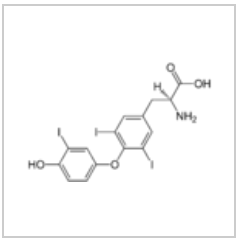
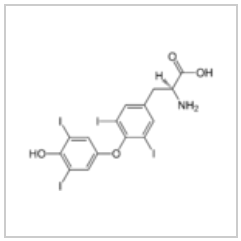
Thyroid hormones

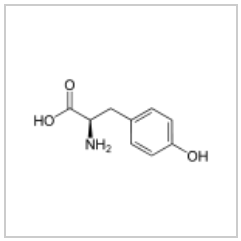
Thyroid hormones – **3, 5, 3'- triiodothyronine** (T3) and **3, 5, 3 ', 5'- tetraiodothyronine** (thyroxine T4) - are iodinated amino acids. In the blood, they are transported mainly bound to plasma protein and act through nuclear receptors in the target organ. They regulate gene expression, tissue differentiation and overall development. In the body, they regulate gene expression by mechanisms similar to steroid hormones.



Triiodothyronine structure



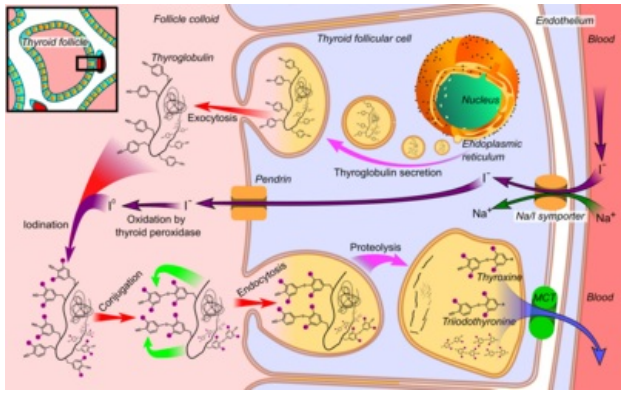
Thyroxine structure



Precursor: tyrosine

Thyroglobulin

Thyroglobulin is a precursor of T4 and T3. It is a large iodinated **glycosylated protein**. It consists of 2 subunits. It contains up to 115 tyrosine residues, each of which can be iodinated. 70% of iodides is in the form of inactive precursors - monoiodotyrosine (MIT), diiodotyrosine (DIT). 30% in the form of iodothyronyl residues - T4 and T3. When there is enough iodine, T4 predominates over T3. Thyroglobulin is synthesized in the basal parts of thyroid cells and moves into the lumen of thyroid follicles, where it is stored as an extracellular colloid. It then re-enters the cells and is hydrolyzed (by acidic peptidases and proteases) to the active hormones T4 and T3. These are released from the basal parts of the cells, apparently by facilitated diffusion. Iodide from inactive precursors - monoiodotyrosine (MIT), diiodotyrosine (DIT) is released by deiodase (NADPH-dependent enzyme).



Synthesis of thyroid hormones

Iodine metabolism

It consists of several steps:

1. ***Iodide*** – thyroid gland is able to concentrate I^- even against the strong electric gradient. It is an energy-intensive process and is connected to a Na^+/K^+ pump. A small amount of iodide also enters the gland by diffusion. The transport mechanism is inhibited by: perchlorate, perrhenate, pertechnate (competitive inhibition - accumulates in the gland), and thiocyanate (competitive inhibition - does not accumulate in the gland).
2. ***Oxidation*** – I^- can oxidize to a higher oxidation state (as the only tissue). The enzyme is thyroperoxidase (tetramer) - it requires hydrogen peroxide as an oxidizing agent.
3. ***Tyrosine iodisation*** – oxidized iodide reacts with tyrosyl residues in thyroglobulin. It is first iodinated in position 3 and then in position 5 - organizational reaction.
4. ***Iodotyrosyl condensation*** – joining two DIT molecules on T4 or one MIT and one DIT on T3.
5. ***Hydrolysis of thyroglobulin*** – stimulates it by TSH, inhibits I^-.

Transportation in blood

Most T4 and T3 in the blood are bound to thyroxine-binding globulin (TBG-major) and thyroxine-binding prealbumin (TBPA). The bond to the transport proteins is **non-covalent**. TBG is formed in the liver and its synthesis increases after stimulation with estrogens. Phenytoin and salicylates compete with the binding of T4 and T3 to TBG. T3 binds to target cell receptors with ten times greater affinity than T4 and is therefore considered the major metabolically active hormone. At the periphery, about 80% of the circulating T4 is converted to T3 or reverse rT3. Other pathways of hormone metabolism are complete deiodination and inactivation by deamination and decarboxylation.

The mechanism of action

Hormones bind to high-affinity specific **receptors in the nucleus of** target cells. A significant effect is to **increase overall proteosynthesis** and induce a **positive nitrogen balance**. Like steroids, thyroid hormones induce or repress proteins by increasing or decreasing gene transcription. T3 and glucocorticoids enhance STH gene transcription. Very high concentrations of T3 **inhibit proteosynthesis** and cause **a negative nitrogen balance**.

Pathophysiology

- Graves disease – hyperthyroidism - is caused by the formation of thyroid-stimulating immunoglobulin, which activates thyroid TSH receptors. Findings - increase in heart rate, nervousness, insomnia, weight loss, loss of appetite, an extension of pulse amplitude.
- **Cretinism** – intrauterine or neonatal hypothyroidism leads to cretinism - multiple congenital defects + irreversible mental retardation.

References

Related articles

- Thyroid gland
- Thyroid diseases
- Graves diseease
- Hypothyroidism

Literature

- TROJAN, Stanislav – TROJAN, Stanislav. *Lékařská fyziologie.* 4. edition. Prague : Grada, 2003. 772 pp. ISBN 80-247-0512-5.
- SILBERNAGL, Stefan – DESPOPOULOS, Agamemnon. *Atlas fyziologie člověka.* 6. edition. Prague : Grada, 2004. 435 pp. ISBN 80-247-0630-X.