PHARMACOLOGY - I

UNIT 2 NOTES

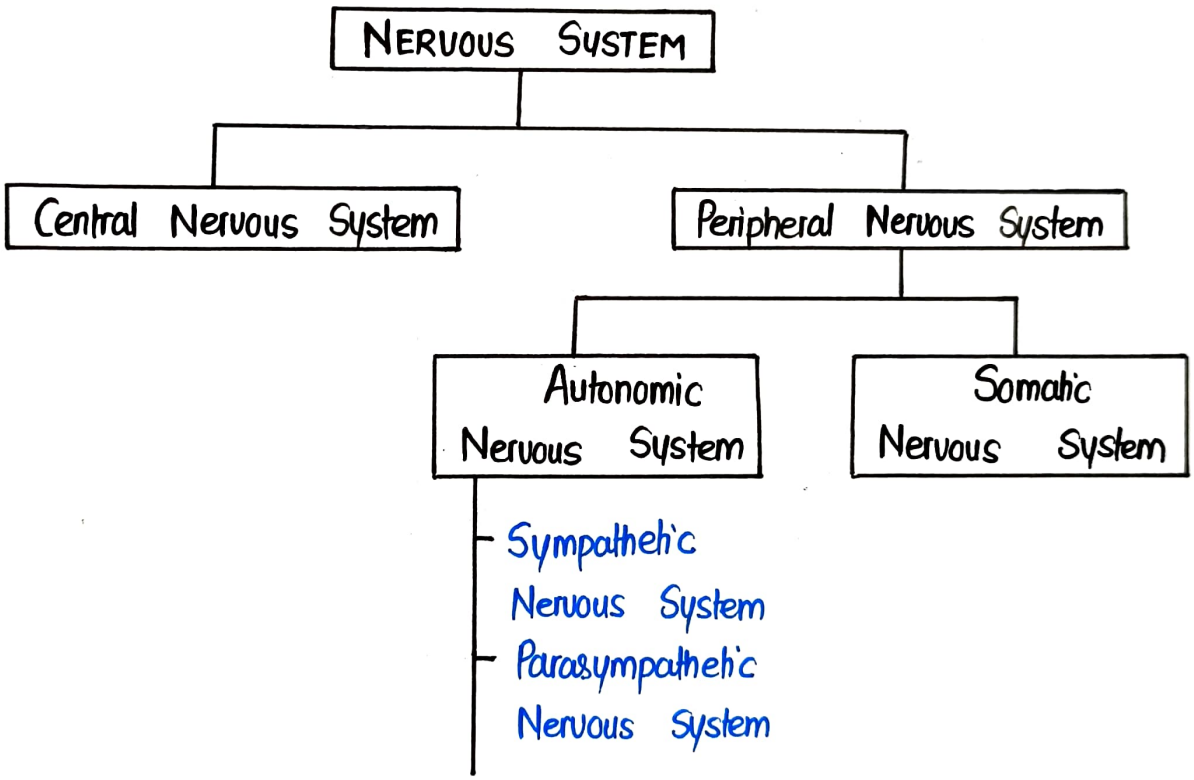
DRUGS ACTING ON PNS

- SYMPATHETIC/PARASYMPATHETIC
- SKELETAL MUSCLE RELAXANTS
- LOCAL ANAESTHETIC
- MYASTHENIA GRAVIS
- GLAUCOMA

IMPERFECT PHARMACY

DRUGS ACTING ON ANS

Drugs acting on the Autonomic Nervous System (ANS) are medications that affect the functions of Sympathetic & Parasympathetic branches of ANS, which control involuntary body functions like heart rate, digestion, respiratory rate, pupil size & glandular activity.



Difference B/w Functions Of Sympathetic & Parasym. N.S.

Organs	Sympathetic	Parasympathetic
Heart	Heart Rate ↑	Heart Rate ↓
Bronchus	Bronchodilation	Bronchoconstriction
GIT	Inhibits Digestion	Stimulate Digestion
Bladder	Relaxes Bladder	Contracts Bladder
Pupil	Dilates (Mydriasis)	Constricts (Miosis)
Glands	↓ Secretion	↑ Secretion

