

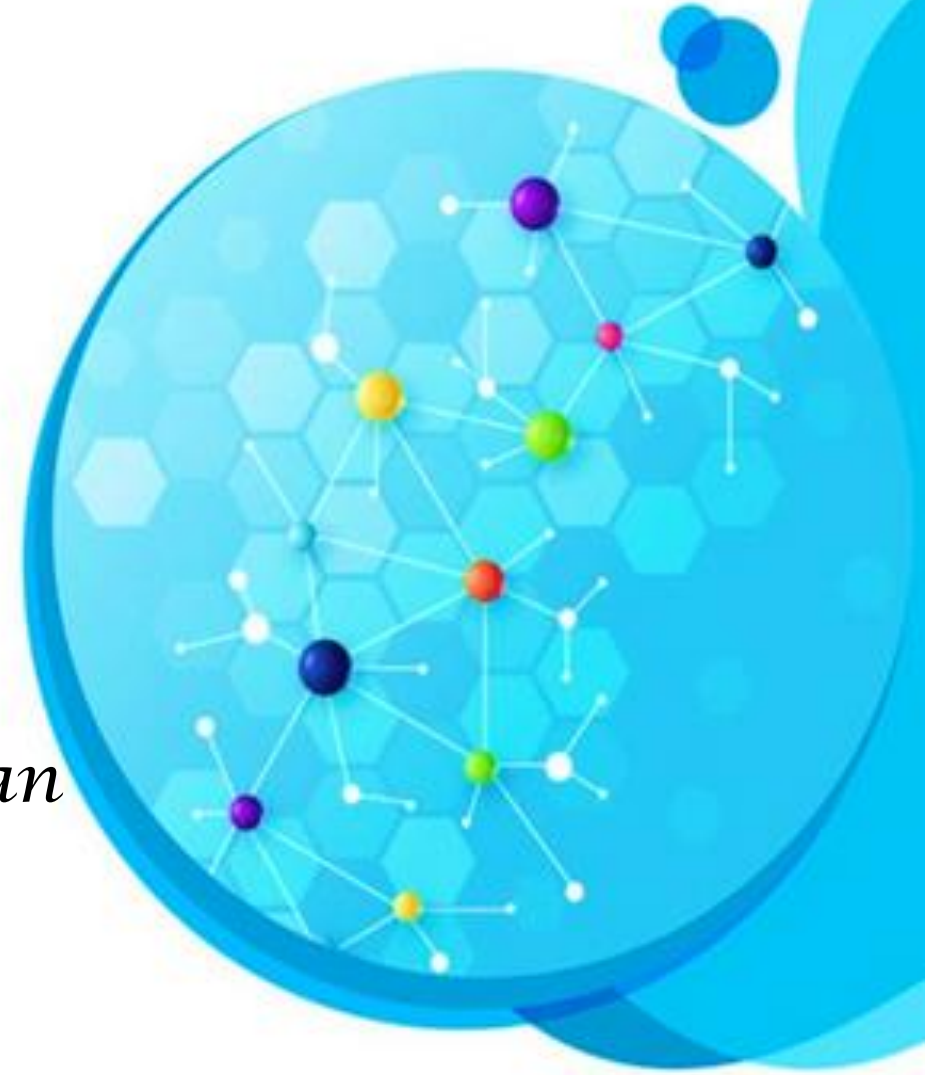
Medical Biochemistry

*Biochemistry of
neurotransmitters*

Asst. Prof. Mohammed Hasan Eleyan

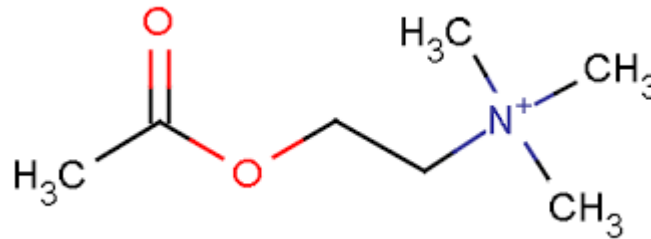
Faculty of Medicine

Al-Azhar University-Gaza



