Pharmacology of Hormones and Hormone Antagonists

Hormones and Hormone Antagonists

Introduction

- Hormones are chemical messengers secreted by endocrine glands that regulate various physiological processes, including growth, metabolism, reproduction, and homeostasis.
- They act at very low concentrations and exert their effects by binding to specific receptors in target tissues.
- Hormones can be steroids, peptides/proteins, or amines based on their structure.
- Hormone therapy involves the use of natural or synthetic hormones to supplement or block the effects of endogenous hormones.
- Hormone antagonists are drugs that block hormone receptors or inhibit hormone synthesis, often used in conditions like hormone-sensitive cancers, endocrine disorders, and for contraception.

Classification

A. Based on Chemical Structure:

1. Peptide and Protein Hormones

- Insulin, Glucagon, Growth hormone, Oxytocin, Vasopressin

2. Steroid Hormones

- Corticosteroids (Glucocorticoids, Mineralocorticoids)
- Sex hormones (Estrogens, Androgens, Progestins)

3. Amino Acid Derivatives (Amine Hormones)

- Thyroid hormones (T3, T4)
- Catecholamines (Epinephrine, Norepinephrine)

B. Based on Therapeutic Use:

1. Replacement Therapy

- For hormone deficiency (e.g., Insulin in diabetes, Levothyroxine in hypothyroidism)

2. Hormone Suppression

- To treat hormone-dependent cancers (e.g., Tamoxifen for breast cancer, Leuprolide for prostate cancer)

3. Hormonal Contraceptives

- Estrogen-progestin combinations

4. Diagnostic Use

- ACTH stimulation test for adrenal function

5. Hormone Antagonists

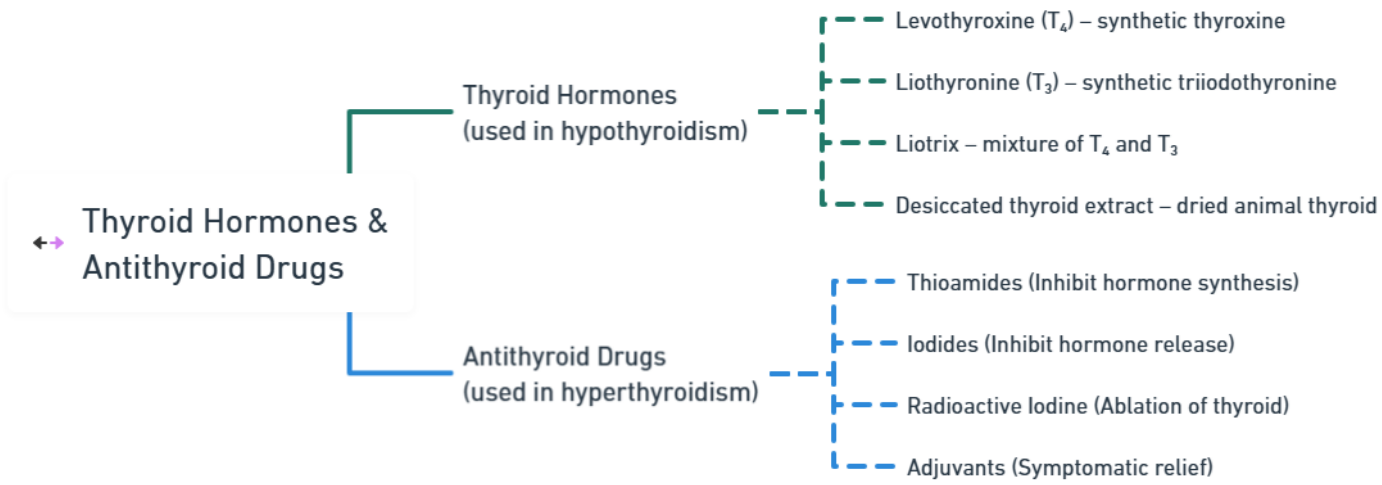
- Estrogen antagonists (e.g., Tamoxifen)
- Androgen antagonists (e.g., Flutamide)
- Corticosteroid antagonists (e.g., Mifepristone for glucocorticoids)

