Lecture title: Serotonin

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Summary:

Serotonin (5-hydroxytryptamine, 5-HT)

Biosynthesis:

Its synthesis comes from dietary tryptophan.

Storage: 5-HT is present in high concentration in **platelets**, the **enterochromaffin cells** and **myenteric plexus of the GI tract** and **CNS**

Metabolism, distribution, and function

1- Serotonin is metabolized by monoamine oxidase (MAO).

2- Approximately 90% of the body's serotonin is found in the GIT in enterochromaffin cells. It is involved in regulating motility.

3- Platelets actively transport serotonin and store it. This keeps the concentration of free 5-HT low in the blood flow.

4- Serotonin is synthesized and stored in the CNS where it acts as a neurotransmitter.

5- Serotonin is also found in venoms and stings. Sensory nerve ends are stimulated by serotonin and this action may be responsible in part for the pain and itch of stings

Serotonin receptors.

include: **5-HT1, 5-HT2, 5-HT3, 5-HT4−7 with** some categories having more than two

receptor subtypes.

Receptors	Site and function	Drugs that act on
$5HT_1$ A,B,C,D, E G_i	**CNS:** sleep, appetite, Mood, thinking and temperature. **Blood vessels:** Vasoconstriction	**Sumatriptan:** Agonist on $5HT_{1D}$ and $5HT_{1B}$ (treat migraine). **Buspirone:** Agonist on $5HT_{1A}$ (treat anxiety).
$5HT_2$ A, B, C Gq	**CNS** **Platelet:** Increase aggregation	**Cyproheptadine:** Antagonist on $5HT_2$ (appetite stimulant). **Ketanserin:** Antagonism of $5HT_{2A}$
$5HT_3$ Na^+/K^+	**CNS:** Vomiting center **GIT:** Regulate the motility	**Ondansetron:** Antagonism of $5HT_3$ (treat nausea and vomiting related to chemotherapy)
$5HT_4$ G_s	**CNS** **GIT:** Regulate the motility Cardiac muscle	**Tegaserod:** Agonist on $5HT_4$ (treat IBS). **Cisapride**: Agonist on 5HT4 **Metoclopramide:** Agonist on $5HT_4$ and antagonized D_2
$5HT_5$	**CNS**	
$5HT_6$ **$5HT_7$**	**CNS**	

Serotonin agonists in nature

Ergot alkaloids (ergotamine, ergometrine, bromocriptine).

Uses:

- Migraine→ ergotamine –partial agonist at 5-HT_{1D} and α1 adrenoceptor → VC (combined with caffeine to increase absorption)
- Hyperprolactinemia → bromocriptine → potent agonist on D2 receptors.
- Postpartum hemorrhage PPH→ ergometrine (ergonovine).
- Cerebral insufficiency → Dihydroergotoxine → antagonism effect on α1 adrenoceptor.

GI prokinetic agents:

These drugs increase GI motility by **increasing ACh release from the vagus nerve**.

a. Cisapride

Mechanism of action: It is an agonist for 5-HT_4 receptor.

Uses: used for gastric/intestinal stasis, reflux esophagitis, and constipation/megacolon in cats.

b. Metoclopramide

Mechanism of action: It is a D2-receptor antagonist/**5-HT_4** agonist.

Uses: It is used for treating vomiting disorders, reflux esophagitis, and gastric stasis, or hypomotility.

Cyproheptadine

Mechanism of action: Its block both 5-HT2 receptors and H1-receptors.

Uses: In cats as an **appetite stimulant**, **feline asthma** or **pruritus**. It also has H1-antihistamine activity, and thus is useful in managing hives. In horses, it is for treating photic head shaking.

Ketanserin

Mechanism of action: It antagonize $5HT_{2A}$ receptors and it has significant α1-adrenergic blocking activity.

Uses:

- Reduces blood pressure. It can be used to reduce intraocular pressure in glaucoma.
- ketanserin does not inhibit platelet aggregation induced by physiologic agonists (collagen and thrombin) and, pathophysiologic stimuli (atherosclerotic plaque). They, therefore, **do not constitute a promising strategy for antiplatelet therapy**.