Acetylcholine

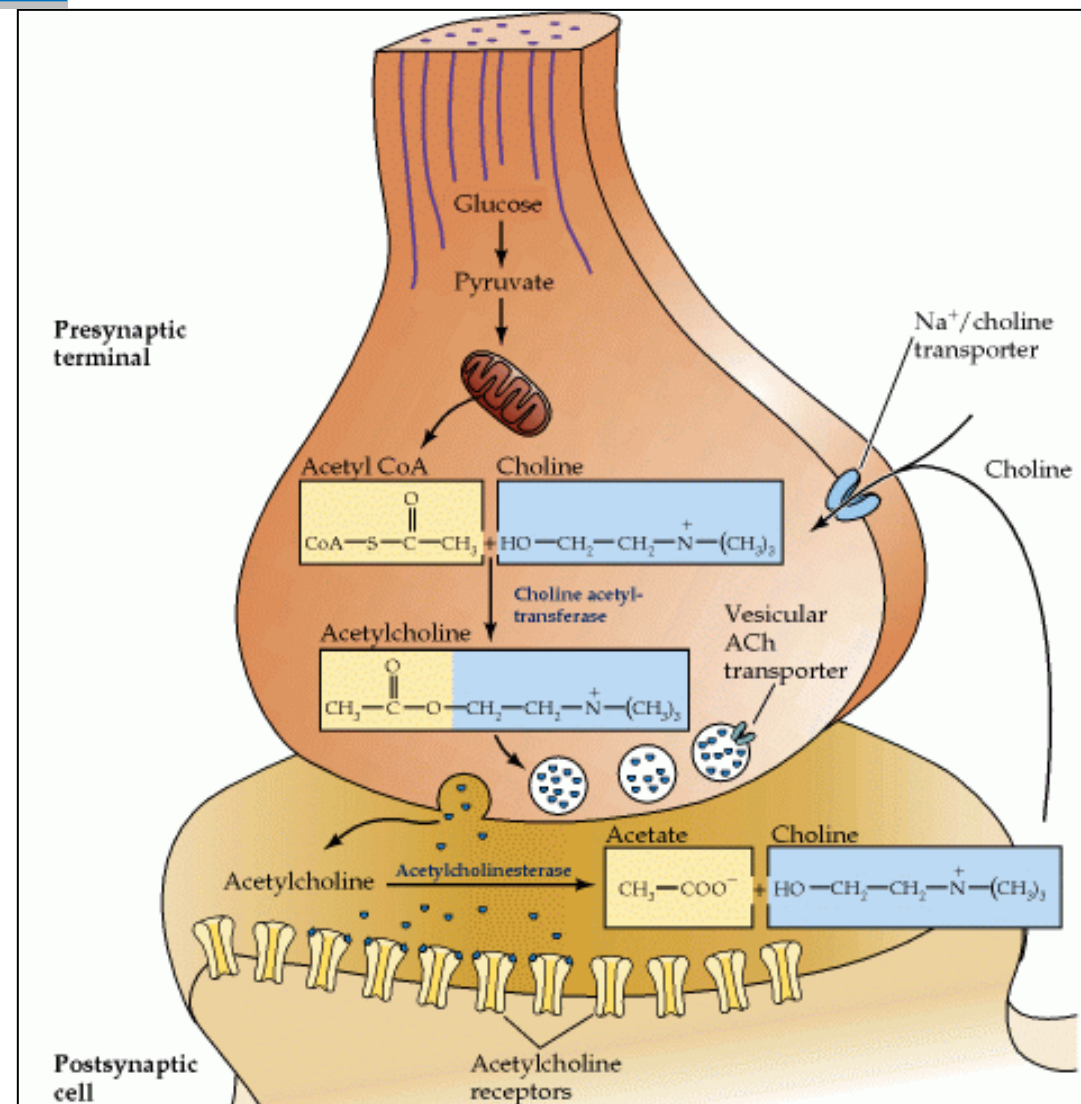
- **Acetylcholine:** a small molecule neurotransmitter consists of Acetyl group and Choline connected by the ester bond between acetyl and choline.



