World Journal of Pharmaceutical and Life Sciences

Impact Factor: 8.21 www.wjpls.org Coden USA: WJPLA7

THYROXINE HORMONE IS AMINO ACID HAVING SINGLE CHIRAL CENTER

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Shri Sarvajanik Pharmacy College, Gujarat Technological University, Arvind Baug, Mehsana-384001, Gujarat, India. **DOI:** https://doi.org/10.5281/zenodo.21026399

How to cite this Article: [1]Dr. Pruthviraj K. Chaudhary*, [1]Dr. Dhiren L. Chaudhari, [1]Jay M. Patel, [1]Krutik P. Patel, [1]Het P. Patel, [2]Dr. Dhrubo Jyoti Sen, [3]Jaspal A. Chaudhary and [4]Dr. Manoj P. Gadhvi (2026). Thyroxine Hormone Is Amino Acid Having Single Chiral Center. World Journal of Pharmaceutical and Life Sciences, 12(6), 376–381.

Article Received on 05/05/2026 **Article Revised on 25/05/2026** **Article Published on 01/06/2026**

ABSTRACT

Thyroid hormones are essential chemicals produced by the butterfly-shaped thyroid gland in your neck. They regulate the body's metabolism, growth, energy levels, and internal temperature. The two primary hormones are: Thyroxine (T4): The main inactive form circulating in the blood. The body converts T4 into T3 as needed. Triiodothyronine (T3): The highly active form that directly impacts your organs, especially your heart, muscles, and brain. How the Process Works: Production: The thyroid gland requires dietary iodine to synthesize both T3 and T4. Regulation: The brain controls this process. The hypothalamus releases TRH, which triggers the pituitary gland to release TSH (Thyroid-Stimulating Hormone). TSH then directs the thyroid to produce T3 and T4. Hypothyroidism (Underactive Thyroid): The thyroid doesn't produce enough hormones. This causes systems to slow down, leading to fatigue, weight gain, constipation, and cold intolerance. Hyperthyroidism (Overactive Thyroid): The thyroid produces too much hormone. This accelerates metabolism, causing weight loss, heat intolerance, anxiety, and rapid heart rate.

KEYWORDS: T3, T4, TSH, Calcitonin, Thyroid Gland, Goiter, Acromegaly, Gigantism, Goiter, Exophthalmic Goiter, Graves' Disease.

Overview: Hyperthyroidism is an overactive thyroid that produces too much thyroid hormone, speeding up your metabolism. **Hypothyroidism** is an underactive thyroid that produces too little hormone, slowing your metabolism down.

Table-1: Difference between Hyperthyroidism & Hypothyroidism.

Feature	Hyperthyroidism (High)	Hypothyroidism (Low)
Hormone Production	Excessively high T_4 and T_3	Dangerously low T_4 and T_3
Metabolism	Speeds up; body burns fuel too quickly	Slows down; body stores fuel/energy
Weight	Unintentional weight loss	Unintentional weight gain
Energy Levels	Hyperactive, anxious, trouble sleeping	Extreme fatigue, sluggishness, depression
Physical Symptoms	Rapid or irregular heartbeat, shaky hands, heat intolerance	Dry skin, constipation, cold intolerance
TSH Levels	Very low (the pituitary gland tries to stop hormone release)	High (the pituitary gland tries to force the thyroid to work)

Normal **Thyroid-Stimulating Hormone (TSH)** levels generally range from 0.4 to 4.0 mIU/L for adults, though this can vary slightly between labs. A high TSH usually indicates an underactive thyroid (hypothyroidism), while a low TSH indicates an overactive thyroid (hyperthyroidism).

This single stereogenic center is located on the α-carbon of the amino acid backbone (the carbon atom that is directly attached to the amino, carboxylic acid, and phenyl groups). This asymmetry results in two enantiomers: biologically active L-thyroxine (levothyroxine) and largely inactive D-thyroxine (dextrothyroxine). If you are looking to learn more about the structure, let me know if you would like to understand: The difference between D- and L-thyroxine. The chemical structure of thyroxine (T4) vs. triiodothyronine (T3). How the stereochemistry affects biological activity. Thyroxine is the tyrosine based hormone produced by the thyroid gland, containing a chiral center in its molecular structure. Thyroxine itself is a chiral molecule due to the presence of an asymmetric carbon atom in its amino acid backbone. This gives rise to two enantiomers: L-thyroxine (levothyroxine) and D-thyroxine (dextrothyroxine).

Thyroxine (T4) has exactly one asymmetric (chiral) carbon atom, located in its amino acid backbone. Location and.

