
Selenium (from selenomethionine)	25 mcg

**Also contains:** Vegetable magnesium stearate and silicon dioxide in a non-GMO vegetable capsule composed of vegetable carbohydrate gum and purified water.

**This product is non-GMO.**

**Contains no:** Gluten, soy, wheat, eggs, dairy, yeast, citrus, preservatives, artificial flavour or colour, or starch.

**Thyroid SAP** contains 120 capsules per bottle.

## DIRECTIONS FOR USE

**Adults (19 years and over):** Take 4 capsules once daily or as directed by your health-care practitioner. Take with meals. Take up to one hour before, or during periods of physical stress. Take a few hours before or after taking other medications or natural health products.

## INDICATIONS

**Thyroid SAP can help:**

- Promote optimal function of the thyroid gland
- Support management of symptoms of thyroid disorders such as Hashimoto's thyroiditis and Graves' disease
- Regulate iodine deficiencies
- Support immune function/system
- Manage PCOS symptoms and prevent risk of PCOS-induced thyroid disorders

## CAUTIONS AND WARNINGS

Consult a healthcare practitioner prior to use if you have a history of non-melanoma skin cancer; or if you are pregnant or have kidney stones. Avoid taking with alcohol or products that cause drowsiness.

## CONTRAINDICATIONS

Do not use this product if you are taking antibiotics or nitroglycerin; or if you are breastfeeding.

## KNOWN ADVERSE REACTIONS

Some people may experience drowsiness. Exercise caution if operating heavy machinery, driving a motor vehicle, or involved in activities requiring mental alertness.

## PURITY, CLEANLINESS, AND STABILITY

All ingredients listed for each **Thyroid SAP** lot number have been tested by an ISO 17025-accredited third-party laboratory for identity, potency, and purity.



Scientific Advisory Panel (SAP):  
adding nutraceutical research  
to achieve optimum health



351, Rue Joseph-Carrier, Vaudreuil-Dorion, Quebec, J7V 5V5  
T 1 866 510 3123 • F 1 866 510 3130 • nfh.ca

The thyroid gland produces thyroid hormone (TH) by synthesizing it through the iodination of tyrosine residues in the glycoprotein thyroglobulin.<sup>[1]</sup> TH regulates metabolic processes necessary for average growth and development and for maintaining adult metabolism. TH hormone level in the body influences body weight and energy expenditure.<sup>[2]</sup> Cretinism is caused by the absence of triiodothyronine (T3) during early human development, leading to growth disturbances and severe mental retardation.<sup>[3]</sup> Low TH levels can reduce cardiac output, increase systemic vascular resistance, and impair immune function, possibly delaying injury repair.<sup>[4]</sup> Levothyroxine, the synthetic form of thyroxine (T4), is the recommended initial treatment for patients with hypothyroidism. However, it is not widely metabolically active compared to T3. The disadvantage of continuous use of liothyronine is that it can lead to cardiac complications such as ischemia and lethal arrhythmias.<sup>[5]</sup> Comparatively, nutraceuticals such as selenium, zinc, *myo*-inositol, and *N*-acetyl-L-cysteine are used for treating thyroid complications and have fewer side effects on general health.<sup>[6]</sup>

### L-TYROSINE

The synthesis of TH involves hydrogen peroxide, and it follows several steps: oxidation of iodide, tyrosine iodination, and finally, pairing of the iodinated tyrosine residues to iodothyronine residues. When there is excessive production of hydrogen peroxide, it may lead the thyroid gland to attack from free radicals.<sup>[7]</sup> In stress-induced mice, supplementation of L-tyrosine helped restore the serum levels of total thyrotropin and triiodothyronine, as well as the dopamine and norepinephrine present in the pallidum, hippocampus, and hypothalamus.<sup>[8]</sup> Similarly, an increase in T3 and T4 concentrations was noticed in ewe and ram lambs after tyrosine supplementation.<sup>[9]</sup> A clinical study on 65 euthyroid individuals showed that daily L-tyrosine supplementation has an excellent capacity to reduce TSH levels and shows a 47% betterment in mood during winter compared to the combinational supplementation of levothyroxine/liothyronine.<sup>[10]</sup>