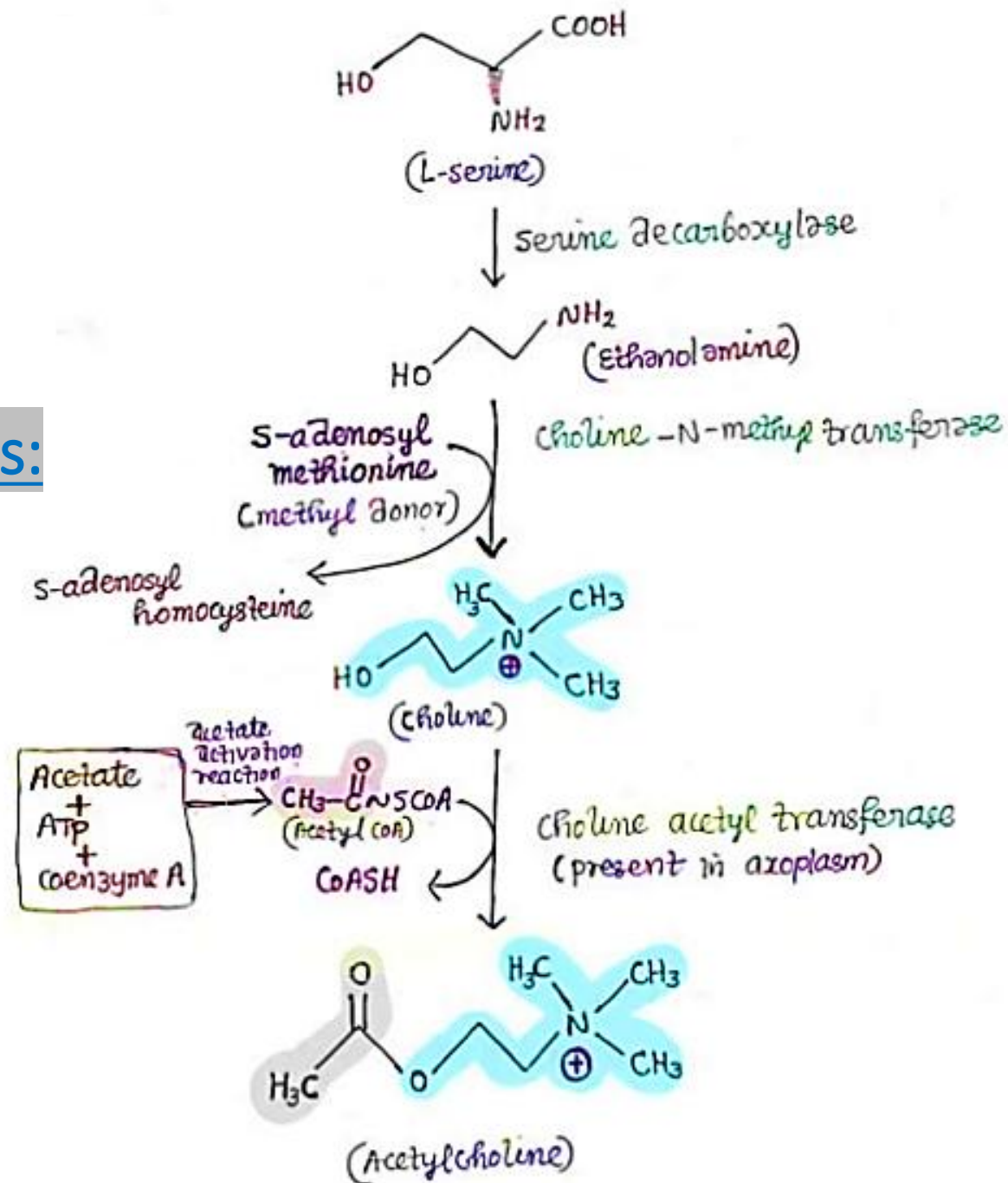
- Acetylcholine is synthesized locally in the cholinergic nerve endings.