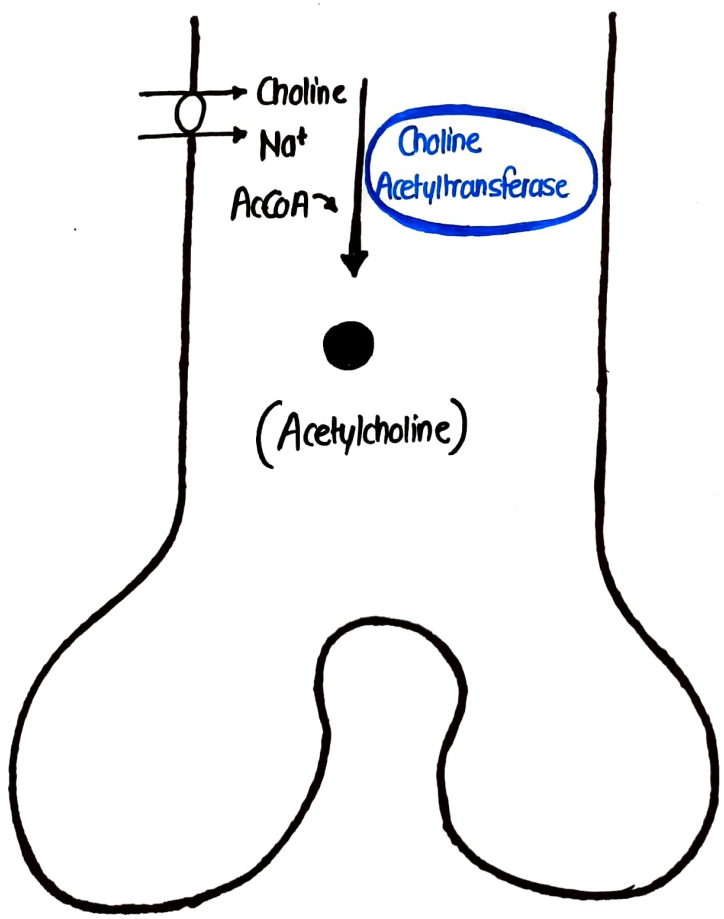
NEUROHUMORAL TRANSMISSION

- Neurohumoral Transmission refers to the process by which nerve cells (neurons) communicate with each other or with effector organs (like muscles or organs) through the release of chemical messengers known as Neurotransmitters.
- It involves following steps :

① SYNTHESIS OF NEUROTRANSMITTER

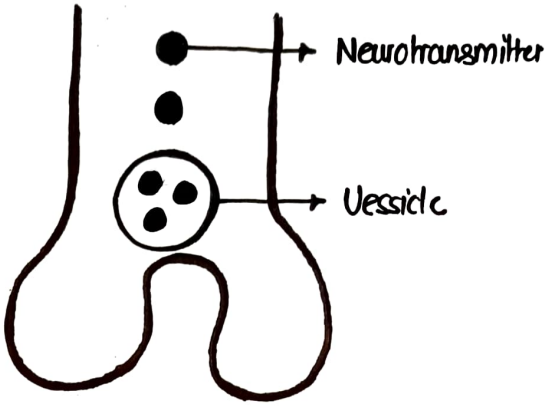
Neurotransmitters are synthesized in the neuron, either in cell body or nerve terminal

Example : Acetylcholine is synthesized from choline & acetyl Co-A by the enzyme choline acetyltransferase



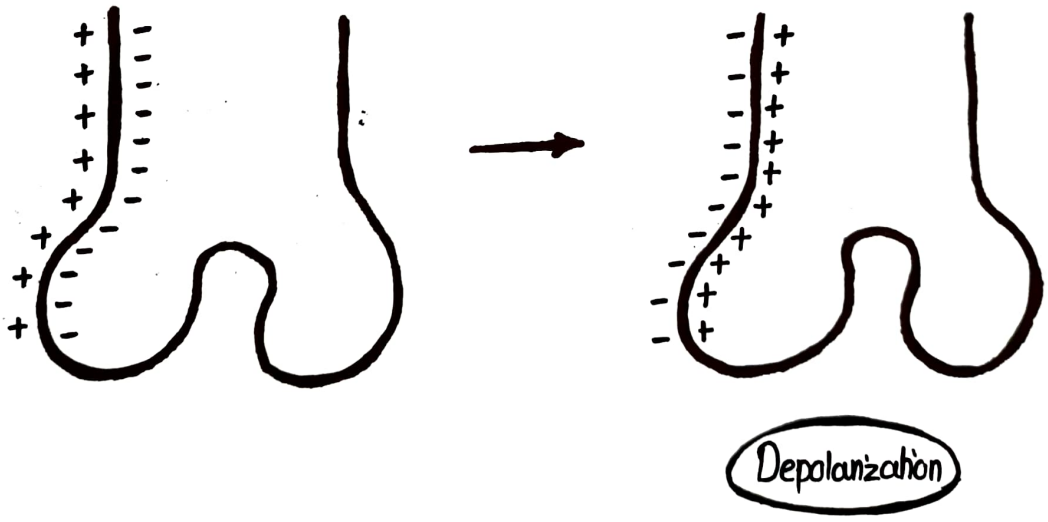
② STORAGE IN VESSICLES

Once synthesized, neurotransmitters are stored in synaptic vessicles in the nerve terminal, ready for release.



