PARASYMPATHOMIMETIC DRUGS

OR

CHOLINERGIC DRUGS

OR

CHOLINOMIMETIC DRUGS

OR

CHOLINOCEPTOR ACTIVATING DRUGS

DEFINITION

These are the group of drugs which produce effects resembling those produced by the stimulation of parasympathetic autonomic nervous system on the target organs

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- Neurotransmitter
- Two types of activities
  - Muscarinic
  - Nicotinic

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SYNTHESIS, STORAGE, RELEASE & INACTIVATION

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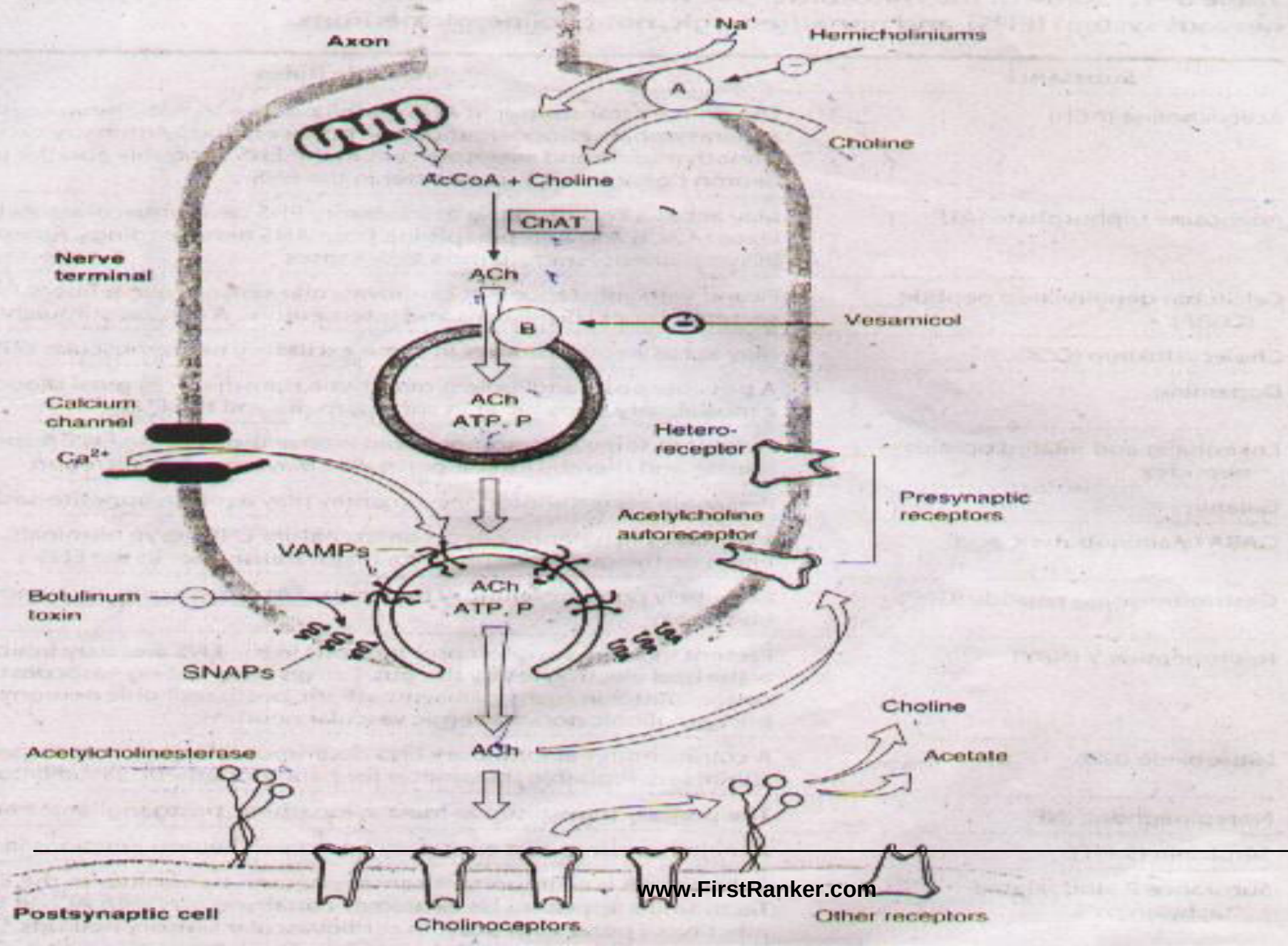

