

Chapter 16. Thyroid & Antithyroid Drugs







Syllabus:

Thyroid: l-Thyroxine, l-Thyronine

Antithyroids: Propylthiouracil, Methimazole

16.1. THYROID HORMONE

Thyroid Glands

-  Largest endocrine gland; Located inferior to cricoid cartilage.
-  Butterfly shaped organ comprising of two Lobes: lobus dexter(right), lobus sinister(left)
-  Weighs 18-60 gms in adults.
-  Histologically it is made up of follicular (T3 & T4) and parafollicular (calcitonin) cells.
-  Functional Unit: Follicle or acinus
-  Hormones: **Triiodothyronine (T3)**, **Thyroxine (T4)** and Calcitonine

Basics Physiological Function of T3/T4:

A) Metabolic Function


- Increase the metabolism of carbohydrate, protein, & Lipids.
- Control the activity of other hormone like insulin, glucagon, glucocorticoids and catecholamine's.
- Increase the oxygen consumption and Heat production.
- Increase the cardiac activity.
- Also affect function of Kidney, liver, and muscle


B) Growth and Development

- Increase the production of growth hormone and potentiating its effects
- Important for skeletal development.
- Essential for normal growth and maturation of CNS

Thyroid disorders is a common disease that can affect 5 to 15% of general population.

Women are more likely prone as compare to men. Disturbance in the **thyroid hormone** leads to thyroid disorders:

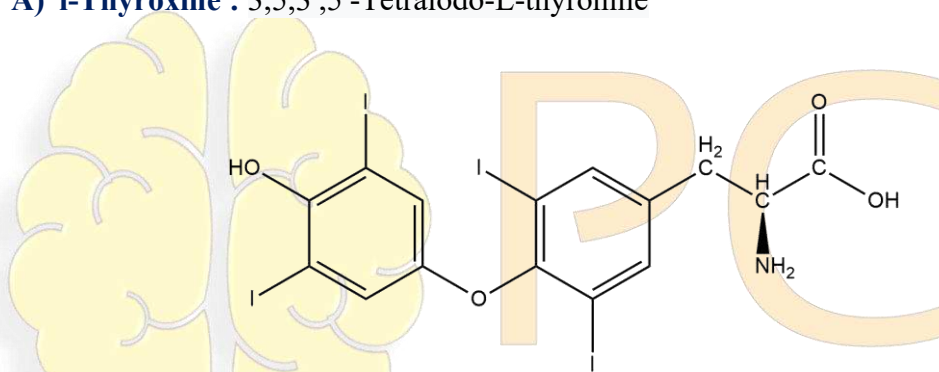
 **Hyperthyroidism:** Increased level of thyroid hormone: Grave's Disease; Toxic Thyroid Nodule (Adenomas); Thyroid Storm

 **Hypothyroidism:** decreased level of thyroid hormone: Hashimotos, Thyroiditis, Cretinism, Myxoedema, Postpartum Thyroiditis, Subacute Thyroiditis, Sick Euthyroidism

Detail Pharmacology: <https://youtu.be/ZopUTwGQ1Oc>

Selected Drugs

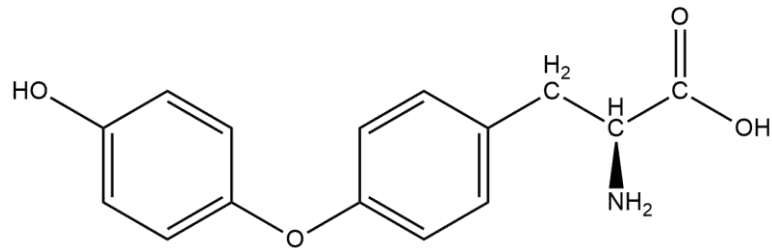
A) l-Thyroxine : 3,5,3',5'-Tetraiodo-L-thyronine



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

MOA: l-thyroxine is a levo-isomer of thyroid hormone (thyroxine) that acts as a replacement in T4 deficiency syndromes such as hypothyroidism. It is chemically identical to natural T4 that increase the metabolic rate and decrease pituitary TSH production. In periphery it converts into T3 (highly active). T4/T3 activates the thyroid hormone receptor (TR- α and TR- β) located at nucleus and regulate the TR-mediated gene transcription.

Use: Used in hypothyroidism condition: Criticism, Myxedema, non-toxic goiter, thyroiditis, thyroid nodule, papillary carcinoma of thyroid

B) Liothyronine**(2S)-2-amino-3-[4-(4-hydroxy phenoxy) phenyl] propanoic acid**

l-thyronine is a levo isomer of triiodothyronine (T3) that is 4 to 5 times more potent than T4. It acts faster and peak effects occurs after 1-2 days while T4 takes 4-5 days.

MOA & Uses: Similar as T4 but can't use frequently.

16.2. ANTITHYROID

These are drugs used to lower the functional capacity of the hyperactive thyroid gland in the hyperthyroidism conditions like Grave's Disease; Toxic Thyroid Nodule (Adenomas); Thyroid Storm

- 1) **Inhibit hormone synthesis (Antithyroid drugs):** Propylthiouracil, Methimazole, Carbimazole
- 2) **Inhibit iodide trapping (Ionic inhibitors)** Thiocyanates (–SCN), Perchlorates (–ClO₄), Nitrates (–NO₃).
- 3) **Inhibit hormone release:** Iodine, Iodides of Na and K, Organic iodide.
- 4) **Destroy thyroid tissue:** Radioactive iodine (131I, 125I, 123I)

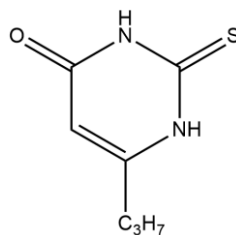
Pharmacology

Antithyroid Drugs: <https://youtu.be/EjSbWyDGQ9I>

Radioactive iodine: https://youtu.be/RNV_GKoD2g4

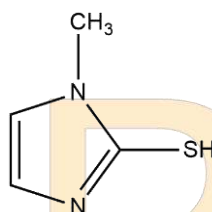
Selected Drugs

A) Propylthiouracil



2,3-dihydro-6-propyl-2-thioxopyridin-4(1H)-one

B) Methimazole



Methyl imidazole-2-thiol

MOA: Antithyroid drugs (Propylthiouracil and Methimazole) bind with the thyroid peroxidase and inhibit the peripheral conversion of T4 into T3 by blocking the oxidation of iodide/iodotyrosyl residues and further inhibit the thyroid hormone synthesis

Uses: Used in hyperthyroidism to control thyrotoxicosis in both Graves' disease and toxic nodular goiter and also used to treatment of thyroid adenoma.