Acetylcholine

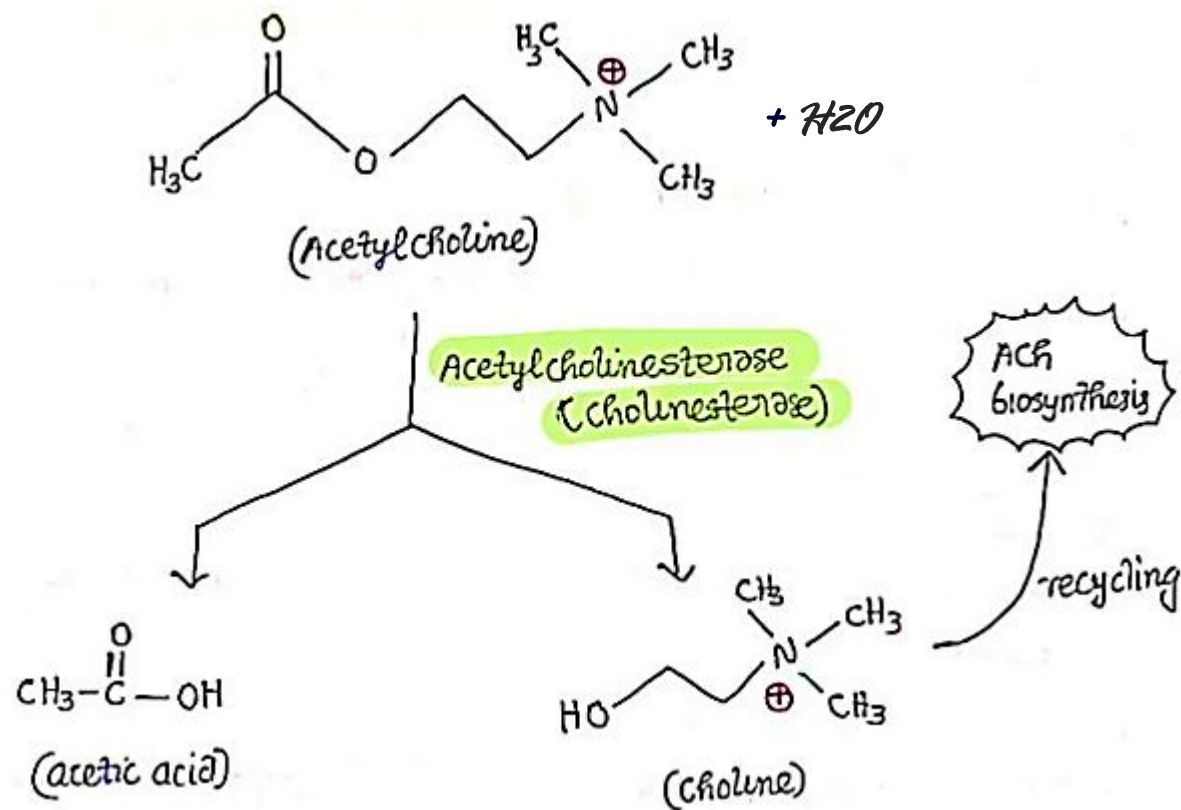
- Sources of choline: from synaptic cleft after Ach degradation or from serine; the brain takes most of choline from the blood.
- Choline is actively taken up by the axonal membrane by Na^+ : choline cotransporter
- Most of the ACh is stored within small clear synaptic vesicles which align mainly near the synaptic membrane.



Acetylcholine synthesis:



Catabolism of Acetylcholine



- Immediately after release, ACh is hydrolyzed by the enzyme cholinesterase and choline is recycled