### INOSITOL

Inositol in the form of *myo*-inositol is the precursor of phosphoinositides, which participate in the intracellular thyroid-stimulating hormone (TSH) signaling.<sup>[11]</sup> *myo*-Inositol is also pivotal in thyroid physiology as it is elucidated that the inositol requirement of a patient affected by thyroid malfunction is significantly higher than that of an average individual.<sup>[12]</sup> A study on diabetic rats supplemented with *myo*-inositol showed a marginal decrease in plasma and myocardial lipid levels and helped improve cardiac performance.<sup>[13]</sup> When *myo*-inositol alone or combined with selenium was tested on human thyroid cells, the cells were protected from apoptosis induced by cytokines such as interferon- $\gamma$ , tumour necrosis factor, and free radicals like hydrogen peroxide.<sup>[14]</sup> A similar cell line-based study on blood mononuclear cells (PBMC) from Hashimoto's thyroiditis (HT)-affected women tested the efficacy of 0.25 to 1  $\mu$ M *myo*-inositol or selenomethionine or a combination of the two. The combinational supplement proved more effective in protecting cells against oxidative stress.<sup>[15]</sup>

### ASHWAGANDHA

Ashwagandha, or *Withania somnifera*, is a traditional medicine with numerous benefits not limited to antistress, anti-inflammatory, antimicrobial, anticancer, and cardioprotective nature.<sup>[16]</sup> It also helps enhance the secretory function of the thyroid gland by boosting triiodothyronine and thyroxine, thus decreasing TSH levels.<sup>[16]</sup> In an animal-based study, ashwagandha extract improved thyroid function by reducing oxidative stress and enhancing hormone levels by lessening the reduced glutathione (GSH), Na<sup>+</sup> / K<sup>+</sup>-ATPase and glutathione peroxidase levels. The histological examination of the thyroid gland showed significant improvement after the ashwagandha treatment.<sup>[17]</sup> The effect of 600 mg/d of ashwagandha extract was tested on patients with elevated serum TSH levels, and the clinical trial revealed that after eight weeks of treatment, the serum thyroid indices returned to normal.<sup>[18]</sup> A systematic review of clinical trials showed that ashwagandha supplementation helped in a significant rise in T3 and T4 levels, subsequently reducing TSH.<sup>[19]</sup>

### COPPER

Thyroid hormone enhances the synthesis and export of hepatic ceruloplasmin, regulating serum copper levels while downregulating intracellular copper-binding proteins.<sup>[20]</sup> There is a strong correlation between serum-free thyroxine and triiodothyronine (FT3) levels and the copper status of an individual. Thus, copper is suggested as a biomarker for detecting thyroid malfunction.<sup>[21]</sup> A study on a Sprague-Dawley rat population fed with copper-deficient and copper-adequate diets showed that a copper deficiency significantly decreased the plasma thyroxine levels and increased hepatic triiodothyronine receptors and body fat.<sup>[22]</sup> A clinical intervention on pregnant women at 12 weeks of gestation showed that women taking supplements containing essential plasma minerals, copper, zinc, and selenium (942–16.44  $\mu$ mol/L, 1759–36.37  $\mu$ mol/L, and 0.75–1.31  $\mu$ mol/L, respectively) were at a lower risk of elevated thyroid peroxidase antibodies, which is an indicator of the autoimmune origin of poor thyroid function.<sup>[23]</sup>

### N-ACETYL-L-CYSTEINE

*N*-Acetyl-L-cysteine (NAC) is an antioxidant that can prevent DNA damage caused by ionizing radiation by acting as a precursor to glutathione, which contains an -SH group. This preventative effect only works if NAC is administered before the radiation exposure.<sup>[24]</sup> When male Wistar rats submitted to left anterior coronary artery occlusion were supplemented with NAC, it helped in restoring redox balance, thereby helping in resolving nonthyroidal illness syndrome (NTIS), and it also helps to maintain proper heart function.<sup>[25]</sup> A similar study on the human population affected by myocardial infarction showed that 1,200 mg of NAC helped restore total antioxidant status and carbonyl content. Thus, NAC helped in reducing oxidative stress in the patients.<sup>[26]</sup> An animal-based study on hyperthyroid rats showed that NAC supplementation significantly reduced fibrosis and apoptosis and helped alleviate inflammatory response.<sup>[27]</sup>