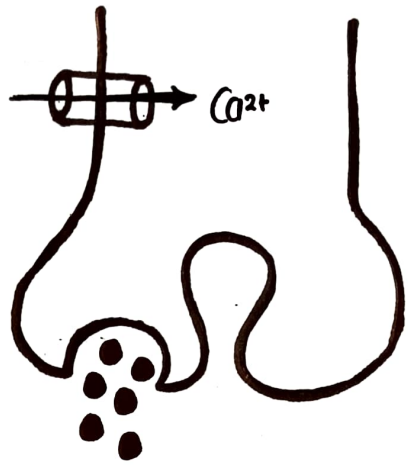
③ NERVE IMPULSE (ACTION POTENTIAL)

When a nerve impulse reaches the nerve terminal it cause depolarisation of membrane



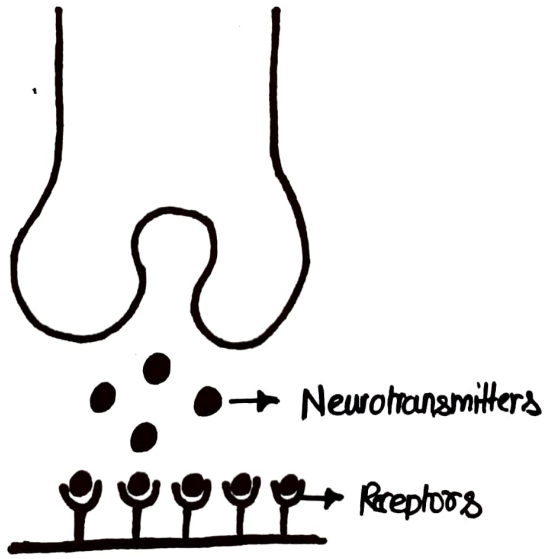
④ Ca^{2+} Influx & Release Of Neurotransmitters

- Depolarisation opens voltage gated calcium channels, allowing Ca^{2+} to enter the neuron
- The increase in Ca^{2+} causes synaptic vessicles to fuse with the membrane & release neurotransmitters into the synaptic cleft.



⑤ Receptor Binding

Neurotransmitter bind to specific receptors on the post synaptic membrane (another neuron, muscle or gland)



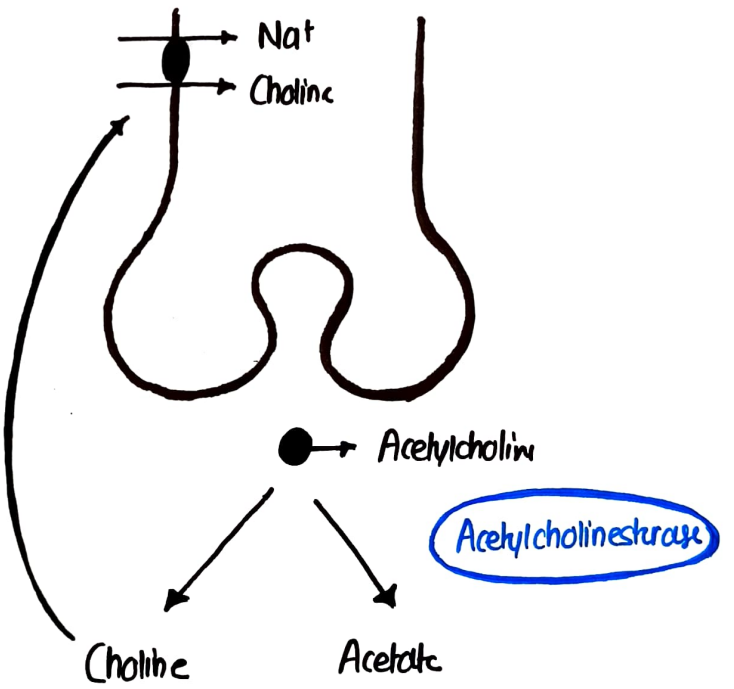
⑥ Post Synaptic Response

- Binding of neurotransmitter to its receptor initiate a response in the target cell (e.g. muscle contraction, gland secretion, another nerve impulse)

⑦ Termination Of Action

After the action has been completed, the neurotransmitter is removed from synaptic cleft either by:

- Enzymatic degradation
- Reuptake into presynaptic neuron



① SYMPATHETIC NERVOUS SYSTEM

- It is known as "Fight or Flight" system.
- This system prepares the body to face stressful or emergency situations.

