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# MEDICINAL CHEMISTRY – I

## UNIT 2

TOPIC :

- **Drugs acting on Autonomic Nervous System**

**Adrenergic Neurotransmitters :**

Biosynthesis and catabolism of catecholamine.

Adrenergic receptors (Alpha & Beta) and their distribution.



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## Drugs Acting on Autonomic Nervous System (ANS)

- The Autonomic Nervous System (ANS) is a part of the Peripheral Nervous System (PNS) that controls involuntary body functions such as heart rate, digestion, glandular secretion, pupil size, and respiratory rate.
- It has two main branches with opposing actions:
  1. Sympathetic Nervous System (SNS) → “Fight or Flight”
  2. Parasympathetic Nervous System (PNS) → “Rest and Digest”
- Drugs acting on the ANS either mimic or block these branches to produce therapeutic effects.

## Adrenergic Neurotransmitters (Catecholamines)

- Chemical messengers released from adrenergic neurons that act on adrenergic receptors ( $\alpha$  and  $\beta$  receptors).
- **Functions:**
  - Mediate “fight or flight” responses:  $\uparrow$  heart rate,  $\uparrow$  blood pressure,  $\uparrow$  blood glucose, bronchodilation.
  - Also regulate mood, movement, renal blood flow, and metabolism.
- **Main Adrenergic Neurotransmitters (Catecholamines):**
  1. **Dopamine (DA)**
    - First catecholamine in synthesis chain.
    - Acts on dopamine ( $D_1$ ,  $D_2$ ) receptors.
    - At high doses → mild effect on  $\beta$  receptors.
    - Functions: CNS role (movement, reward), renal vasodilation, precursor for norepinephrine.
  2. **Norepinephrine (Noradrenaline)**
    - Primary neurotransmitter released by sympathetic postganglionic neurons.
    - Acts mainly on  $\alpha_1$  and  $\beta_1$  receptors.
    - Functions:  $\uparrow$  heart rate,  $\uparrow$  contractility, vasoconstriction →  $\uparrow$  blood pressure.
  3. **Epinephrine (Adrenaline)**

- Hormone from adrenal medulla.
- Acts on  $\alpha_1$ ,  $\beta_1$ ,  $\beta_2$  receptors.
- Functions:
  - $\uparrow$  heart rate & cardiac output ( $\beta_1$ ).
  - Bronchodilation ( $\beta_2$ ).
  - Vasoconstriction ( $\alpha_1$ ) + skeletal muscle vasodilation ( $\beta_2$ ).
  - $\uparrow$  blood glucose via glycogenolysis.

## Biosynthesis of Catecholamines

1. **Phenylalanine**  $\rightarrow$  **Tyrosine** (enzyme: *Phenylalanine hydroxylase*).
2. **Tyrosine**  $\rightarrow$  **DOPA** (enzyme: *Tyrosine hydroxylase*).
3. **DOPA**  $\rightarrow$  **Dopamine** (enzyme: *DOPA decarboxylase*).
4. **Dopamine**  $\rightarrow$  **Norepinephrine** (enzyme: *Dopamine  $\beta$ -hydroxylase*).
5. **Norepinephrine**  $\rightarrow$  **Epinephrine** (enzyme: *Phenylethanolamine N-methyl transferase*).

## Catabolism (Breakdown) of Catecholamines

- **Main enzymes:**
  1. **Monoamine Oxidase (MAO):**
    - Found in mitochondria of neurons & other tissues.
    - Removes amino group  $\rightarrow$  inactivates catecholamines.
  2. **Catechol-O-Methyl Transferase (COMT):**
    - Found in liver, kidney, other tissues.
    - Methylates catechol group  $\rightarrow$  inactivates catecholamines.

## Adrenergic Receptors

- G-protein coupled receptors (GPCRs) activated by catecholamines (NE, Epi, DA).

### Types and Functions:

#### 1. $\alpha$ -Adrenergic Receptors

- **$\alpha_1$  receptors:** Vasoconstriction,  $\uparrow$  BP, pupil dilation, bladder sphincter contraction.
- **$\alpha_2$  receptors:** Inhibit NE release (presynaptic),  $\downarrow$  insulin release.

#### 2. $\beta$ -Adrenergic Receptors

- **$\beta_1$  receptors:**  $\uparrow$  heart rate,  $\uparrow$  contractility,  $\uparrow$  renin release.
- **$\beta_2$  receptors:** Bronchodilation, vasodilation in skeletal muscle,  $\uparrow$  glycogenolysis.
- **$\beta_3$  receptors:** Lipolysis in adipose tissue, thermogenesis.

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