Configuration

The Asymmetric Center: It is the α-carbon atom of the alanine side chain. The Four Groups: This α-carbon is bonded to four distinct groups: an amino group (NH_2), a carboxyl group (-COOH)), a hydrogen atom (-H), and the bulky iodinated aromatic ring system (the thyronine group). Bioactive Isomer: Naturally occurring thyroxine exists as the L-isomer (levothyroxine). The mirror-image D-isomer is physiologically largely inactive.

Thyroxine (T4) contains exactly one asymmetric chiral center. It is located at the α-carbon of its alanine/amino acid side chain, where the amino group, the carboxyl group, a hydrogen atom, and the large diiodophenol ring are all attached. The **Two Enantiomers:** Because of this single chiral center, thyroxine exists as two non-superimposable mirror images (enantiomers): L-Thyroxine (Levothyroxine): The naturally occurring, biologically active form of the hormone produced by the human thyroid gland. It is widely prescribed as a medication for hypothyroidism. D-Thyroxine (Dextrothyroxine): The non-naturally occurring mirror image. It has minimal thyroid hormone activity, although historical medical uses have targeted cholesterol reduction. **Chirality & Pharmaceutical Importance:** Only the L-enantiomer is fully recognized by human thyroid receptors. Because of the structural differences between these asymmetric centers, regulatory bodies require strict control over optical purity in commercial pharmaceutical products to ensure maximum efficacy and medicinal safety.

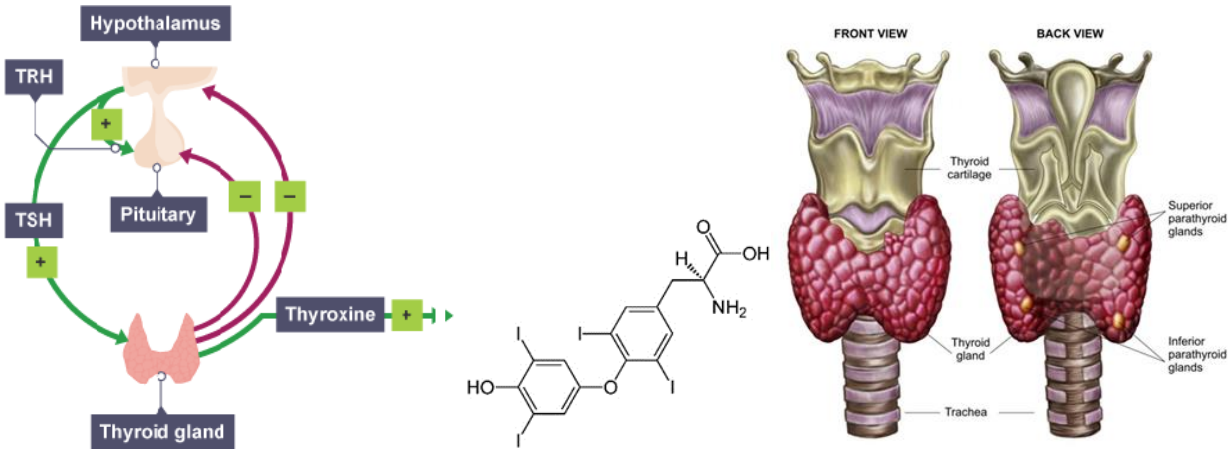

Figure-1: Thyroxine & Thyroid gland.

If you would like to explore this further, I can help you with: Analytical methods used to separate and quantify the D and L enantiomers (like chiral HPLC): The specific R/S spatial configuration of the α-carbon. How the chiral center of thyroxine compares to other thyroid hormones like Triiodothyronine (T_3).

Standard TSH Reference Ranges

Optimal ranges can fluctuate depending on your age, life stage, or if you are pregnant. Common benchmarks include:

Adults: 0.4 to 4.0 mIU/L (though some doctors prefer an optimal zone of 0.5 to 2.5 mIU/L for symptom management).

During Pregnancy: Typically tighter ranges (e.g., 0.1 to 2.5 mIU/L in the first trimester).

Older Adults: Ranges often have a higher upper limit (up to 6.0–7.0 mIU/L in the elderly).