KEY FUNCTIONS

- Increases Heart Rate
- Dilates Bronchi (Improves Airflow)
- Dilates Pupil (Mydriasis)
- Inhibits Digestion
- Inhibits Salivation
- Stimulates Glucose release from Liver
- Relaxes Bladder (Urine retention)
- Causes vasoconstriction (raises BP)
- stimulates sweating

NEUROTRANSMITTERS

- Preganglionic : Acetylcholine (ACH)
- Post Ganglionic : Norepinephrine or Epinephrine

ADRENERGIC NEUROTRANSMITTERS

- Adrenergic Neurotransmitters are chemical messengers released by Adrenergic Neurons, which primarily act on adrenergic receptors (alpha & beta receptors) in the Sympathetic Nervous System.
- These neurotransmitters are involved in "Fight or Flight" responses like increasing heart rate, blood pressure & energy availibility.
- They are also known as Catecholamines.
- The three main adrenergic neurotransmitters are:

① Dopamine
② Norepinephrine
③ Epinephrine

① DOPAMINE

- It is the first catecholamine in the synthesis chain.
- It acts on dopaminergic receptors (D_1, D_2).
- It has mild action on β_1 & α_1 receptors at higher doses.
- It plays important role in renal vasodilation, CNS functions (mood, movement) & precursor to norepinephrine.

② NOR- EPINEPHRINE

- They are also known as Noradrenaline.
- It is the primary neurotransmitter released by sympathetic postganglionic neurons.
- It acts mainly on α_1, α_2 & β_1 receptors.
- Primary functions include:
  - Increases heart rate & contractility. (β_1)
  - Vasoconstriction (α_1) - increases BP.

③ EPINEPHRINE

- It is also known as Adrenaline.
- It acts on α_1, α_2 β_1 & β_2 receptors.
- Functions :

- Increases Heart Rate & Cardiac Output (β_1)
- Bronchodilation (β_2)
- Vasoconstriction (α_1) & vasodilation in skeletal muscles (β_2)
- Raises blood glucose levels (stimulates glycogenolysis)

BIOSYNTHESIS OF CATECHOLAMINES

Phenylalanine

↓ Phenylalanine Hydroxylase

Tyrosine

↓ Tyrosine Hydroxylase

DOPA

↓ Dopa Decarboxylase

Dopamine

↓ Dopamine Hydroxylase

Nor- Epinephrine

↓ N- Methyl transferase

Epinephrine

STEPS

- First Phenyalanine is converted into Tyrosine by the enzyme 'Phenylalanine Hydroxylase'
- Tyrosine is converted into DOPA by the enzyme 'tyrosine hydroxylase'
- DOPA is then converted to Dopamine by the enzyme 'DOPA decarboxylase'
- Dopamine is then converted to Norepinephrine by the enzyme 'Dopamine β- hydroxylase'
- Nor- Epinephrine is then finally converted to Epinephrine by the enzyme 'N- methyl transferase'.