Thyroid and Antithyroid Drugs

Introduction

- The thyroid gland is a butterfly-shaped endocrine gland located in the neck. It synthesizes and secretes thyroid hormones:
    - Thyroxine (T_4)
    - Triiodothyronine (T_3)
      These hormones play a critical role in regulating metabolism, growth and development, thermogenesis, cardiovascular function, and neurological function.
- Thyroid function is regulated by the hypothalamic-pituitary-thyroid axis:
    - TRH (thyrotropin-releasing hormone) from hypothalamus → stimulates
    - TSH (thyroid-stimulating hormone) from anterior pituitary → stimulates
    - Thyroid gland → releases T_3 and T_4.
- Disorders of thyroid function include:
    - Hypothyroidism: Decreased thyroid hormone production
    - Hyperthyroidism (Thyrotoxicosis): Excessive production of thyroid hormones
- Thyroid drugs include hormone replacement therapy (e.g., levothyroxine) for hypothyroidism, and antithyroid drugs (e.g., methimazole, propylthiouracil) for hyperthyroidism.

Classification



Thyroid Hormones (used in hypothyroidism):

- **Levothyroxine (T_4)** – synthetic form of thyroxine
- **Liothyronine (T_3)** – synthetic triiodothyronine
- **Liotrix** – a mixture of T_4 and T_3
- **Desiccated thyroid extract** – dried animal thyroid (rarely used now)

Antithyroid Drugs (used in hyperthyroidism):

A. Thioamides (Inhibit hormone synthesis):

- Methimazole (MMI)
- Propylthiouracil (PTU)

B. Iodides (Inhibit hormone release):

- Lugol's iodine (iodine + potassium iodide)
- Saturated solution of potassium iodide (SSKI)

C. Radioactive Iodin (Ablation of thyroid):

- Iodine-131

D. Adjuvants (Symptomatic relief):

- Beta-blockers (e.g., Propranolol)
- Glucocorticoids
- Calcium channel blockers (for heart rate control)

Mechanism of Action

Thyroid Hormones:

- **Levothyroxine (T_4)** is converted to **T_3**, the active form, in peripheral tissues.
- T_3 binds to nuclear thyroid hormone receptors and modifies transcription of genes involved in metabolism, growth, protein synthesis, and energy production.

Antithyroid Drugs:

1. Thioamides (MMI, PTU):

- Inhibit thyroid peroxidase enzyme.
- Block iodination of tyrosine residues in thyroglobulin and coupling of iodotyrosines (MIT and DIT) to form T_3 and T_4.
- PTU also inhibits peripheral conversion of T_4 to T_3.

2. Iodides (Lugol's iodine, SSKI):

- In high concentrations, iodides inhibit thyroid hormone release.
- Also reduce size and vascularity of thyroid gland.
- Effect is transient (known as Wolff-Chaikoff effect).

3. Radioactive Iodine (I-131):

- Emits beta radiation that selectively destroys thyroid follicular cells.
- Used for definitive treatment of hyperthyroidism and thyroid cancer.

4. Beta-blockers (Propranolol):

- Do not inhibit hormone synthesis, but reduce symptoms like tachycardia, anxiety, and tremors.
- At high doses, propranolol also inhibits peripheral conversion of T_4 to T_3.

Pharmacokinetics

Thyroid Hormones

A. Levothyroxine (T_4):

- Oral absorption: ~70–80%
- Half-life: ~7 days (allows once-daily dosing)
- Metabolized in liver, excreted in bile and urine
- Delayed onset: 1–3 weeks to see full effect

B. Liothyronine (T_3):

- More potent but shorter half-life (~1 day)
- Faster onset, useful in myxedema coma

Antithyroid Drugs:

A. Methimazole:

- Oral, long half-life (~6–13 hrs), allows once-daily dosing
- Crosses placenta and into breast milk

B. Propylthiouracil (PTU):

- Oral, shorter half-life (~1–2 hrs), requires multiple daily doses
- Crosses placenta but preferred in first trimester due to lower teratogenicity

C. Iodides:

- Rapid onset (within 24 hrs)
- Maximal effect in 10–15 days
- Short-lived effect (escape phenomenon)

D. Radioiodine (I-131):

- Oral administration
- Concentrated in thyroid, half-life: ~8 days
- Effects appear after 2–4 weeks, peak at 2–3 months

Pharmacodynamics

Thyroid Hormones:

- Increase basal metabolic rate
- Stimulate cardiac output, oxygen consumption, protein synthesis

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