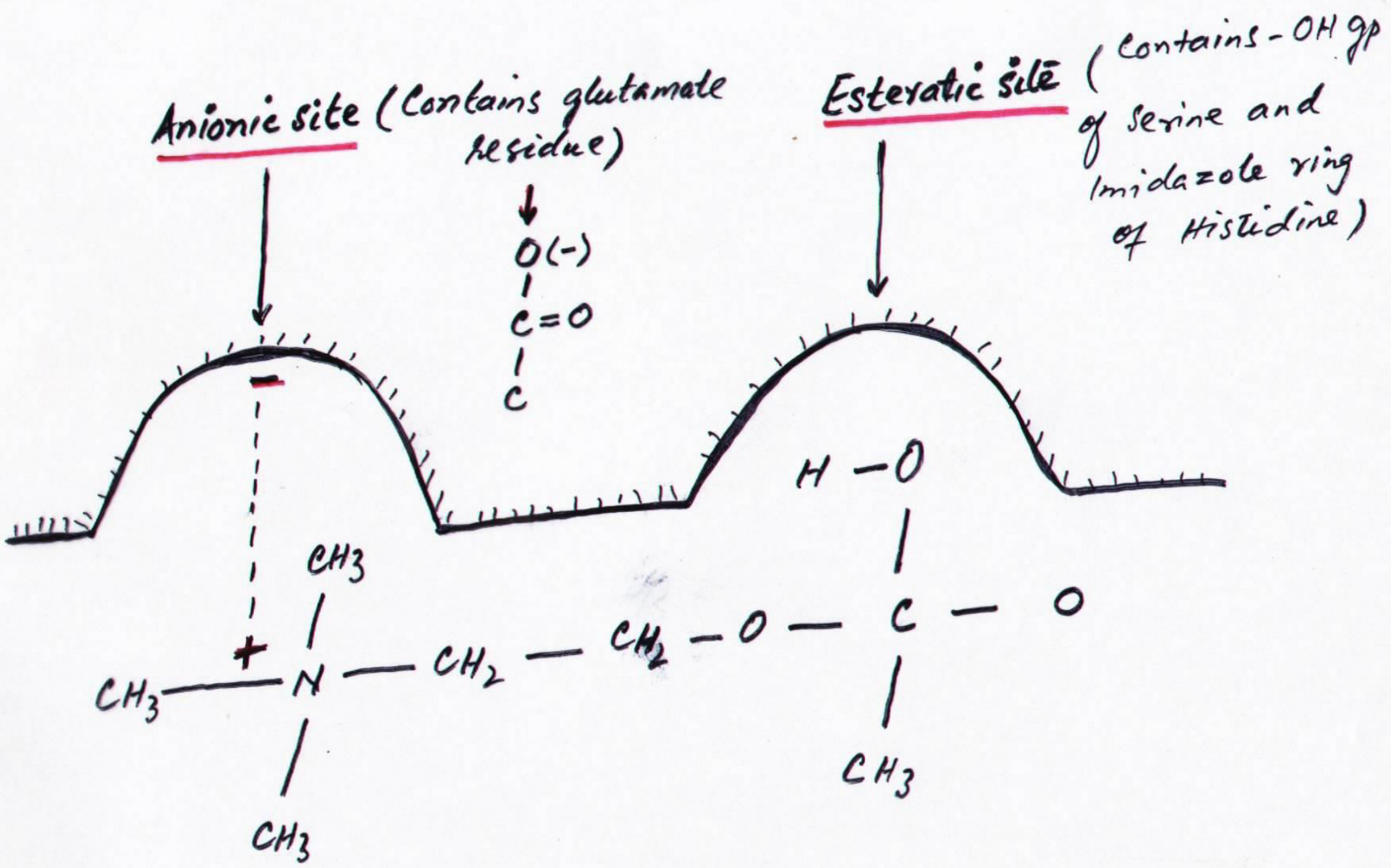

INTERACTION OF ACETYL CHOLINE AND THE EZYME CHOLINESTERASE RESPONSIBLE FOR ITS HYDROLYSIS AND INACTIVATION.

