DEPTH OF BIOLOGY

PHARMACOLOGY- 2nd

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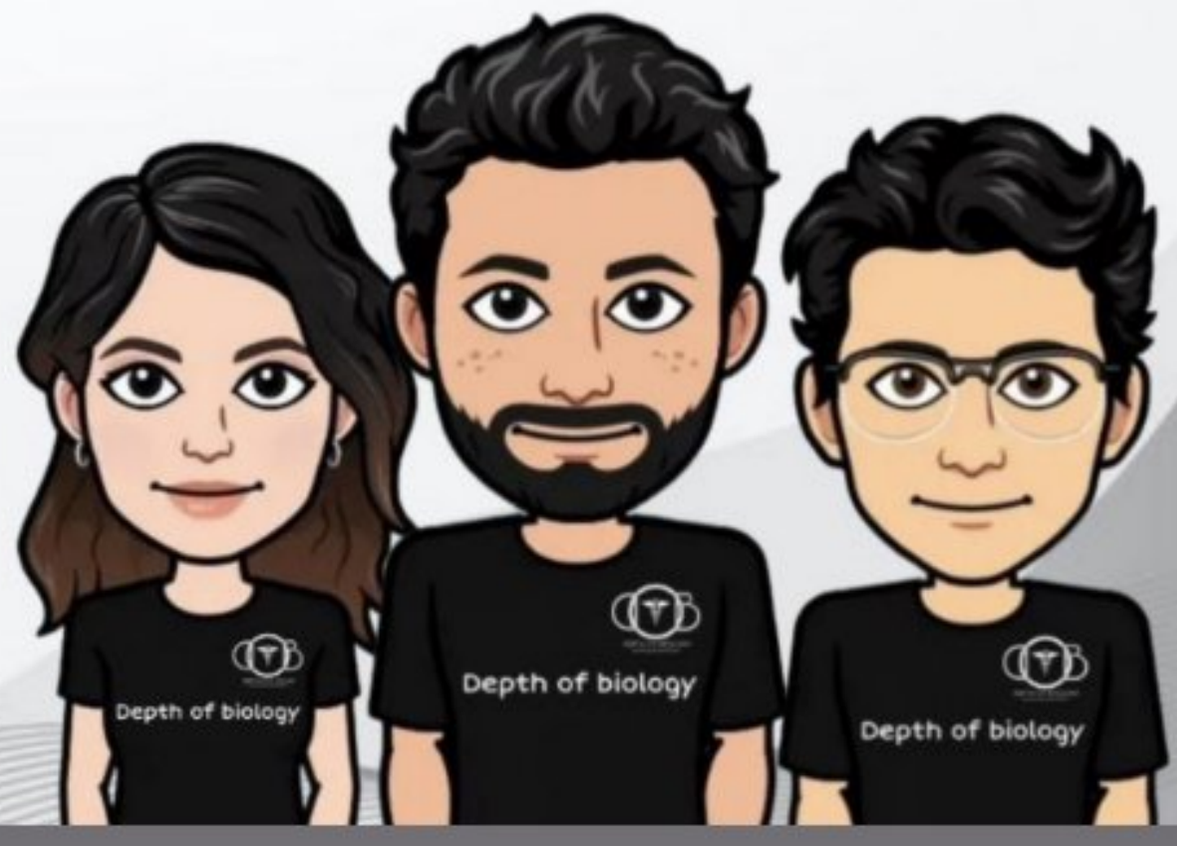
LET'S CONNECT AND GROW TOGETHER

DOB COMMUNITY



UNIT-III

3. Autocoids and related drugs

a. Introduction to autacoids and classification

b. Histamine, 5-HT and their antagonists.

c. Prostaglandins, Thromboxanes and Leukotrienes.

d. Angiotensin, Bradykinin and Substance P.

e. Non-steroidal anti-inflammatory agents

f. Anti-gout drugs

g. Antirheumatic drugs

UNIT- I **10 Hours**

Antihistaminic agents: Histamine, receptors and their distribution in the humanbody

H_1–antagonists: Diphenhydramine hydrochloride*, Dimenhydrinate, Doxylamines cuccinate, Clemastine fumarate, Diphenylphyraline hydrochloride, Tripelenamine hydrochloride, Chlorcyclizine hydrochloride, Meclizine hydrochloride, Buclizine hydrochloride, Chlorpheniramine maleate, Triprolidine hydrochloride*, Phenidamine tartarate, Promethazine hydrochloride*, Trimeprazine tartrate, Cyproheptadine hydrochloride, Azatidine maleate, Astemizole, Loratadine, Cetirizine, Levocetrazine Cromolyn sodium

H_2-antagonists: Cimetidine*, Famotidine, Ranitidin.

Gastric Proton pump inhibitors: Omeprazole, Lansoprazole, Rabeprazole, Pantoprazole

Autacoids -

Synthesis → Release
Action

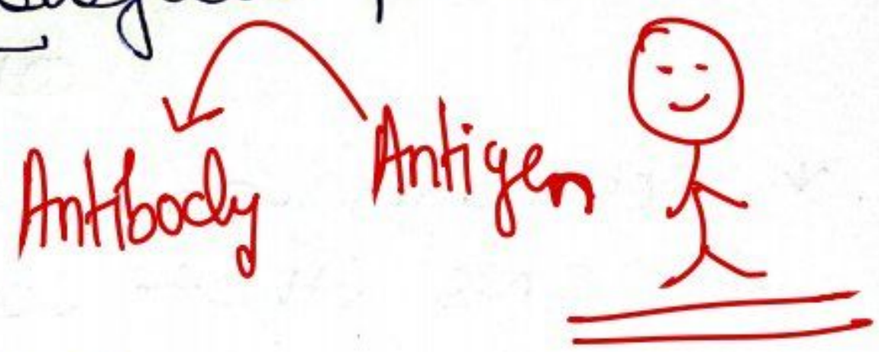
Autacoids ⇒ Autos - self
Akos - remedy or healing or Therapy or Treatment