### IODINE

In a healthy adult, the human body typically contains 15 to 20 milligrams of iodine; 70–80% of this amount is found in the thyroid gland. The sodium/iodine symporter (NIS) transfers iodide into the thyroid gland through the basolateral membrane of the thyroid cell.<sup>[28]</sup> Approximately 38% of the world's population has iodine deficiency, which is preventable and the leading cause of mental retardation, especially for women and their infants.<sup>[29]</sup> When fed an iodine-deficient diet for a prolonged period, animals showed nodular and cyst formation in the thyroid glands, and overstimulation of the thyroid gland was observed.<sup>[30],[31]</sup> A human trial

evaluated the effect of 150  $\mu$ g of iodine in the form of potassium iodate. The supplementation resulted in a significant decrease in thyroglobulin levels.<sup>[32]</sup> Likewise, a study on pregnant women with mild iodine deficiency showed that a daily supplement of 150  $\mu$ g of iodine can improve their iodine levels and positively affect maternal thyroglobulin.<sup>[33]</sup>

### ZINC

Zinc is crucial for the metabolism of TH. It helps regulate the activity of specific enzymes called deiodinases, which produce hormones that control the thyroid gland. It also plays a role in producing hormones that stimulate the thyroid gland and helps modify the structures of essential proteins necessary for synthesizing TH.<sup>[34]</sup> Zinc-deficient rats were observed to develop an abnormality in the thyroid status. In combination, zinc and thyroid function affect overall growth.<sup>[35]</sup> Zinc deficiency decreased serum triiodothyronine and free thyroxine concentrations by approximately 30% compared to zinc-adequate controls.<sup>[36]</sup> A clinical trial on hypothyroid patients supplemented with 30 mg zinc gluconate, 250 mg magnesium oxide, and one 25,000 IU vitamin A twice weekly resulted in significant improvement in free thyroxine levels and decreased anthropometric indices and serum hs-CRP.<sup>[37]</sup> Similarly, another intervention showed that zinc, alone or in combination with selenium, helped increase mean free and total triiodothyronine levels in hypothyroid female patients.<sup>[38]</sup>

### SELENIUM

Selenium is abundantly found in the thyroid gland and has been established to play a crucial role in the gland's functioning. In autoimmune diseases such as Graves' disease and Hashimoto's thyroiditis, a common phenomenon observed is low selenium status.<sup>[39]</sup> Selenium deficiency can cause a decrease in the thyroid gland's glutathione peroxidases activity, resulting in oxidative damage in cells, followed by necrosis and invasion of the thyroid tissue by macrophages and T lymphocytes. As a result, the thyroid gland undergoes chronic inflammation, which destroys it through TGF-dependent processes, leading to an atrophy of the gland.<sup>[40]</sup> A prospective clinical trial explored the potential of selenium supplementation on female patients with autoimmune thyroiditis and thyroid peroxidase antibodies. The supplementation helped normalize the antibody levels and improved the inflammatory activity.<sup>[41]</sup> Another clinical trial showed that 80  $\mu$ g/d of sodium selenite can help in a significant decrease of thyroid echogenicity and thyroid peroxidase antibodies.<sup>[42]</sup>