MECHANISM OF ACTION

G –protein linked (Muscarinic)

Ion channel (Nicotinic)

PHOSPHO – INOSITOL SYSTEM

BINDING OF DRUG WITH RECEPTOR
(ALPHA-1 ADRENDERGIC, MUSCARINIC- CHOLINERGIC)

ACTIVATION OF PHOSPHOLIPASE-C

PHOSPHATIDYL INOSITOL 4-5 BIPHOSPHATE

DIACYL GLYCEROL
(CONFINEDTO MEMBRANE)

ACTIVATION OF PROTEIN KINASEC
INTRACELLULAR

ENTRY OF Ca++ THROUGH THE CA++

CHANNEL

INOSITOL 1.4.5 TRIPHOSPHATE
(DIFFUSES INTO CYTOSOL)

RELEASE OF Ca++ FROM
SOURCES

FORMATION OF Ca++ CALMODULI
COMPLEX

ALTERATION IN THE ACTIVITY OF C
DEPENDENT ENZYMES

EFFECT

CHOLINERGIC RECEPTORS

Muscarinic

M1 = Nerves, Stomach, Brain

Antagonist: Pirenzepine

M2 = Heart, Nerves, Smooth Muscle.

Antagonist: Gallamine

M3 = Glands, Endothelium, Smooth Muscle.

M_4 and M_5 newly discovered, role not yet known

Nicotinic

Neuromuscular Junction

Agonist: Phenyl Trimethyl Ammonium

Antagonist: Tubocurarine

Autonomic Ganglia, Adrenal Medulla

Agonist: Dimethyl phenyl piperazinium

Antagonist: Hexamethonium

CLASSICIFICATION

A. Directly Acting

B. Indirectly Acting

A. Directly Acting Cholinergic Drugs :

I. Choline Esters

Acetylcholine

Carbachol

Methacholine

Bethanechol

II. Cholinomimetic Alkaloids

a. Mainly Muscarinic Agonists

Natural Alkaloids:

Muscarine
Pilocarpine
Arecholine

Synthetic Alkaloid:

Oxotramorine

b. Mainly Nicotinic Agonists

Natural Alkaloids:

Nicotine
Lobeline

Synthetic Alkaloids:

Dimethyiphenyipiperazinium(DMPP)

B. Indirectly Acting Cholinergic Drugs (Anticholinesterases)

I- Reversible

a. Carbamates

b. Alcohols

II- Irreversible

I- Reversible

a. Carbamates

Tertiary amines

Physostigmine

Quaternary Ammonium compounds

Neostigmine

Pyridostigmine

Distigmine

Ambenonium

Demecarium

b. Alcohols

Edrophonium

c. Miscellaneous

Tacrine

Donepezil

Galantamine

Rivastigmine

II. Irreversible Anticholinesterases (Organophosphorus Compounds)

1) Therapeutically useful:
   Ecothiophate

2) War Gases:
   Sarin
   Tuban,
   Soman

3) Insecticides:-
   Parathion
   Malathion
   Diisopropyl Flurophosphate (DFP)
   Tetramethyl Pyrophosphate (TMPP)
   Octamethyl Pyrophosphotetraamide (OMPA)