CATABOLISM OF CATECHOLAMINES

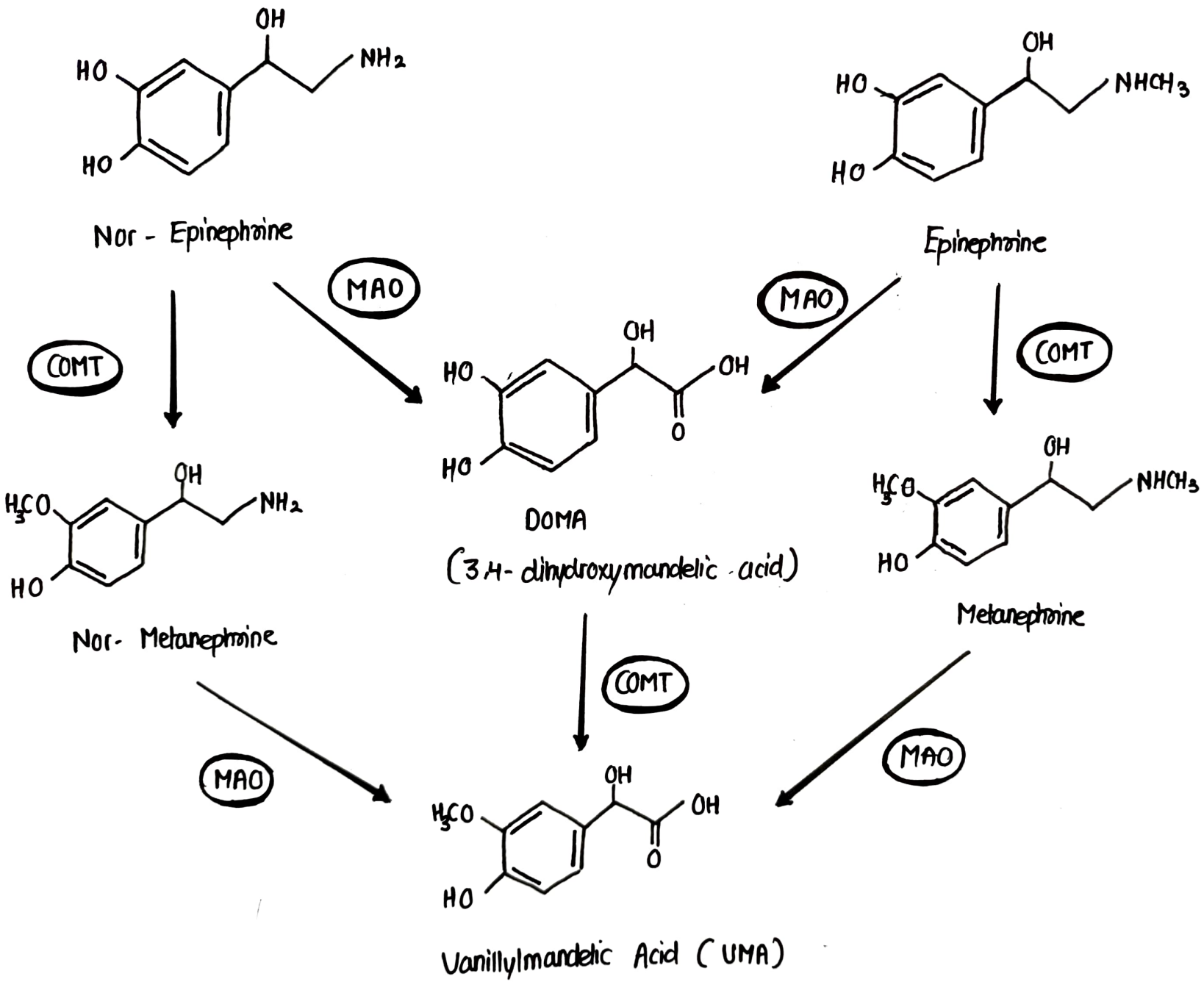
- Catabolism of catecholamines refers to breakdown or degradation of catecholamines like Dopamine, Norepinephrine and Epinephrine after they have performed their functions in body.
- This breakdown is mainly done by two enzymes:

① Monoamino Oxidase (MAO)

- Found in almost all body tissues.
- It breaks down catecholamines by removing the amine ($-NH_2$) group.

② Catechol - O- Methyltransferase (COMT)

- Found in Liver & kidneys.
- Adds a methyl group to catechol ring.


OH
HO
NH2
HO
Nor - Epinephrine
OH
HO
NHCH3
HO
Epinephrine
MAO
MAO
COMT
COMT
OH
HO
OH
O
HO
DOMA
(3,4- dihydroxymandelic acid)
OH
H3CO
NH2
HO
Nor- Metanephrine
OH
H3CO
NHCH3
HO
Metanephrine
COMT
MAO
MAO
OH
H3CO
OH
O
HO
Vanillylmandelic Acid (VMA)

ADRENERGIC RECEPTORS

- Adrenergic Receptors are class of G-Protein-Coupled Receptors (GPCRs) that are targeted by the catecholamines i.e. norepinephrine and Epinephrine.
- These receptors mediate the physiological response of sympathatic nervous system & are involved in wide range of processes including heart rate regulation, smooth muscle contraction or relaxation etc.

TYPES OF ADRENERGIC RECEPTORS

Adrenergic Receptors are broadly classified into two main types:

① Alpha (α) adrenergic receptors
② Beta (β) adrenergic receptors

① α Adrenergic Receptors

- They are mainly responsible for smooth muscle contraction & vasoconstriction.
- They are of two types

(a) α_1 Receptors
(b) α_2 Receptors

② β Adrenergic Receptors

- They usually cause smooth muscle relaxation & increases heart activity.
- They are of 3 types:

