

Unit-IV/Part-A

Drug Acting on Endocrine system

Presented By;-

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Specialization:- Pharmaceutical Chemistry

Endocrine system

- ▶ **Definition:-**The endocrine system is a network of glands and specialized cells that produce and secrete hormones directly into the bloodstream.
- ▶ These hormones regulate various physiological processes, including growth, metabolism, reproduction, stress response, and homeostasis.

Major Endocrine Glands and Their Hormones:

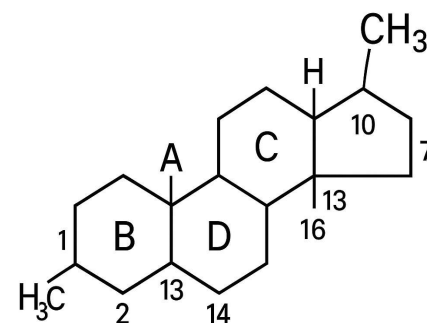


Gland	Hormones Secreted	Functions
Pituitary (Master gland)	Anterior lobe: GH, TSH, ACTH, FSH, LH, Prolactin Posterior lobe: ADH, Oxytocin	Controls other glands, growth, reproduction.
Pineal gland	Melatonin	Regulates sleep-wake cycle (biological clock).
Thyroid gland	T3 (Triiodothyronine), T4 (Thyroxine), Calcitonin	Regulates metabolism, growth, and calcium levels.
Parathyroid glands	Parathyroid hormone (PTH)	Regulates blood calcium and phosphate levels.
Adrenal glands	Cortex: Cortisol, Aldosterone, Androgens Medulla: Adrenaline (Epinephrine), Noradrenaline	Stress response, metabolism, blood pressure regulation.
Pancreas (Islets of Langerhans)	Insulin, Glucagon, Somatostatin	Blood glucose regulation.
Gonads (Ovaries & Testes)	Ovaries: Estrogen, Progesterone Testes: Testosterone	Reproduction, secondary sexual characteristics.
Thymus	Thymosin	Maturation of T-lymphocytes (immune system).

Steroids

Definition:-Steroids are a class of **lipid-based organic compounds** characterized by a **cyclopentanoperhydrophenanthrene nucleus** (also called the steroid nucleus), which is a structure composed of **17 carbon atoms arranged in four fused rings**:

1. Three cyclohexane rings (A, B, C)
2. One cyclopentane ring (D)



Steroid Nucleus

Nomenclature of Steroids



The nomenclature of steroids is based on the **International Union of Pure and Applied Chemistry (IUPAC)** guidelines. Key points:

1. Parent Hydrocarbon:

- The base structure is called “**gonane**” (C17 steroid nucleus).
- If methyl groups are added at C-10 and C-13, it is called “**estrane**” (C18), “**androstane**” (C19), or “**pregnane**” (C21), depending on the carbon count.

2. Numbering of Steroid Skeleton:

- Carbons are numbered from **C-1 in ring A** to **C-17 in ring D**, with side chains numbered beyond C-17.
- **C-18 and C-19 are methyl groups** attached at C-10 and C-13, respectively.

3. Ring Designation:

- The rings are named **A, B, C, D** from left to right.

4. Unsaturation and Functional Groups:

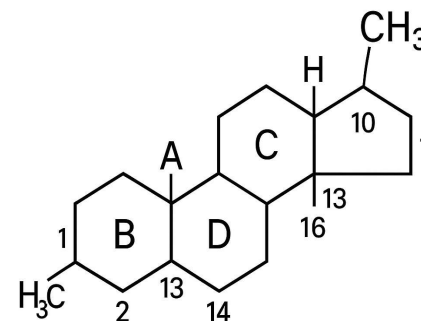
- Double bonds are indicated by suffix “**-ene**”, e.g., **androst-4-ene** (double bond at C4-C5).
- Ketones are indicated by “**-one**”, e.g., **testosterone = androst-4-en-17 β -ol-3-one**.
- Hydroxyl groups are indicated by “**-ol**”, e.g., **estradiol**.

5. Prefixes for Substituents:

- Substituents are specified with their positions (e.g., **17 α -methyltestosterone**).
- Stereochemistry (α or β orientation) is important and indicated in the name.

6. Example of Steroid Nomenclature:

- **Testosterone:** androst-4-en-17 β -ol-3-one
(An androstane skeleton, double bond at C4, hydroxyl at C17 in β orientation, and ketone at C3.)



Steroid Nucleus

Stereochemistry in steroids

Stereochemistry in steroids

Steroids, ubiquitous in nature and vital in medicine, possess a characteristic 17-carbon skeletal structure arranged in four fused rings (A, B, C, D). The intricate three-dimensional arrangement of atoms, known as stereochemistry, plays a crucial role in their biological activity and medicinal applications.

1. Steroid structure and stereochemical notation

- Steroids have a core structure of four fused rings: three six-membered cyclohexane rings (A, B, C) and one five-membered cyclopentane ring (D).
- Substituents above the plane of the rings are denoted by a solid line (β -configuration), while those below the plane are indicated by a dashed line (α -configuration).
- The IUPAC (International Union of Pure and Applied Chemistry) numbering system is used to identify specific carbon atoms in the steroid nucleus.

2. Ring fusions and conformation

- The fusion of adjacent rings (A/B, B/C, C/D) can be either cis or trans, determining the overall shape of the steroid molecule.
- In most naturally occurring saturated steroids, the B/C and C/D ring junctions are trans-fused.
- The A/B ring junction can be either cis or trans, depending on the orientation of the hydrogen atom at C-5.
- The cyclohexane rings typically adopt a more stable "chair" conformation, although boat conformations can exist at higher energy.
- However, the rigid ring system of steroids prevents the "ring-flip" phenomenon observed in simple cyclohexanes.

3. Chirality and isomers

- Steroids possess multiple chiral centers (asymmetric carbon atoms), leading to the possibility of numerous stereoisomers (e.g., 64 for Gonane, Oestrane, and Androstane).
- These isomers can have drastically different biological activities, including potency, target specificity, and side effects.
- Medicinal chemists must carefully consider the stereochemistry of steroid drugs, as different stereoisomers can have different interactions with biological receptors and metabolic enzymes.



Metabolism of Steroids

1. **Phase I** Reactions (Modification of Structure)

- **Oxidation, reduction, or hydroxylation** occurs primarily in the liver.
- **Enzymes involved:** Cytochrome P450 monooxygenases (CYP450).
- **Examples:**
 - Testosterone → Dihydrotestosterone (DHT) (via **5 α -reductase**).
 - Testosterone → Estradiol (via **aromatase, CYP19A1**).
 - Cortisol → Cortisone (via **11 β -hydroxysteroid dehydrogenase**).
- These reactions often **activate or deactivate the hormone**.

2. **Phase II** Reactions (Conjugation)

- Conjugation with **glucuronic acid (glucuronidation)** or **sulfate (sulfation)** occurs.
- **Enzymes involved:**
 - UDP-glucuronosyltransferases (UGTs).
 - Sulfotransferases (SULTs).
- **Purpose:** Makes steroids more **water-soluble**, aiding renal or biliary excretion.



Thank You

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