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ACETYLCHOLINE

NOT USED AS A DRUG

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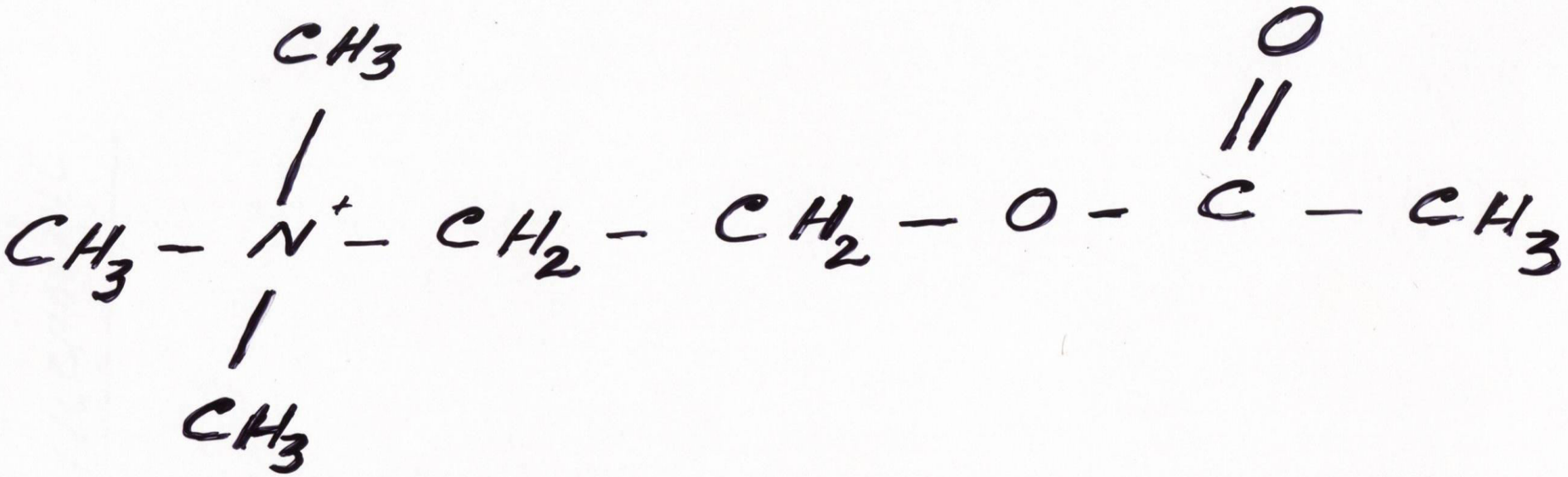
CHEMISTRY



ACETYLCHOLINE.

PHARMACOKINETICS

- Acetylcholine & other Choline esters have a permanently charged **quaternary ammonium group** in their structure
- All are **hydrolysed in the GIT**
- The tertiary natural cholinomimetic alkaloids (pilocarpine, nicotine, lobeline) are well absorbed from most sites of adm. Muscarine, a quaternary amine is less completely absorbed from the GIT and is toxic too.
- **Excretion** mainly by the kidneys

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Pharmacological Actions/ Organ system effects:

