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MEDICINAL CHEMISTRY – I

UNIT 3

TOPIC :

- **Cholinergic neurotransmitters :**

Biosynthesis and catabolism of acetylcholine.

Cholinergic receptors (Muscarinic & Nicotinic) and their distribution.

Cholinergic Neurotransmitters

- Cholinergic neurotransmitters are chemical messengers that transmit nerve impulses by binding to cholinergic receptors (nicotinic or muscarinic) on the target cell.
- Major neurotransmitter: Acetylcholine (ACh)
It is the primary neurotransmitter of the cholinergic system.
- Functions of Acetylcholine:
 - Neuromuscular junction – activates skeletal muscle contraction.
 - Autonomic nervous system – regulates involuntary functions (e.g., heart rate, digestion, glandular secretion).
 - Central nervous system (CNS) – supports higher brain functions such as memory, learning, and attention.

Biosynthesis of Acetylcholine (ACh)

- Location: Takes place mainly in the nerve terminals of cholinergic neurons.
- Key enzyme: Choline acetyltransferase (ChAT).
- Substrates required:
 - Choline (derived from diet or recycled after ACh breakdown)
 - Acetyl-CoA (produced in mitochondria)

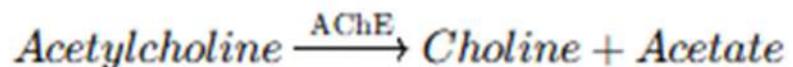
Reaction:



Catabolism of Acetylcholine

- Location: Occurs mainly in the **synaptic cleft** immediately after neurotransmission.
- Key enzyme: **Acetylcholinesterase (AChE)** – a very fast-acting enzyme.

Reaction:



Fate of products:

- **Choline** → taken back into the presynaptic neuron (recycled for ACh synthesis).
- **Acetate** → diffuses away and enters metabolic pathways.
- **Importance:**
 - Ensures **rapid termination** of ACh action at the synapse.
 - Prevents continuous stimulation of receptors (which could cause paralysis or toxicity).
 - The breakdown occurs within **milliseconds**.

Cholinergic Receptors

- Cholinergic receptors are **specialized proteins** located on the surface of cells (neurons, muscles, glands) that bind **acetylcholine (ACh)** and mediate its physiological effects.
- **Major types:**
 1. **Muscarinic receptors (M₁–M₅)** – belong to **G-protein coupled receptor family**.
 2. **Nicotinic receptors (NN, NM)** – belong to **ligand-gated ion channel family**.

1. Muscarinic Receptors (M₁–M₅)

- GPCR type → act through **second messengers**.
- Subtypes and distribution:

Subtype	Coupling (G-protein)	Major Distribution	Function
M₁	Gq	CNS (hippocampus, cortex), autonomic ganglia, gastric parietal cells	↑ Cognitive functions (memory, learning), ↑ Gastric acid secretion, neuronal excitation
M₂	Gi	Heart (atria, SA & AV)	↓ Heart rate (bradycardia)

		node), CNS	conduction, ↓ neurotransmitter release
M₃	Gq	Smooth muscle (bronchi, bladder, GIT), exocrine glands, eye (pupil)	Smooth muscle contraction, ↑ glandular secretion (saliva, tears, sweat), miosis (pupil constriction)
M₄	Gi	CNS (striatum, hippocampus)	Inhibits neurotransmitter release, role in motor control
M₅	Gq	CNS (substantia nigra, brain vasculature)	May modulate dopamine release, vasodilation in cerebral blood vessels

2. Nicotinic Receptors

- **Ligand-gated ion channels** (Na^+/K^+ channel).
- Subtypes:

Subtype	Location	Function
NN (Neuronal Nicotinic)	Autonomic ganglia (sympathetic & parasympathetic), adrenal medulla	Mediates transmission in ganglia, stimulates catecholamine release (adrenaline, noradrenaline)
NM (Muscle Nicotinic)	Neuromuscular junction (skeletal muscle)	Mediates skeletal muscle contraction