

# Thyroid and anti-thyroid drugs

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Thyroid hormones are **iodinated amino acids** derived from L-Tyrosine, synthesized in the thyroid gland and stored as amino acid residues of **thyroglobulin**.

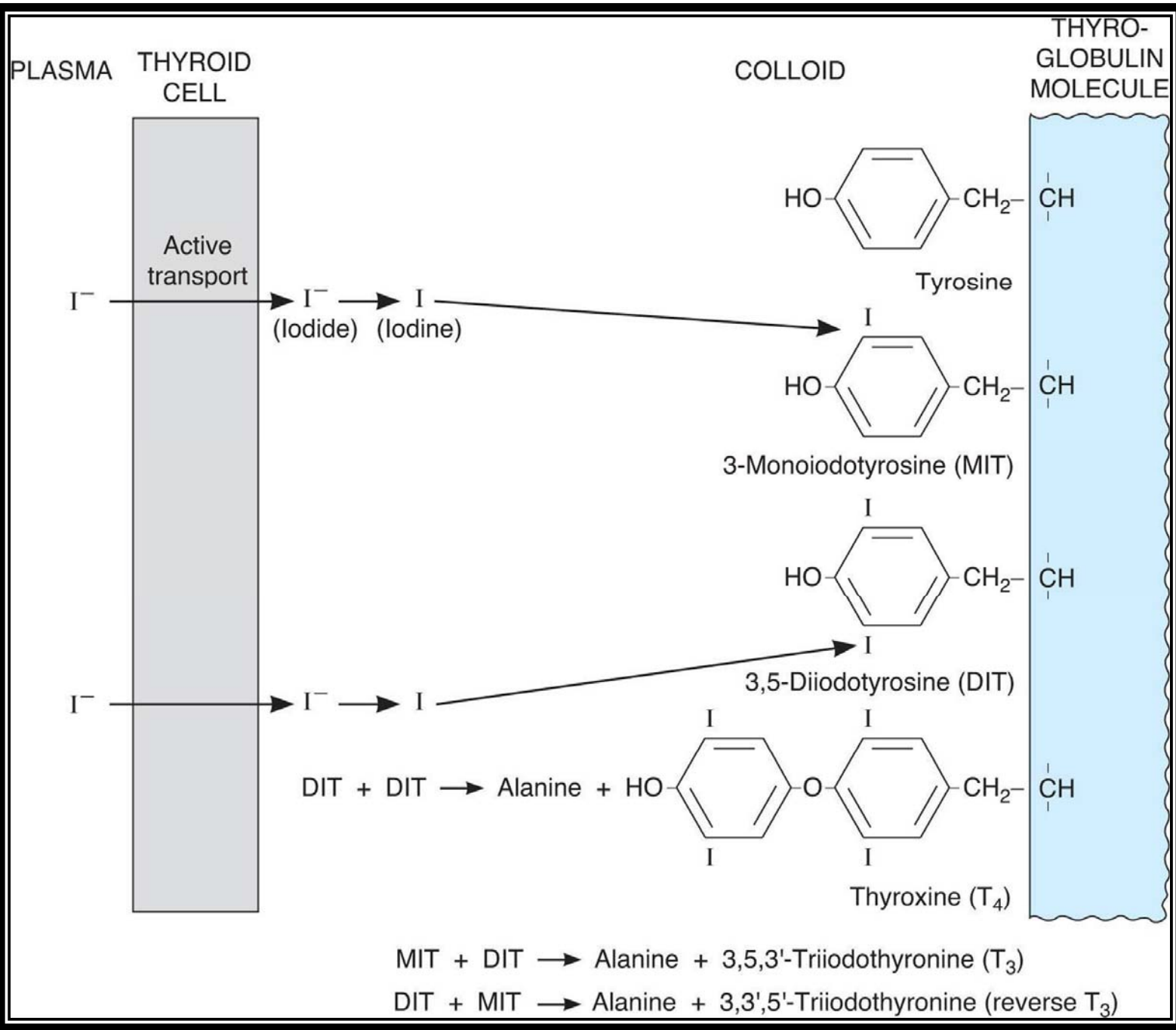
Thyroxine (T<sub>4</sub>) and Tri-iodothyronine are the principal thyroid hormones. Chemically they are amino acids containing iodinated diphenyl ethers.