Locally

* Site of action - locally
  * Local hormone → short action

* It is differ from hormones ⇒
  - these are [not produced by specific gland]
  - [not transported by circulation]
  - [Don't act on distant target]

* Involve in Physiological + Pathological processes
  → Injury



* Released during → allergy
  → Hypersensitivity
  → Inflammation

Classification :-

a] Amines autocoids - Histamine*, 5-Hydroxytryptamine [Serotonin]

b] Lipid derived autocoids - Prostaglandin, Leukotriens, Platelets activated factor

c] Peptide autocoids - Plasmakinins [Bradykinin, Kallidine]
Angiotensin

* Consider as autocoids → Cytokinins - Interleukin, TNF α

Peptides → Gastrin, Somatostatin

* ~~Autocoid~~ - Histamine → Histamine lecture Medicinal chemistry Unit-1

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* 5-Hydroxytryptamine [5-HT] - Serotonin

- Found in - Animal and Plant tissue
  eg - Banana, Pineapple, Tomato
- Serotonin - Mood Stabilizing hormone [Discovered 1948 *]

→ Distribution - In human -
90% - Intestine
other - Brain, Platelet

Serotonin ✗

* Serotonin cannot cross CNS, but those found BBB in CNS that synthesized in CNS and act in CNS.

* 5HT receptor → $5HT_1$, $5HT_2$, $5HT_3$, $5HT_4$
$5HT_5$, $5HT_6$, $5HT_7$

(R) → Macromolecule → Pharmacolog. Activity ✗

☆ $5HT_3$ - ligand gated ion channel
☆ $5HT_1$, $5HT_2$, $5HT_4$, $5HT_5$, $5HT_6$, $5HT_7$ - GPCR

Functions of 5-HT receptor

- $5HT_1$ - ↓se Serotonergic neural (Neuron.) activity
- $5HT_{2A}$ - Vascular Smooth muscle contraction
  - Platelet aggregation
- $5HT_3$ - Emesis, GUT Peristalsis↑, Bradycardia (<60 bpm)
  Pain, Itch

* Ondersetron block $5HT_3$ receptor → Anti emetic effect

- $5HT_4$ - Intestinal secretion

→ Renzapride [Prokinetic] → selective agonist
drug. Peristalsis↑

*Synthesis → It is occur in Enterochromaffin cells

Storage
Release
and
metabolism

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Tryptophan [amino acid]

↓ store

Serotonergic neuron

↓ release

Serotonergic synapse

Serotonin transporter (SERT) ↓ (Amine pump) (Active Transp.)

Serotonergic nerve ending

→ vesicles {store}

active transport → 0 0 0 platelets → MAO (destroyed) (metabolism) 2

5HT

→ Pharmacological action → DEPTH OF BIOLOGY

* Potent depolarizer of nerve ending

a) CVS - • Large vessicles – constricted
Arteriole – dilate

• Triphasic response on BP (a) Initial ↓ BP – due to ↑ vagal activity → Activity (Vagus Nerve)

(b) ↑ in BP – due to vasoconstriction

(C) ↓ in BP – due to arteriolar dilation

b) Gastrointestinal tract –

- ↑ gastric motility + contraction = diarrhoea

– Activation of 5HT receptor → Ach release = ↑ Intestine motility affect

Prokinetic effect

c) Gland – 5HT = ↓ gastric secretion = ↓ acid and ↓ pepsin

– ↑ mucus production = ulcer

Protective effect

d) Nerve ending – 5HT → activate afferent nerve ending = tingling + pain

Sensation

e) Platelets – $5HT_2$ → promote platelet aggregation

f) CNS – Injected IV. = no effect because ≠ BBB penetration

Injected directly on Brain = sleepiness

↓ Body temp., hunger

g) Other – Emesis = $5HT_3$ receptor at GUT

Pathophysiological role –

a) Neurotransmitter –

Action – Sleep, temp regulation, Mood, pain, cognitive function, Behavioural activity, Vomitting, thought, Appetite.

b) Precursor of melatonin. –

Action – 1) Precursor of melatonin at Pineal gland

2) Regulate biological clock

3) maintain circardian rythum

c) Neuro endocrine function - regulate anterior pituitary hormone

d) Nausea - vomitting - Especially for - Cytotoxic drug Radiotherapy

e) migraine - start vasoconstrictor phase of migraine = inflammation of neuron

f) Heamostatic control - Platelet - 5-HT = ↑ platelet aggregation = clot

g) Hypertension - 5HT is responsible for = preeclamptic ↑ in BP

h) Intestinal motility - Enterochromaffin cell = ↑ peristalsis + reflux

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Antagonist ⇒ Anti + Agonist ⇒ inhibit activity of agonist

→ Cyproheptadin

action - 1) Primary action = 5HT-2A receptor

2) Additional activity = H1 Antihistaminic, Anticholinergic, sedative

3) It ↑ appetite = used in children & poor eater = ↑ weigh

4) Side effect = drowsiness, dry mouth, weight gain, confusion

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→ ~~Ketanserin~~ = Selective $5HT_2$ receptor blocking activity

- Antagonize 5HT induced activity =

↓ Vaso constriction, platelet aggrn ↓

Contraction of airway and smooth muscles

X

→ Clozapine - action - weak dopaminergic activity

- Atypical antipsychotic = block $5HT_2$

→ Ondansetron - Prototypical selective = $5HT_3$ antagonist

- Effectively control = nausea ; vomitting (cytotoxic + radiography)

X X

- anticancer drg induced.

X