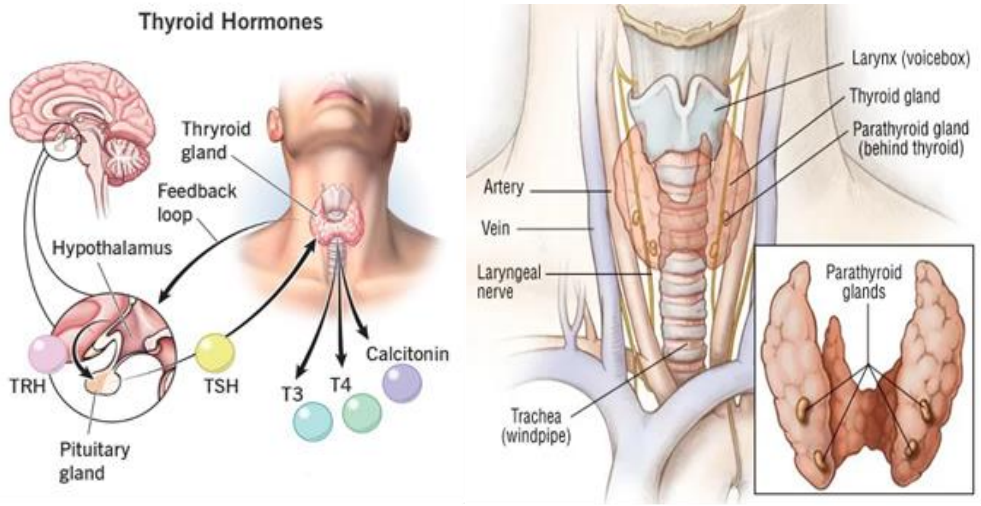

Figure-2: Thyroid Gland with T3, T4, TSH & Calcitonin.

Interpreting Your Results

High TSH (> 4.0 mIU/L): Your pituitary gland is working harder to signal a sluggish thyroid. This commonly points to hypothyroidism.

Low TSH (< 0.4 mIU/L): Your pituitary is slowing down because your thyroid is producing too much hormone, often indicating hyperthyroidism.

Thyroxine (T4) [CAS: 51-48-9] is an iodine-based amino acid hormone that controls your body's metabolic rate, heart function, and brain development. Its chemical structure features a core "thyronine" skeleton made of two linked tyrosine molecules, containing exactly four iodine atoms.

Molecular Formula: $C_{15}H_{11}I_4NO_4$.

Molar Mass: 776.874g/mol.

Chemistry: The thyroxine molecule consists of two aromatic benzene rings connected by a central ether (oxygen) linkage: **Inner Ring (Phenolic Ring):** Contains a hydroxyl –OH group and two iodine atoms at positions 3 and 5.

Outer Ring (Tyrosyl Ring): Contains two additional iodine atoms at positions 3' and 5'.

Thyroxine (T_4) is a chiral molecule due to the presence of a single asymmetric carbon atom in its alanine side chain. This structural asymmetry gives rise to two mirror-image enantiomers: levothyroxine (L-thyroxine) and dextrothyroxine (D-thyroxine). Here are the critical stereo chemical details of thyroxine: Active Enantiomer: L-thyroxine is the naturally occurring, physiologically active isomer produced by the thyroid gland. It is responsible for regulating metabolism, growth, and development. Inactive Enantiomer: D-thyroxine is the non-natural mirror image. It has significantly reduced hormonal activity and is not used for hormone replacement, though historically it was investigated for its lipid-lowering properties.

Absolute Configuration: Using the Cahn-Ingold-Prelog (CIP) priority rules, the chiral center at the α-carbon of the alanine side chain for the natural L-isomer corresponds to the (S)-configuration.

Amino Acid Tail: Attached to the inner ring is an alanine side chain (CH_2-CH(NH_2)-COOH). The full chemical name, 3,3',5,5'-tetraiodothyronine, literally points to the locations of the four iodine atoms. Thyroxine acts largely as a pro-hormone. Once released by the Thyroid Gland, enzymes in your body strip away one iodine atom to convert it into T3 (triiodothyronine)—the highly active form of the hormone. Thyroxine (T4) synthesis is a multi-step process in the thyroid gland's follicular cells. It requires dietary iodine, the protein thyroglobulin, and the enzyme thyroid peroxidase (TPO). TPO oxidizes iodide, attaches it to tyrosine residues (organification), and couples them into T4. Proteolytic enzymes then release T4 into the bloodstream.

Iodide Trapping and Transport: Action: Thyroid follicular cells actively take up circulating iodide from the blood via the Sodium/Iodide Symporter (NIS).Transport: Iodide is then transported into the colloid-filled lumen of the thyroid follicle via a transporter protein called pendrin.