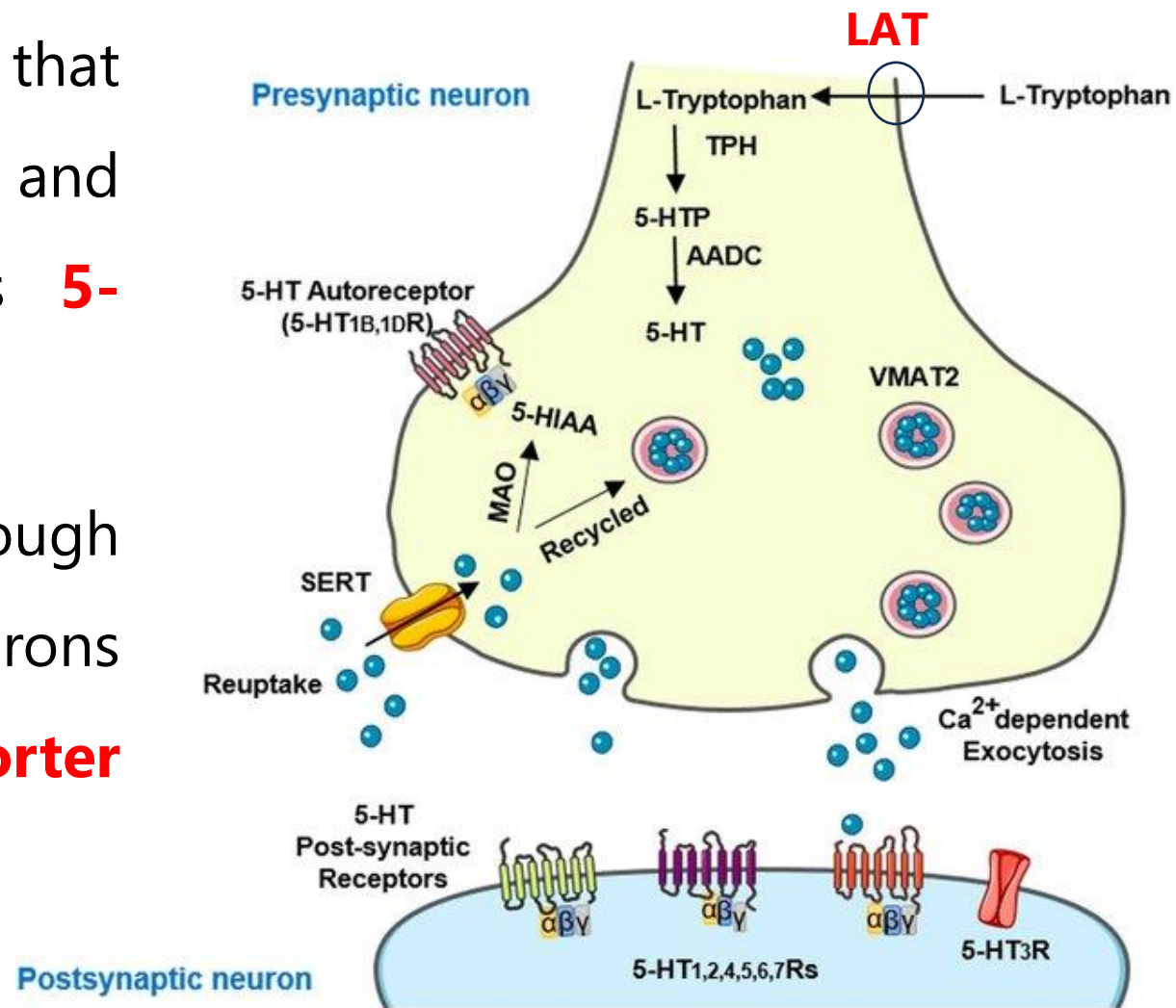
Tryptophan-Derived Neurotransmitters

Serotonin and melatonin

Serotonin

Tryptophan, an essential amino acid obtained from the diet.

- Serotonin is a ubiquitous monoamine that acts as both a neurotransmitter and hormone, which is also known as **5-hydroxytryptamine (5-HT)**.
- The synthesis of 5-HT is initiated through an active uptake of tryptophan in neurons by **L-type Amino Acid Transporter (LAT1/LAT2)**.





Serotonin synthesis

- Serotonin is synthesized from the amino acid Tryptophan.
- The synthesis of serotonin involve two reactions:

1) Hydroxylation:

- Tryptophan $\longrightarrow$ 5- Hydroxytryptophan
- The enzyme catalyzes this reaction is **Tryptophan Hydroxylase**.
- The Co- factor is Tetrahydrobiopterin, which converted in this reaction to Dihydrobiopterin.

2) Decarboxylation:

- 5- hydroxytryptophan $\longrightarrow$ Serotonin
- The enzyme is **hydroxytryptophan decarboxylase**.
- Serotonin is synthesized in CNS, & Chromaffin cells.