### **Biosynthesis**

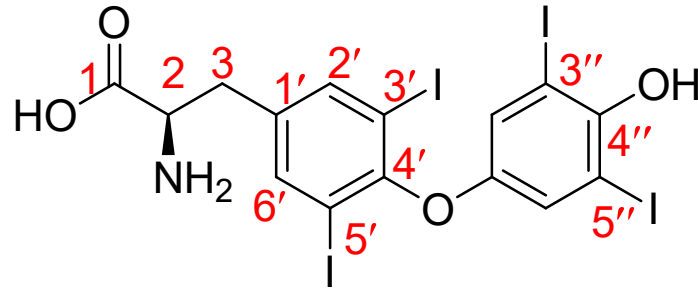
The thyroid hormones are synthesized and stored in the thyroid follicle as part of thyroglobulin molecule, which is a glycoprotein (m.w. 660 KD)

The formation of thyroid hormones involves the following steps.

- Active uptake of iodide by the follicular cells.
- Oxidation of iodide and formation of iodotyrosine residues of thyroglobulin.
- Formation of iodothyronines from iodotyrosine
- Proteolysis of thyroglobulin and release of T<sub>4</sub> and T<sub>3</sub>.
- Conversion of T<sub>4</sub> to T<sub>3</sub>.



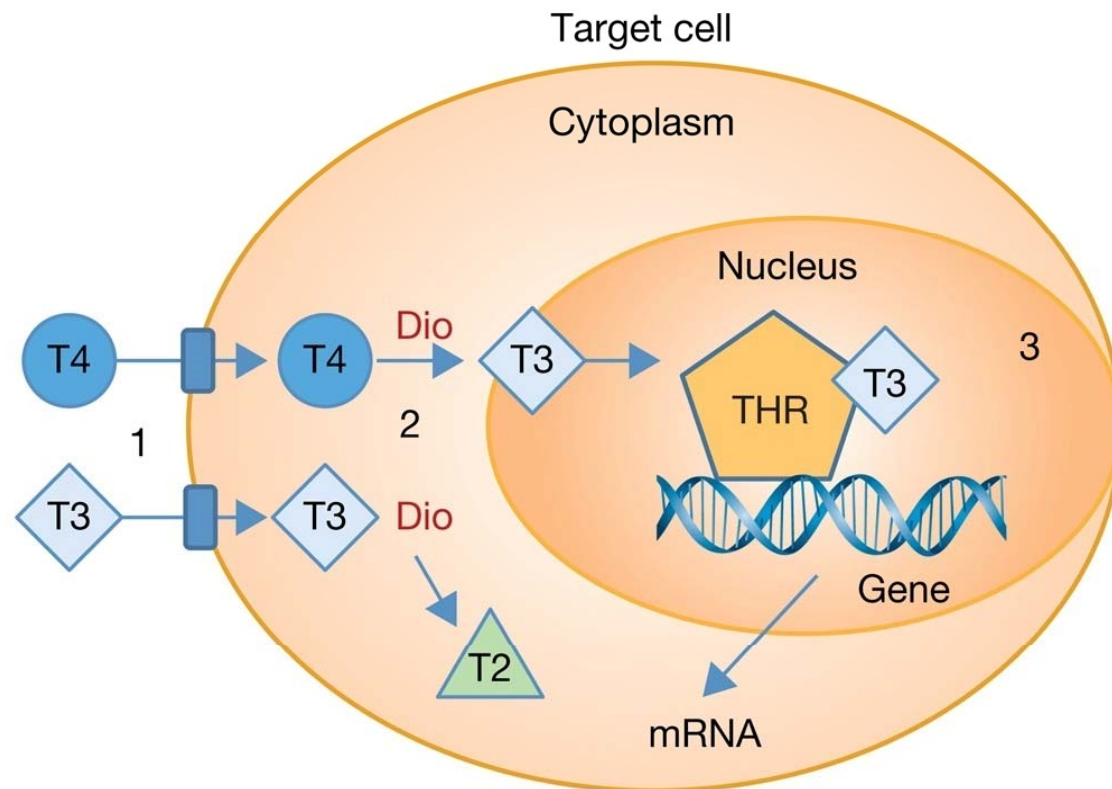
## L-Thyroxine



**L-2-amino-3-[4'-(4''-hydroxy-3'',5''-diiodophenoxy)-3',5'-diiodophenyl]propanoic acid**

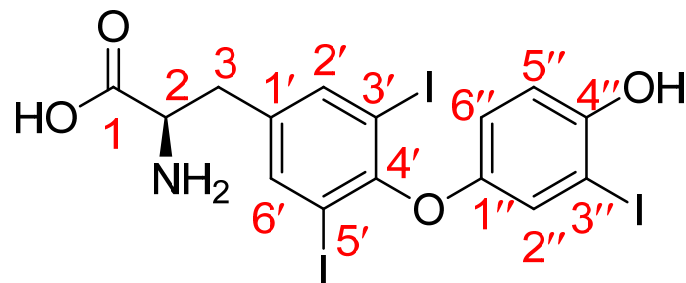
- Levothyroxine is a synthetically prepared levo-isomer of the thyroid hormone thyroxine ( $T_4$ , a **tetra-iodinated tyrosine** derivative) that acts as a replacement in deficiency syndromes such as **hypothyroidism**.
- $T_4$  is the major hormone secreted from the thyroid gland and is chemically identical to the naturally secreted  $T_4$ .
- In the fetus and newborn, it is required for the **growth and development** of all tissues including bones and the brain. In adults, it helps to maintain **brain function, food metabolism, and body temperature**.