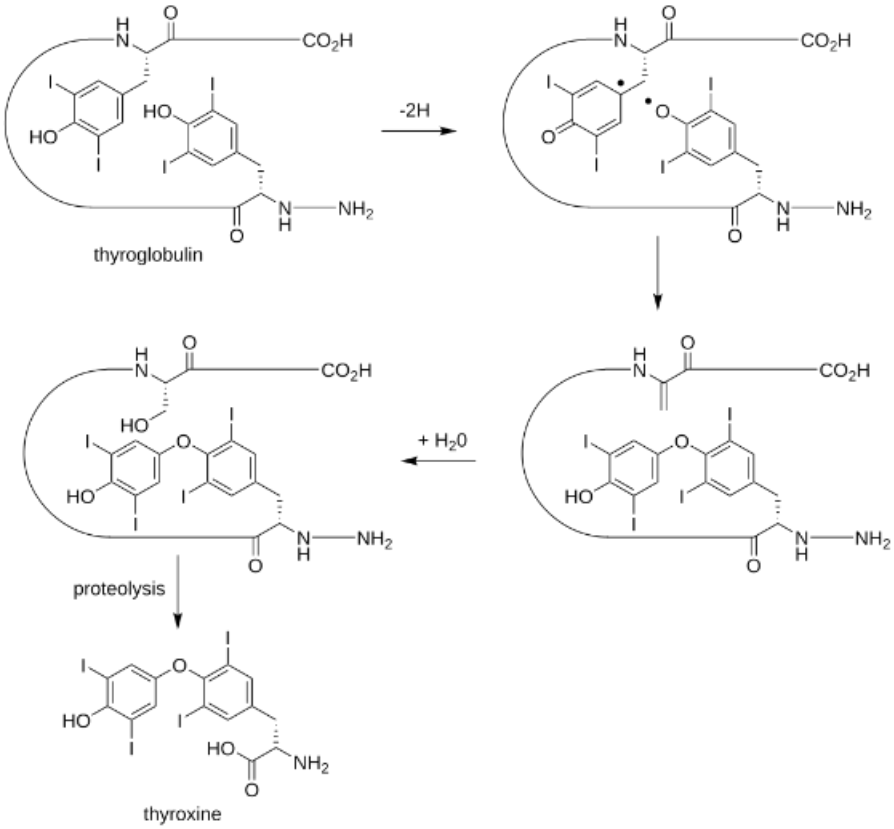

Figure-3: Biochemistry of Thyroxine biosynthesis.

Iodination (Organification)

Oxidation: In the colloid, the enzyme Thyroid Peroxidase (TPO) oxidizes the transported iodide into active iodine.

Attachment: TPO then attaches the iodine to tyrosine amino acid molecules that form the backbone of a large glycoprotein called thyroglobulin. Yield: This step creates monoiodotyrosine (MIT, one iodine) and diiodotyrosine (DIT, two iodines).

Coupling Reaction: Action: TPO facilitates the joining together of MIT and DIT residues while still attached to the thyroglobulin protein.

Yield: Combining one MIT and one DIT forms triiodothyronine (T3). Combining two DIT molecules forms thyroxine (T4).

Storage and Release

Storage: The newly formed T4 and T3 remain bound to the thyroglobulin protein in the follicular lumen, acting as an extensive storage reservoir. Secretion: When thyroid-stimulating hormone (TSH) signals the need for hormones, the follicular cells engulf thyroglobulin via endocytosis. Proteolytic enzymes inside cellular lysosomes chop the T4 off its thyroglobulin backbone, allowing free thyroxine to enter the bloodstream.

Graves' disease is an autoimmune disorder that causes the thyroid gland to produce too much thyroid hormone (hyperthyroidism). The immune system mistakenly attacks the thyroid, causing body metabolism to speed up. Common symptoms include unintentional weight loss, rapid heartbeat, tremors, anxiety, heat intolerance, and an enlarged thyroid gland (goiter). Graves' disease affects multiple systems in the body. While a racing metabolism is the primary driver, other unique manifestations occur outside the thyroid.

Thyroid Eye Disease (Graves' ophthalmopathy): Roughly 20% of patients experience inflammation and buildup behind the eyes, leading to dry eyes, bulging eyes (proptosis), light sensitivity, and double vision.

Skin Changes (Pretibial myxedema): Rarely, thick, red, or lumpy skin can develop on the shins or top of the feet. General **Hyperthyroidism:** Sleep disturbances, muscle weakness, frequent bowel movements, and changes in the menstrual cycle.

Biochemistry

Acromegaly is a rare, slow-progressing hormonal disorder in adults caused by a benign (noncancerous) pituitary tumor that produces excess growth hormone. This leads to the abnormal enlargement of bones, cartilage, and organs, most commonly resulting in swollen hands, feet, and distinct facial changes. Because the changes happen very gradually, it often takes years for symptoms to become obvious. Understanding the condition requires looking at how it presents, its causes, and how it is treated.