Break down of serotonin

- Serotonin is degraded in two reactions

1) Oxidation:



2) Dehydrogenation



1 Oxidative Deamination (by MAO)

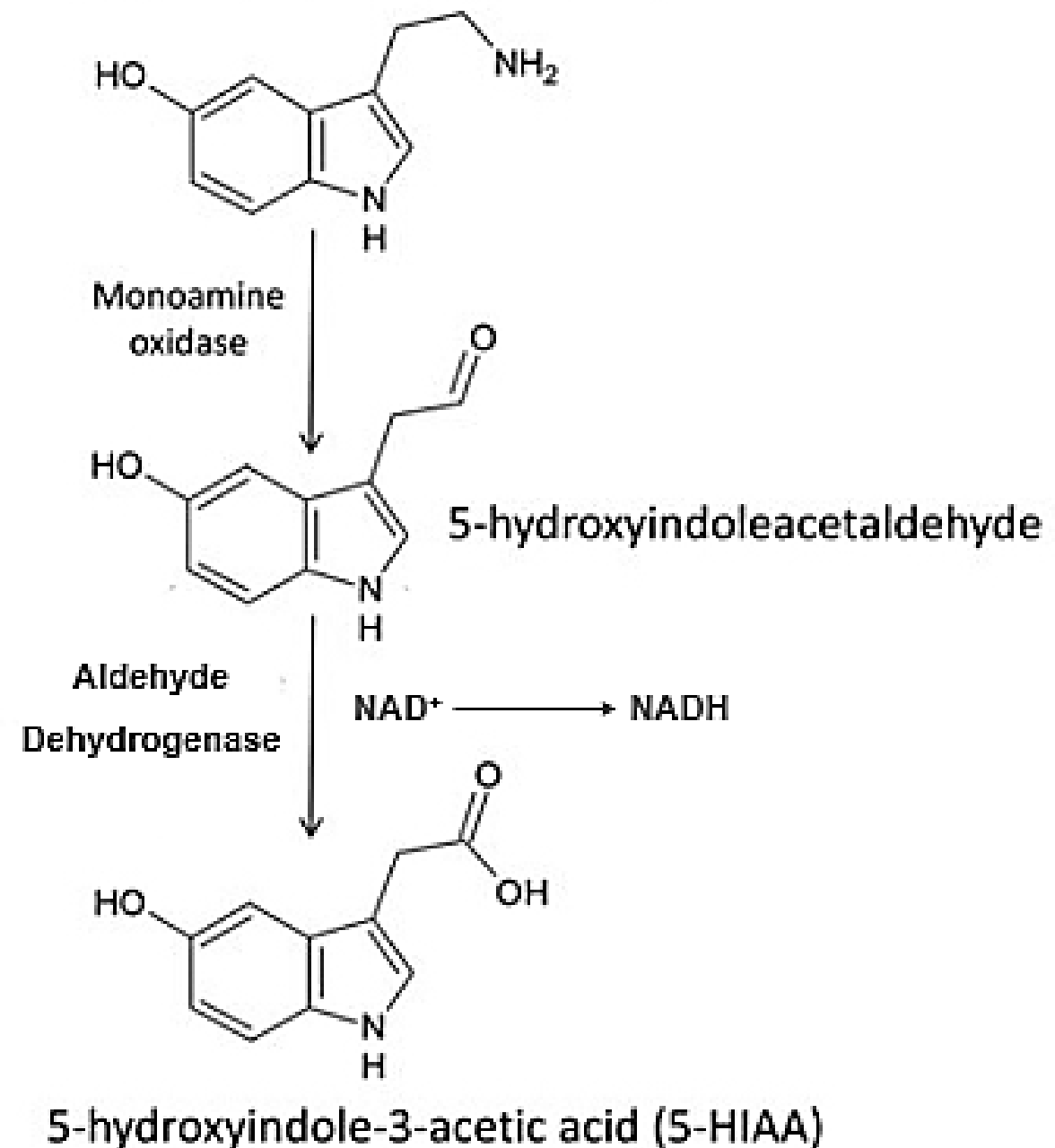
- **Location:** Primarily in **presynaptic neurons** and **peripheral tissues (liver, intestine, lungs, kidneys)**
- 5-HIAL rapidly diffuses out of the neuron into the **extracellular space** and **circulates in the bloodstream**.

2 Aldehyde Oxidation (by Aldehyde Dehydrogenase, ALDH)

- **Location:** Mainly in the **liver and peripheral tissues** (some activity in neurons).

