

Medicinal Chemistry - II

Unit - I

[DEPTH OF BIOLOGY]

Antihistaminic Agents.



Histamine

Tissue

amine

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Allergen

Human
(Allergy)

Allergy $\rightarrow$ Abnormal response
of our Immune system towards
Certain Allergen (pollen).

Allergen / Antigen

Indoor
Outdoor

eg $\rightarrow$ drug

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Histamine Receptor $\Rightarrow$ H_1 , H_2 , H_3 , H_4

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Allergen
(from Indoor/outdoor)

Enter into
Blood stream

B-cell.

IgE
Antibodies

(Antibodies)

[Mast Cell]

Histamine (granule form).

Antigen compete with
Antibodies
↓
& then Antigen rupture
the Cell memb.

Antigen

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[running nose
watery eyes]

Allergy
rxn.
start.

Released Histamine

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[DEPTH OF BIOLOGY]

[DEPTH OF BIOLOGY]

Storage of Histamine

⇒ Stored in Mast Cell (Granule form)

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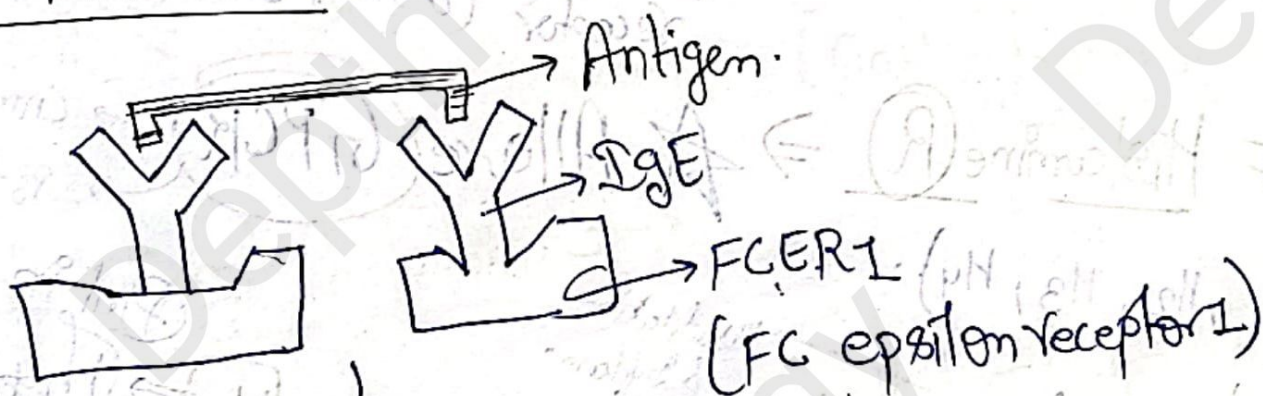
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Inactive Complex of (Histamine & Heparin)

Release of Histamine

⇒ How?

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This is the type of High affinity IgE.

Activate Tyrosine Protein Kinase.

(Antibody & Antigen strong binding with the Help of (FCεR1)).

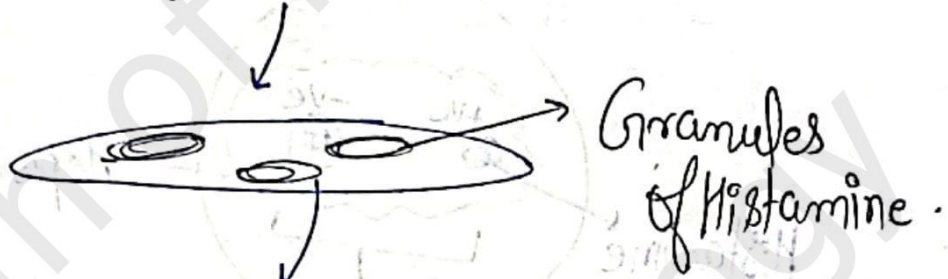
PIP₂ (DAG).

IP₃

Activation of Phospholipase C

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Release
Trigger (start) the Ca^{2+} .



Entry of Nat Ion.

Histamine release

Histamine
receptor (& bind with the R).

Histamine (R) $\Rightarrow$ All are GPCR. $\rightarrow$ CAMP Pathway. $\rightarrow$ IP3-DAG

(H_1 , H_2 , H_3 , H_4):

Ant in blood Vessel, Heart, CNS, Brain (H_1) $\rightarrow$ Vasodilation & Inflamm. $\rightarrow$ IP3-DAG pathway follows.

Ant in Thymus Hemopoietic Cell (Inflamm., Allergies). (H_4)

Histamine

Heart force of contrac.

H_2

Ant in Heart Smooth Muscle, [PARIETAL CELL]

Vasodilation Gastric acid & HCl secretion.

[CAMP PATHWAY] increase

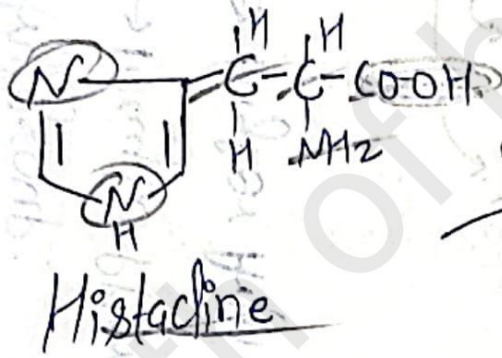
H_3

Ant in CoNS, PNS Heart, Lung.