Table-2: Difference between Goiter & Exophthalmic Goiter.

Feature	Goiter [Simple, Endemic]	Exophthalmic Goiter [Graves' Disease]
Primary Cause	Lack of iodine in diet	Autoimmune disorder where immune system attacks thyroid
Thyroid Activity	Hypothyroidism [under secretion of thyroixne]	Hyperthyroidism [over secretion of thyroixne]
Eye Symptoms	Normal eye appearance	Exophthalmos: Protruding of eye balls
Metabolism	Slow metabolism leading to weight gain and fatigue	Accelerated metabolism leading to weight loss despite increased appetite, nervousness and rapid heart rate
Primary Treatment	Iodine Supplement, thyroid hormone replacement or surgery.	Anti-thyroid medication or radioactive therapy or surgery

Signs: Physical Changes: Enlarged hands and feet (often requiring larger ring and shoe sizes), a protruding jaw (prognathism), prominent brow, thickened lips, and widening gaps between teeth.

Soft Tissue Growth: Thickened skin, excessive sweating, and an enlarged tongue.

Other Health Issues: Joint and muscle pain, deepening of the voice (due to vocal cord swelling), severe headaches, and vision changes (from the tumor pressing on the optic nerve).While they are caused by the same mechanism, the difference lies in when the excess hormone occurs.

Gigantism: Occurs in children whose growth plates have not yet fused. It causes extreme overall height.

Acromegaly: Occurs in adults after the growth plates in the bones have closed. It does not increase height, but rather causes bones and tissues to thicken and alter in shape.

A **goiter** is an abnormal enlargement of the thyroid gland, which is a small, butterfly-shaped gland located at the base of your neck. While it is usually painless, goitre can sometimes cause a cough, a tight feeling in the throat, or difficulty swallowing and breathing. A goiter does not necessarily mean your thyroid gland is malfunctioning, but it can indicate an underlying issue.

Common causes include

Iodine Deficiency: The most common cause worldwide; the thyroid enlarges to capture more of the limited iodine needed to produce hormones.

Autoimmune Diseases: Conditions like Hashimoto's disease (which causes hypothyroidism) and Graves' disease (which causes hyperthyroidism).

Thyroid Nodules: Lumps that develop within the gland, either singly or in clusters.

Thyroiditis: Inflammation of the thyroid gland.

Exophthalmic goiter, widely known as **Graves' Disease**, is an autoimmune disorder that causes the thyroid gland to become enlarged and overactive (hyperthyroidism). This over-secretion of thyroid hormones leads to an increased metabolic rate, while the autoimmune response specifically causes the characteristic protrusion of the eyeballs.

The disease affects multiple systems in the body, presenting with a combination of hormonal, physical, and ophthalmic signs.

Eye Issues (Exophthalmos): Bulging, swollen, or protruded eyeballs, which can cause double vision, dryness, and light sensitivity.

Figure-4: Goiter, Exophthalmic Goiter, Cretinism and Acromegaly.

Thyroid Swelling (Goiter): An enlarged thyroid gland that creates a visible lump or swelling in the front of the neck. **Hyperthyroidism:** Rapid or irregular heartbeat, unexplained weight loss despite an increased appetite, nervousness, heat intolerance, trembling hands, and fatigue. The condition occurs when the immune system mistakenly attacks the thyroid gland. It produces antibodies known as thyroid-stimulating

immunoglobulins (TSI) that force the thyroid to produce excessive amounts of thyroid hormones (T_3 and T_4). Both genetic predisposition and environmental triggers play a role in its development.

Diagnosis and Treatment: To diagnose exophthalmic goitre, doctors rely on physical exams, blood tests (to measure TSH, T_3, and T_4 levels), and sometimes radioactive iodine uptake scans.

Medications: Anti-thyroid medications (like methimazole) or beta-blockers to control symptoms.

Radioactive Iodine Therapy: Taking radioactive iodine orally to shrink the thyroid gland over time.

Surgery: Partial or complete removal of the thyroid gland (thyroidectomy).

Eye Care: Artificial tears, corticosteroids, or in severe cases, orbital surgery to relieve pressure behind the eye.

CONCLUSION

Thyroid hormone is the hormone that controls your body's metabolism, the process in which your body transforms the food you eat into energy. The two main hormones your thyroid releases — thyroxine (T4) and triiodothyronine (T3) — collectively make up thyroid hormone.

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