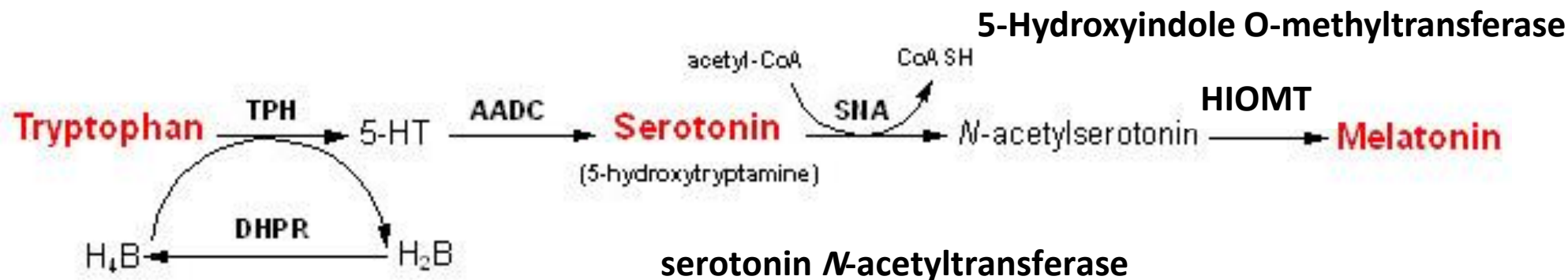
3 Excretion of 5-HIAA in Urine

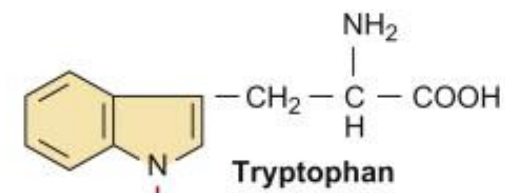
Serotonin (5-hydroxytryptamine)



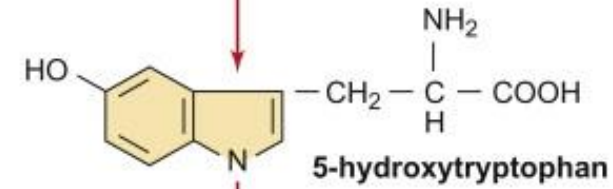
Melatonin

- Serotonin synthesized in the **pineal gland** serves as a precursor for the synthesis of **melatonin**, which is a neurohormone involved in regulating
 - Sleep patterns
 - Seasonal and circadian (daily) rhythms
 - Dark-light cycle

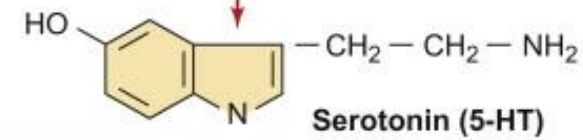




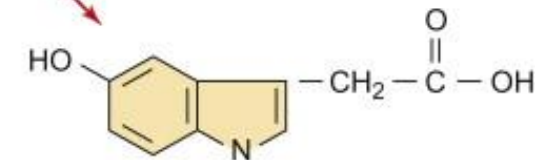
Tryptophan
hydroxylase



Aromatic amino
acid decarboxylase

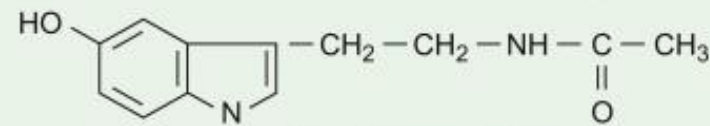


Monoamine oxidase +
aldehyde dehydrogenase



5-hydroxyindoleacetic acid

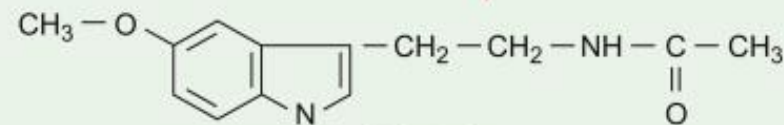
5-HT
N-acetyltransferase **Pineal**



N-acetyl serotonin

SAM

5-hydroxyindole-
O-methyltransferase



Melatonin



Thanks