### POTENTIAL OF THE SYNERGY

Trace elements—including selenium, zinc, copper, iron, manganese, and iodine—can synergistically act and help in alleviating the oxidative stress on the thyroid gland and help in decreasing the incidence of thyroid diseases such as Hashimoto's thyroiditis, dysthyroidism, and thyroid cancer.<sup>[43]</sup> A clinical study explored the synergistic efficiency of 2 g *myo*-inositol, 0.5 mg L-tyrosine, 0.2 mg folic acid, 55  $\mu$ g selenium, and 40  $\mu$ g chromium in women with PCOS, and it proved that the combinational treatment helped in improving PCOS symptoms. This study suggests that the increased risk of thyroid diseases in PCOS patients, such as nodular goitre and autoimmune thyroiditis, can also be resolved by a synergistic approach.<sup>[44]</sup> The combination of zinc and selenium proves to be efficient in treating thyroid-related complications.<sup>[38]</sup>

### REFERENCES

- Cheng, S.-Y., J.L. Leonard, and P.J. Davis. "Molecular aspects of thyroid hormone actions." *Endocrine Reviews*, Vol. 31, No. 2 (2010): 139–170.
- Mullur, R., Y.-Y. Liu, and G.A. Brent. "Thyroid hormone regulation of metabolism." *Physiological Reviews*, Vol. 94, No. 2 (2014): 355–382.
- Zhang, J., and M.A. Lazar. "The mechanism of action of thyroid hormones." *Annual Review of Physiology*, Vol. 62 (2000): 439–466.
- Razvi, S. "Novel uses of thyroid hormones in cardiovascular conditions." *Endocrine*, Vol. 66, No. 1 (2019): 115–123.
- Blond, B., and L. Wartofsky. "Treatment with thyroid hormone." *Endocrine Reviews*, Vol. 35, No. 3 (2014): 433–512.
- Benveniste, S., U. Feldt-Rasmussen, D. Bonfiglioli, and E. Asanovich. "Nutraceutical supplements in the thyroid setting: Health benefits beyond basic nutrition." *Nutrients*, Vol. 11, No. 9 (2019): 2214.
- Benveniste, S., S. Sabbi, F. Resta, B. Licchelli, and E. Guastamacchia. "Role of iodine, selenium and other micronutrients in thyroid function and disorders." *Endocrine, Metabolic & Immune Disorders Drug Targets*, Vol. 9, No. 3 (2009): 277–294.
- Wang, Z., J. Li, Z. Wang, L. Xie, Y. Zhang, Y. Chen, J. Su, and Z. Li. "L-Tyrosine improves neuroendocrine function in a mouse model of chronic stress." *Neuroscience Research*, Vol. 7, No. 18 (2012): 1413–1419.
- Mohamed, M.Y., S.N.A. Azeem, A.-M.K. Khairy, M.G. Gabr, M.A. El-Baroudy, and A.E.-H.A.A. El-Naby. "Effect of L-tyrosine oral administration to growing Ossimi lambs." *Egyptian Journal of Agricultural Research*, Vol. 90, No. 1 (2012): 383–393.
- Palinkas, L.A., K. Reedy, M. Smith, M. Angell, G.B. Steel, D. Reeves, D. Shurtell, H.S. Case, N.Y. Do, and H.L. Reed. "Psychoneuroendocrine effects of combined thyroid and triiodothyronine versus tyrosine during prolonged Antarctic residence." *International Journal of Circumpolar Health*, Vol. 66, No. 5 (2007): 402–417.
- Fallahi, P., S.M. Ferrari, G. Elia, F. Ragusa, S.R. Paparo, C. Caruso, G. Guglielmi, and A. Antonelli. "myo-Inositol in autoimmune thyroiditis, and hypothyroidism." *Reviews in Endocrine and Metabolic Disorders*, Vol. 19, No. 4 (2018): 349–354.
- Benveniste, S., M. Norcia, and V. Unfer. "The role of inositol in thyroid physiology and in subclinical hypothyroidism management." *Frontiers in Endocrinology*, Vol. 12 (2021): 662582.