Muscarinic Actions

Nicotinic Actions

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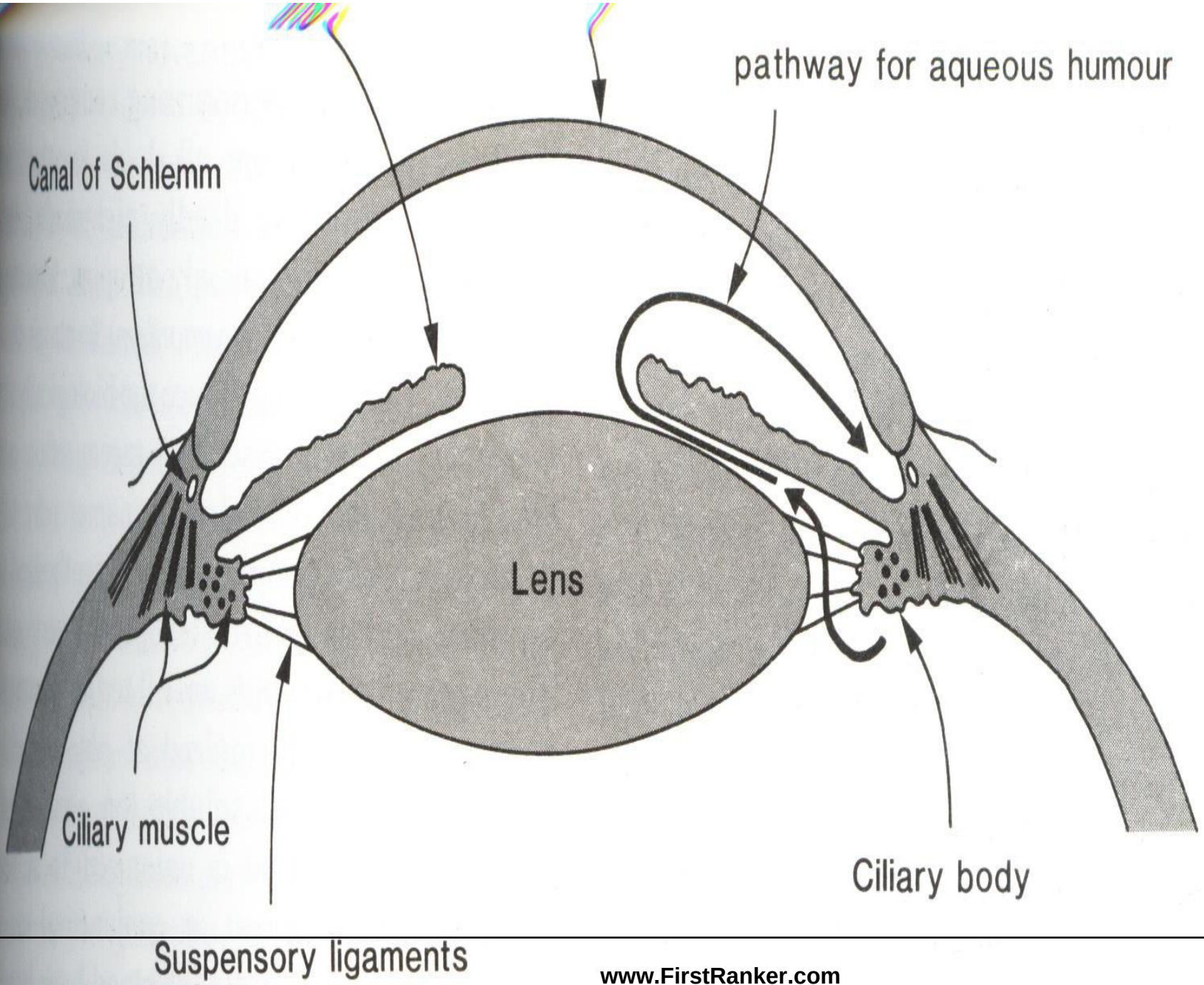
EYE:

- Miosis (constriction of pupil).
- Spasm of accommodation
- Decrease in intraocular pressure.
- Conjunctival hyperaemia
- Lacrimation



CVS (Heart & B.V)

Respiratory system

Gastro intestinal tract

Urinary bladder

Exocrine glands

Central Nervous System

Peripheral nervous system

N.M .Junction

CARBACHOL

- Ester of carbamic acid
- Has both muscarinic and nicotinic actions
- Muscarinic actions are prominent on eye, GIT & urinary bladder
- DOA more than 30 min

- Therapeutic uses:

Glaucoma

METHACHOLINE

- Has methyl group in its structure
- Has both muscarinic and nicotinic actions (very mild nicotinic actions)
- Muscarinic actions are prominent on CVS
- Longer DOA as compared to ACh
- Therapeutic uses: given SC for the relief of paroxysmal atrial tachycardia

BETHANECHOL

- Structure related to Ach, acetate is replaced by carbamate & choline is methylated
- Has no nicotinic actions
- Muscarinic actions are prominent on eye, GIT & urinary bladder
- Prolonged DOA
- Therapeutic uses:
  - Post operative Gastric distension
  - Paralytic ileus
  - Bladder atonia

MUSCARINE

- Quaternary amine (*Amanita muscaria*)
- Less complete absorption from the GIT
- Very toxic & can even enter the brain
- Rx : Atropine

PILOCARPINE

- Tertiary amine (Pilocarpus jaborandi leaves)
- Has muscarinic actions
- Therapeutic uses:
  - Glaucoma
  - To reduce the effect of mydriatics
  - To break adhesions

Not used for systemic diseases → increased tracheobronchial secretions leading to pulmonary oedema

NICOTINE & LOBELINE

- Plant derivatives
- Actions are mainly on nicotinic receptors (CNS, PNS, NMJ)
- CNS, have important effects on brainstem and cortex.
- PNS – autonomic ganglia.
- NMJ, immediate depolarization of the end plate – increase in permeability to Na and K ions.