(a) β_1 Receptors
(b) β_2 Receptors
(c) β_3 Receptors

Distribution & Functions Of Adrenergic Receptors

Receptor	Location	Functions
α_1	Blood Vessels, Iris, Bladder Liver	Vasoconstriction, Mydriasis Urinary Retention
α_2	Presynaptic Terminals, Pancreas, Platelets CNS	Inhibits NE ↓ Insulin ↓ BP
β_1	Heart, kidney	↑ HR, ↑ Contractility ↑ renin
β_2	Lungs, Uterus, Blood Vessels Liver	Bronchodilation, Vasodilation Tocolysis, Glycogenolysis
β_3	Adipose Tissue, Bladder	Thermogenesis, Bladder Relaxation

SYMPATHOMIMETIC AGENTS

- Sympathomimetic Agents are drugs or substances that mimic the effects of the sympathetic nervous system by stimulating adrenergic receptors (α & β receptors)
- They either directly activate these receptors or increase the levels of natural neurotransmitters like norepinephrine or epinephrine.

SYMPATHOMIMETIC AGENTS

Direct Acting

- Norepinephrine
- Epinephrine
- Phenylphrine*
- Dopamine
- Methyldopa
- Clonidine
- Dobutamine
- Isoproterenol
- Terbutaline
- Salbutamol*
- Bitolterol
- Naphazoline
- Oxymetazoline
- Xylometazoline

Indirect Acting

- Hydroxyamphetamine
- Pseudoephedrine
- Propylhexedrine

Mixed Acting

- Ephedrine
- Metaraminol

① Direct Acting Sympathomimetic Agents

These are those agents that directly stimulate adrenergic receptors by mimicking the action of epinephrine / nor-epinephrine.

Mechanism Of Action

Direct-acting sympathomimetics bind directly to adrenergic receptors & mimic the effect of sympathetic nervous system activation.

- α_1 : Vasoconstriction, Pupil dilation
- α_2 : ↓ Blood Pressure
- β_1 : ↑ Heart Rate & Contractility
- β_2 : Bronchodilation, Uterine Relaxation

Examples

- Epinephrine : $\alpha_1, \alpha_2, \beta_1, \beta_2$
- Nor-Epinephrine : $\alpha_1, \alpha_2, \beta_1$
- Phenylephrine : α_1 selective
- Dobutamine : β_1 selective

PHARMACOKINETICS

- Absorption : Catecholamines (e.g. epinephrine) are poorly absorbed orally, some (e.g. albuterol) are effective via inhalation or orally.
- Distribution : Varies : lipophilic agents can cross tissues well.
- Metabolism : Metabolised mainly by MAO & COMT.
- Excretion : Excreted as inactive metabolites in urine

Uses

- Cardiac Arrest
- Acute Hypotension
- Heart Failure
- Bronchial Asthama / COPD
- Nasal Decongestion

Adverse Effect

- Hypertension
- Tachycardia
- Hyperglycemia
- Insomnia
- Anxiety

② Indirect Acting Sympathomimetic Agents

MOA

Indirect acting sympathomimetics do not bind directly to adrenergic receptors, instead, they increase the levels of catecholamines at synaptic cleft by:

- Stimulating release of norepinephrine from presynaptic nerve terminals
- Inhibiting reuptake of norepinephrine, epinephrine
- Inhibiting its breakdown by enzymes like MAO or COMT.

Pharmacokinetics

- Absorption: Many are well absorbed orally
- Distribution: Lipophilic agents can cross the blood-brain barrier causing CNS effects.
- Metabolism: Metabolised in liver by various pathways (MAO, CYP450 enzymes).
- Excretion: Excreted mainly via urine

Uses

- Miosis
- Allergic Rhinitis
- Local Vasoconstriction

Adverse Effect

- Insomnia
- Anxiety
- Seizures
- Hypertension

Examples

- Hydroxyamphetamine
- Pseudoephedrine
- Propylhexedrine

③ Mixed Acting Sympathomimetic Agents

MOA

Mixed acting parasympathomimetic agents act by :

- Directly stimulating adrenergic receptors.
- Promoting the release of endogenous catecholamines.

Example

- Ephedrine
- Metaraminol

PHARMACOKINETICS

- Absorption : Well absorbed orally
- Distribution : Crosses blood brain barrier
- Metabolism : Partially metabolized in liver
- Excretion : Excreted unchanged in urine.