- Xiang, H., C.E. Heyliger, and J.H. McNeill. "Effect of myo-inositol and T3 on myocardial lipids and cardiac function in streptozotocin-induced diabetic rats." *Diabetes*, Vol. 37, No. 11 (1988): 1542–1548.
- Ferrari, S.M., G. Elia, F. Ragusa, S.R. Paparo, C. Caruso, S. Benveniste, P. Fallahi, and A. Antonelli. "The protective effect of myo-inositol on human macrocytes." *Reviews in Endocrine and Metabolic Disorders*, Vol. 19, No. 4 (2018): 355–362.
- Benveniste, S., T. Vicchio, F. Di Bari, R. Vita, P. Fallahi, S.M. Ferrari, S. Catania, C. Costa, and A. Antonelli. "Favorable effects of myo-inositol, selenomethionine or their combination on the hydrogen peroxide-induced oxidative stress of peripheral mononuclear cells from patients with Hashimoto's thyroiditis: Preliminary in vitro studies." *European Review for Medical & Pharmacological Sciences*, Vol. 21, No. 2 Suppl. (2017): 89–101.
- Wicinski, M., A. Fajkiewicz-Madajczyk, Z. Kurant, D. Kurant, G. Gryczka, M. Falkowska, M. Winińska, M. Szupski, I. Ohla, J. Zabrzyński. "Can ashwagandha benefit the endocrine system?—A review." *International Journal of Molecular Sciences*, Vol. 24, No. 2 (2023): 1653.
- Abdel-Wahhab, K.G., H.H. Mourad, F.A. Mannaa, F.A. Morsy, L.K. Hassan, and R.F. Taher. "Role of ashwagandha methanolic extract in the regulation of thyroid profile in hypothyroidism modelled rats." *Molecular Biology Reports*, Vol. 46, No. 4 (2019): 3627–3640.
- Sharma, A.K., I. Basu, and S. Singh. "Efficacy and safety of ashwagandha root extract in subclinical hypothyroid patients: A double-blind, randomized placebo-controlled trial." *The Journal of Alternative and Complementary Medicine*, Vol. 24, No. 3 (2018): 243–248.
- Logresti, A.L., and S.J. Smith. "Ashwagandha (*Withania somnifera*) for the treatment and enhancement of mental and physical conditions: A systematic review of human trials." *Journal of Herbal Medicine*, Vol. 28 (2021): 100434.
- Mittag, J., T. Behrends, K. Nordström, J. Anselmo, B. Venström, and L. Schomburg. "Serum copper as a novel biomarker for resistance to thyroid hormone." *Biochemical Journal*, Vol. 443, No. 1 (2011): 103–109.
- Ye, Y., Y. Li, Q. Ma, Y. Li, H. Zeng, Y. Luo, Y. Liang, et al. "Association of multiple blood metals with thyroid function in general adults: A cross-sectional study." *Frontiers in Endocrinology*, Vol. 14 (2023): 1134208.
- Lukaski, H.C., C.B. Hall, and M.J. Marchello. "Body temperature and thyroid hormone metabolism of copper-deficient rats." *The Journal of Nutritional Biochemistry*, Vol. 6, No. 8 (1995): 445–451.
- Pap, V., J. Kraljic, W. Marek, and M. Rayman. "Plasma mineral (selenium, zinc or copper) concentrations in the general pregnant population, adjusted for supplement intake, in relation to thyroid function." *British Journal of Nutrition*, Vol. 125, No. 1 (2021): 71–78.
- Kurashige, T., M. Shimamura, and Y. Nagayama. "N-Acetyl-L-cysteine protects thyroid cells against DNA damage induced by external and internal irradiation." *Radiation and Environmental Biophysics*, Vol. 56, No. 4 (2017): 439–441.
- Lehnen, T.E., M.V. Santos, A. Lima, A.L. Maia, and S.M. Wajner. "N-Acetylcysteine prevents low T3 syndrome and attenuates cardiac dysfunction in a male rat model of myocardial infarction." *Endocrinology*, Vol. 158, No. 10 (2017): 1502–1510.
- Leung, A., E.M. Pearce, and L.E. Braverman. "Role of iodine in thyroid physiology." *Expert Review of Endocrinology & Metabolism*, Vol. 5, No. 4 (2009): 591–600.
