THYROID AND ANTITHYROID DRUGS

The thyroid gland is a large endocrine gland located deep in the neck, close to the upper portion of trachea. The gland is a source of two fundamental different types of hormones namely thyroxine (T4) and triiodothyroxine (T3), which are iodine containing derivatives of L-thyroxine. Both are vital for normal growth development and control of essential functions such as energy metabolism and protein synthesis. Thyroid gland is the only organ in mammals that has a capability to incorporate iodine into organic substances.

Thyroxine was first isolated in crystalline form from a hydrolysate of thyroid gland by Kendall in 1915. Later its structure was established by Harington in 1927 and a year later Harington and Barger synthesized the hormone.

Bio-synthesis of Thyroid Hormone

Thyroid hormone 3, 3’- α-Diiodo - L - thyrone (T2) and 3, 3’, 5’-Triiodo-L- thryone (T3) are formed in a giant prohormone molecule thyroglobulin, an iodinated glycoprotein. The formation of thyroid hormone depends on an exogenous supply of iodine. The iodine atom plays an unique role in the conformational preferences for T3 and T4 because of their large steric bulkiness. The formation of thyroid hormones involves the following complex sequences:

i) Active uptake of iodide by follicular cells.

ii) Oxidation of iodide and formation of iodotyrosine.

iii) Coupling of iodotyrosine residue.

iv) Proteolysis of thyroglobulin and release of iodothyronines. (T4 and T3)
Fig. 27.1 Biosynthesis of Thyroxine

**Thyroid Hormones**

Synthetic, crystalline thyroid hormones are more uniformly absorbed than biological preparations and contain more precisely measured amount of active ingredients in their dosage forms.
Levothyroxine sodium (Levothroid, Unithroid, Thyronorm)

\[
\begin{align*}
\text{HO} & \quad \text{O} & \quad \text{CH}_2\text{C} & \quad \text{NH}_2 & \quad \Theta & \quad \Theta \\
\text{I} & & \text{I} & & \text{COONa} & & \\
\text{HO} & \quad \text{O} & \quad \text{CH}_2\text{CH}_2\text{COOH} & \quad \text{NH}_2
\end{align*}
\]

o - (4-Hydroxy -3,5 - diiodophenyl) -3,5 - diiodo-L-Tyrosine mono sodium salt

Liothyronine (T\textsubscript{3}) (Cytomel, Tertroxin, Triostat)

\[
\begin{align*}
\text{HO} & \quad \text{O} & \quad \text{CH}_2\text{C} & \quad \text{NH}_2 \\
\text{I} & & \text{I} & & \\
\text{HO} & \quad \text{O} & \quad \text{CH}_2\text{CH}_2\text{COOH}
\end{align*}
\]

o - (4- Hydroxy -3- iodophenyl) -3,5 - diiodo - L - Tyrosine

Liothyronine has a rapid onset of action. It is used in condition where rapid and short duration of action is required.

**ANTITHYROID DRUGS**

Antithyroid drugs can either directly or indirectly interfere with the synthesis, release or action of thyroid hormones and used to control hyperthyroidism. A number of linear and heterocyclic derivatives of thiourea inhibit the production of thyroid hormone by the thyroid gland. The mechanism of action is that of preventing iodination of tyrosine or coupling between iodotyrosine. They also inhibit the conversion of thyroxine to liothyronine in the periphery.

**Classification**

i) Thioureylenes
   a) Thio uracil derivatives: eg. Methyl thiouracil, Propyl thiouracil.
   b) Imidazoles: eg. Methimazole, Carbimazole.

ii) Ionic inhibitors: eg. Thiocyanates, Perchlorates, Nitrates.

iii) Radioactive iodine: eg. \(^{131}\text{I}\)

   v) Iodides: eg. Lugol solutions, Colloid iodine, saturated solution of potassium iodide.
Propyl Thiouracil (Prothiugil)

![Propyl Thiouracil](image)

2,3 - Dihydro - 6 - propyl -2- thioxopyrimidin - 4 - one

Methyl Thiouracil (Thioryl, Tiorala)

![Methyl Thiouracil](image)

2,3 - Dihydro - 6 - methyl - 2 - thioxopyrimidin - 4 - one

Methimazole (Nortnyx)

![Methimazole](image)

1,3 - Dihydro - 1 - methyl - 2H - imidazol - 2 - thione