Uses

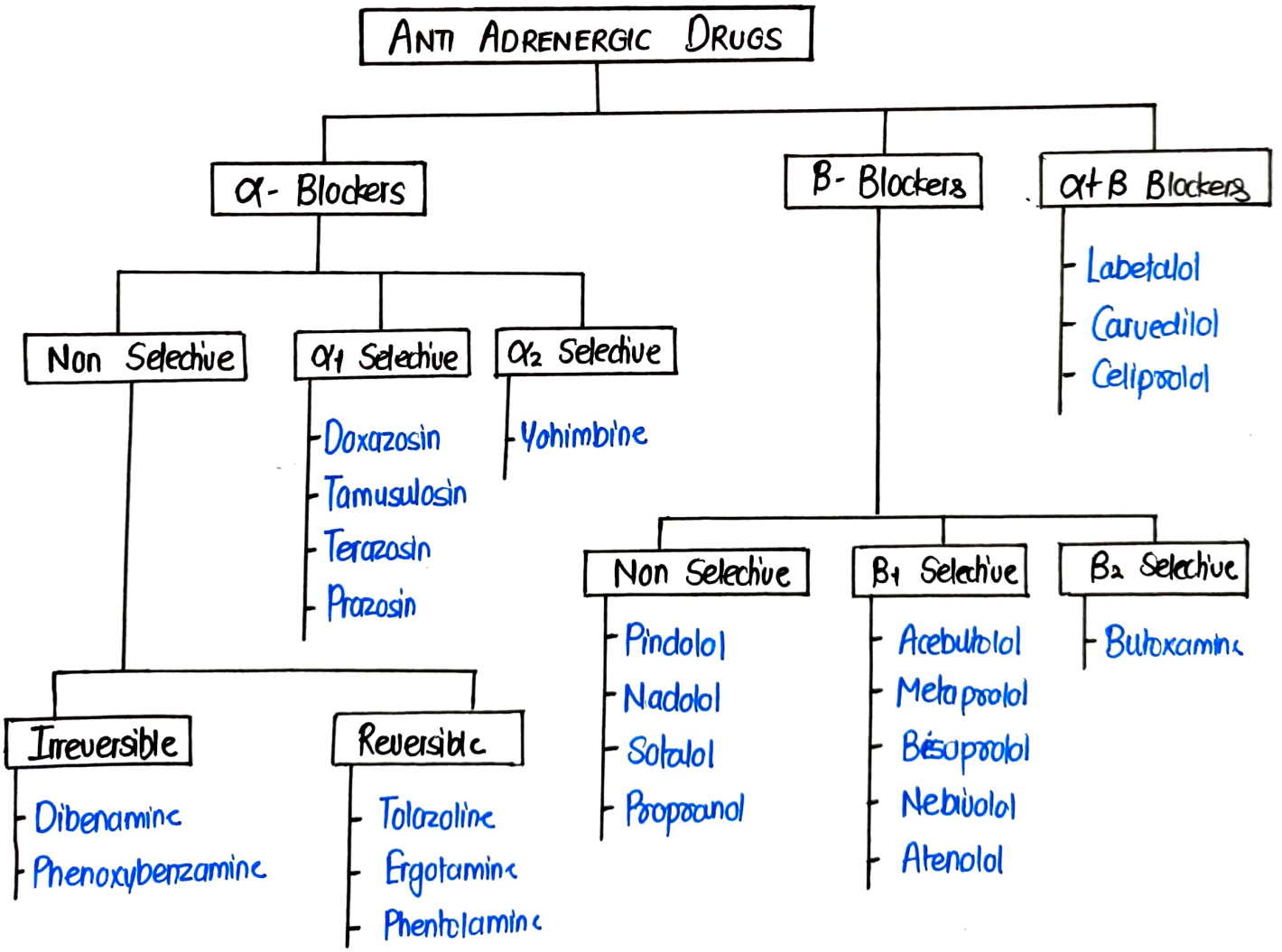
- Hypotension
- Nasal Congestion
- Bronchial Asthama
- Mild CNS stimulation

Adverse Effect

- Hypertension
- Tachycardia
- Nausea
- Vomiting

SYMPATHOLYTICS

- They are also known as :
  - Adrenergic Antagonist
  - Adrenergic Blocking Agents
  - Antiadrenergic Drugs
- These are the drugs that block the effect of adrenaline & noradrenaline on adrenergic receptors in body.
- They work by binding to adrenergic receptors without activating them thus preventing stimulation by body's natural catecholamines.



① α Blockers

MOA

Alpha blockers inhibits alpha adrenergic receptors by binding to them, thus preventing the action of endogenous catecholamines.

Types

They are of following types:

① α_1 Blockers
② α_2 Blockers
③ Non selective α Blockers

Pharmacokinetics

- Absorption : Most are well absorbed orally
- Distribution : Widely distributed, some cross the blood brain barrier
- Metabolism : Mostly metabolized in liver
- Excretion : Excreted via urine & feaces

Uses

- Hypertension
- Urinary Retention
- Migraine

Adverse Effect

- Hypotension
- Dizziness
- Fatigue
- Sexual Dysfunction

Example

- Doxazosin
- Prazosin etc.