- Shallier, R.T., and J.K. Stevenson. "Development of carcinoma of the thyroid in iodine-deficient mice." *Cancer*, Vol. 19, No. 8 (1966): 1063–1080.
- Isler, H. "Effect of iodine on thyroid tumors induced in the rat by a low-iodine diet." *Journal of the National Cancer Institute*, Vol. 23 (1959): 679–693.
- Ma, Z.F., B.J. Venn, P.I. Manning, C.M. Cameron, and S.A. Skeaff. "Iodine supplementation of mildly iodine-deficient adults lowers thyroglobulin: A randomized controlled trial." *The Journal of Clinical Endocrinology & Metabolism*, Vol. 101, No. 4 (2016): 1733–1744.
- Manousos, S., R. Egertsen, L. Huhtelin, and H.P. Nyström. "A randomized, double-blind study of iodine supplementation during pregnancy in Sweden: Pilot evaluation of maternal iodine status and thyroid function." *European Journal of Nutrition*, Vol. 60, No. 6 (2021): 3411–3422.
- Sera, J.S., J.B. Ross, J.C. Freitas, A.P. Andrade, M.F. Feitosa, L.C. Fontenelle, A.R.S. de Oliveira, M.C. Cruz, and D.N. Marengo. "The role of zinc in thyroid hormones metabolism." *International Journal for Vitamin and Nutrition Research*, Vol. 89, No. 1–2 (2019): 80–88.
- Freake, H.C., K.E. Govoni, K. Guda, C. Huang, and S.A. Zinn. "Actions and interactions of thyroid hormones and zinc status in growing rats." *The Journal of Nutrition*, Vol. 131, No. 4 (2001): 1135–1141.
- Kralik, A., K. Eder, and M. Kirchgesner. "Influence of zinc and selenium deficiency on parameters relating to thyroid hormone metabolism." *Hormone and Metabolic Research*, Vol. 28, No. 5 (1996): 223–226.
- Rabbani, E., F. Golgiri, L. Janani, N. Moradi, S. Fallah, B. Abiri, and M. Vafa. "Randomized study of the effects of zinc, vitamin A, and magnesium co-supplementation on thyroid function, oxidative stress, and hs-CRP in patients with hypothyroidism." *Biological Trace Element Research*, Vol. 199, No. 11 (2021): 4078–4083.
- Mahmoudianfar, S., M. Vafa, F. Golgiri, M. Khoshnati, M. Gohari, Z. Solati, and M. Djafari. "Effects of zinc and selenium supplementation on thyroid function in overweight and obese hypothyroid female patients: A randomized double-blind controlled trial." *Journal of the American College of Nutrition*, Vol. 34, No. 5 (2015): 391–399.
- Gorini, F., L. Sabatino, A. Pingitore, and C. Vassalle. "Selenium: An element of life essential for thyroid function." *Molecules*, Vol. 26, No. 23 (2021): 7084.
- Gärtner, R., and R. Gärtner. "Selenium and thyroid." *Best Practice & Research. Clinical Endocrinology & Metabolism*, Vol. 23, No. 6 (2009): 815–827.
- Gärtner, R., B.C.H. Gassner, J.W. Dietrich, B. Krebs, and M.W.A. Angstweber. "Selenium supplementation in patients with autoimmune thyroiditis decreases thyroid peroxidase antibody concentrations." *The Journal of Clinical Endocrinology & Metabolism*, Vol. 87, No. 4 (2002): 1687–1691.
- Nacamulli, D., C. Mian, D. Petricca, F. Lazzarotto, S. Barolli, D. Pozza, S. Masiero, et al. "Influence of physiological dietary selenium supplementation on the natural course of autoimmune thyroiditis." *Clinical Endocrinology*, Vol. 73, No. 4 (2010): 555–559.
- Wroblewski, M., J. Wroblewska, J. Nuckiewicz, M. Pawlowska, R. Wesolowski, and A. Wozniak. "The role of selected trace elements in oxidative homeostasis in patients with thyroid diseases." *International Journal of Molecular Sciences*, Vol. 24, No. 5 (2023): 4840.