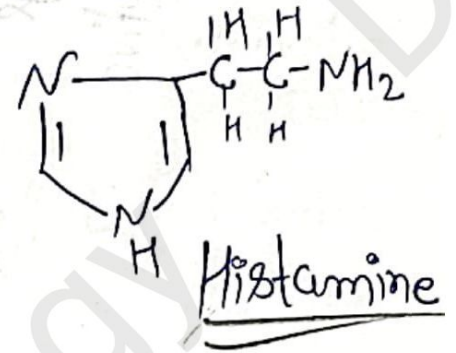
Inhibition of Histamine

Biosyn of Histamine

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Decarbox[•]
-CO₂



★ Anti-Histamine ⇒ (a) Receptor block.



(H₁, H₂ Antagonist)
(Gastric Proton Pump Inhibitor)

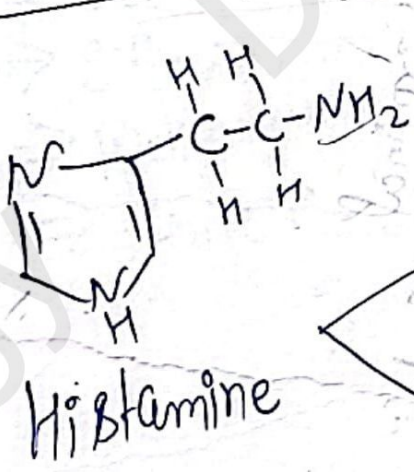
(b) Enzyme Inhibition ⇒

~~Phospholipase C~~ ~~DAH~~

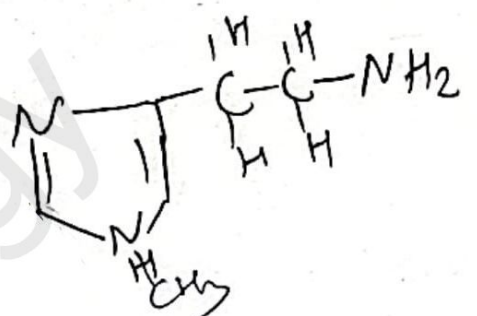
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Metabolism of Histamine →

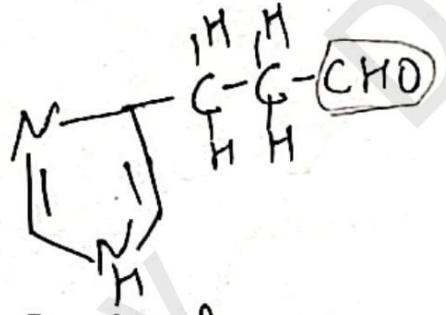
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Histamine N-Methyltransferase



Diamine Oxidase (DAO)



Imidazole Acetaldehyde

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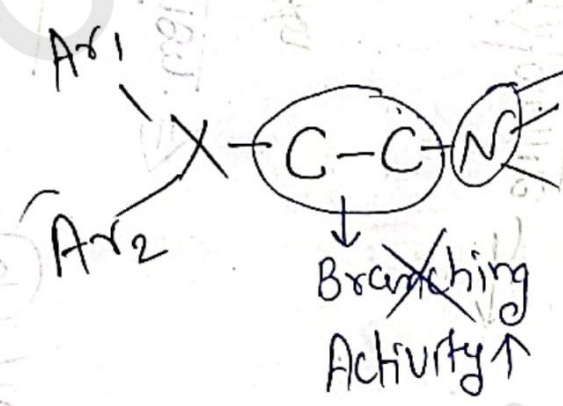
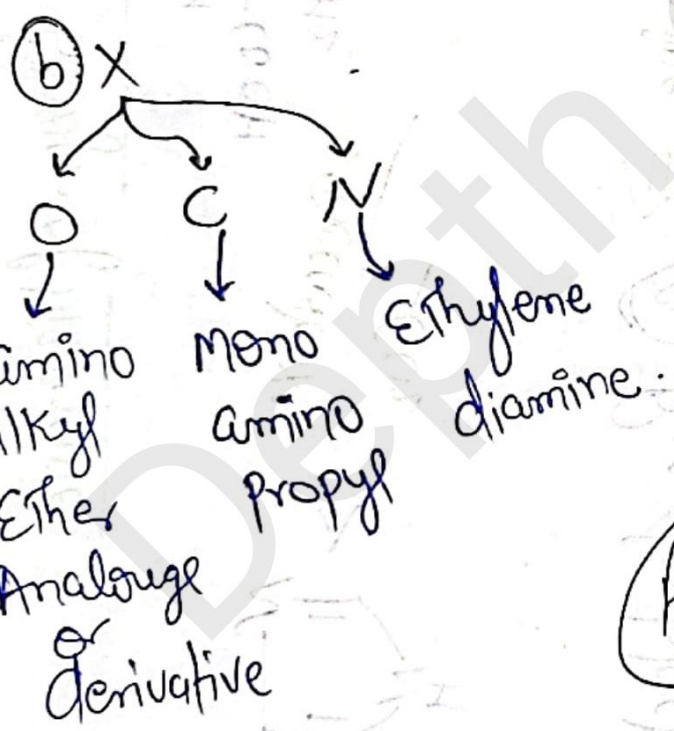
S.A.R

① Aryl group.

Ar₁ → may be Phenyl & Heteroatom

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Ar₂ → Aryl or Aryl Methyl.



Terminal Nitrogen atom
If Nitrogen contain 3° Amine
It's Activity ↑
[3° > 2° > 1°]

Ar₁ & Ar₂
essential for the activity.

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