**MOA:** It is converted to its active metabolite, L-triiodothyronine ( $T_3$ ).  $T_4$  and  $T_3$  bind to thyroid receptor proteins in the cell nucleus and cause metabolic effects through the control of DNA transcription and protein synthesis.



**Uses:** Levothyroxine is used to treat hypothyroidism.

## L-Thyronine



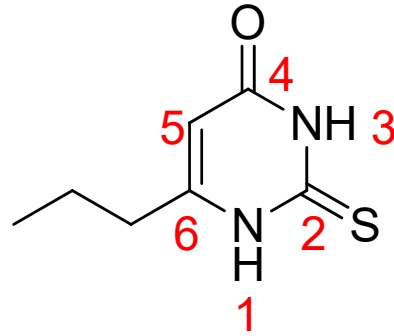
IUPAC: L-3-[4'-(4''-hydroxy-3''-iodophenoxy)-3',5'-diiodophenyl]alanine

Levothyronine is synthetic triiodothyronine (T3), thyroid hormone. Levothyronine has properties of levothyroxine; however, it acts faster and binds less with blood proteins.

**MOA:** Similar to L-thyroxine

**Uses:** Levothyroxine is used to treat hypothyroidism.

## Propylthiouracil



**MOA** IUPAC: **2,3-dihydro-6-propyl-2-thioxo-4(1H)-pyrimidinone**

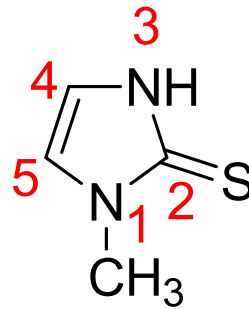
○ Propylthiouracil binds to thyroid peroxidase and thereby inhibits the conversion of iodide to iodine.

○ Thyroid peroxidase normally converts iodide to iodine (via hydrogen peroxide as a cofactor) and also catalyzes the incorporation of the resulting iodide molecule onto both the 3 and/or 5 positions of the phenol rings of tyrosines found in thyroglobulin.

○ Thyroglobulin is degraded to produce thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>), which are the main hormones produced by the thyroid gland. Therefore propylthiouracil effectively inhibits the production of new thyroid hormones.

**Uses:** Used to manage hyperthyroidism which is due to an overactive thyroid gland (Grave's disease)

## Methimazole



**MOA**      **IUPAC: 1-methyl-2,3-dihydro-1H-imidazole-2-thione**

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