② B- BLOCKERS

MOA

Beta Blockers block β- adrenergic receptors, preventing the effect of catecholamines

TYPES

① β_1 Selective
② β_2 Selective
③ Non Selective β Blockers

PHARMACOKINETICS

- Absorption : Generally well absorbed orally
- Distribution : Widely distributed, some cross blood brain barrier.
- Metabolism : Metabolised in liver
- Excretion : Excreted via feaces & urine.

USES

- Hypertension
- Angina
- Arrythmias
- Heart failure
- Glaucoma

Examples

- Propranol
- Sotalol
- Metoprolol
- Atenolol

Adverse Effect

- Bradycardia
- Hypotension, Fatigue, Depression

PARASYMPATHETIC SYSTEM

- The Parasympathetic Nervous System is part of Autonomic Nervous System.
- It's often called the 'rest & digest' system because it slows down the heart rate, increases digestion & promotes activities that occurs when body is at rest.

KEY FUNCTIONS

- Slows Heart Rate
- Stimulates Digestion
- Promotes Gland Secretion
- Constricts Pupils
- Contracts the bladder
- Stimulates sexual arousal
- Constricts bronchi

Note: Parasympathetic System is also known as 'Cholinergic System'

CHOLINERGIC NEUROTRANSMITTERS

- A Cholinergic Neurotransmitter is a chemical messenger that transmits signals across a synapse & bind to Cholinergic receptors on the target cell & produce a response.
- Acetylcholine is the major Cholinergic Neurotransmitter.

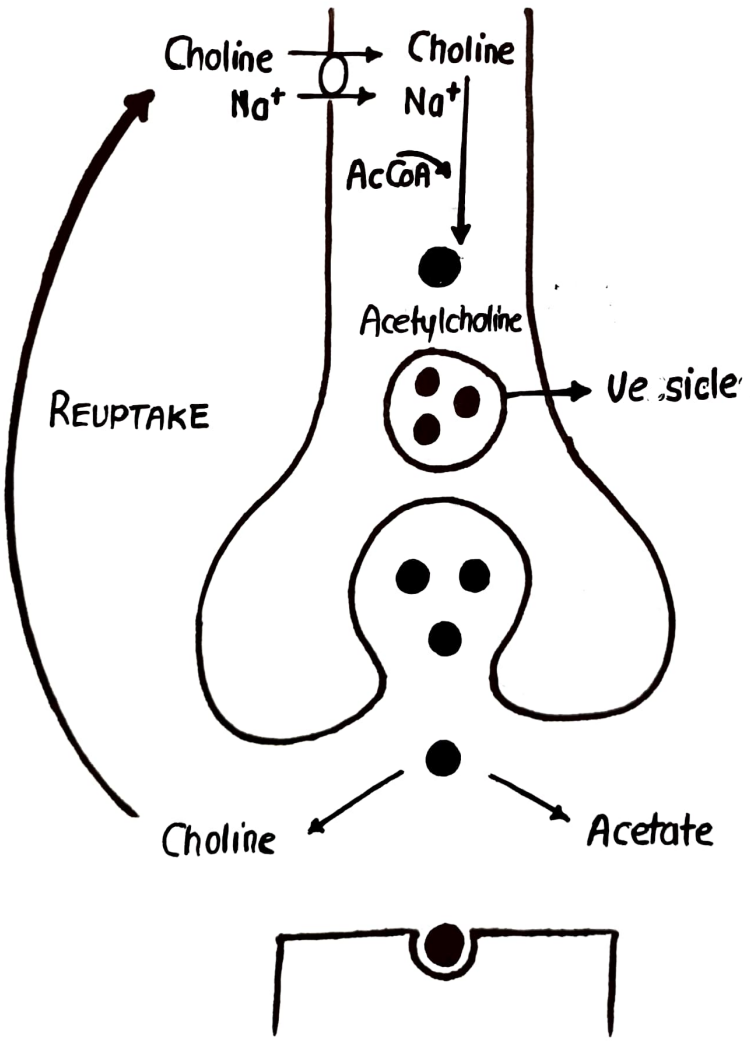
ACETYLCHOLINE

- Acetylcholine is the primary neurotransmitter in the Cholinergic System which is responsible for transmitting signals between nerve cells.
- It plays a crucial role in :
- Activating muscles (at neuromuscular junction)
- Regulating Involuntary body functions (like heat rate & digestion)
- Supporting brain functions (such as memory, attention & arousal in the Central Nervous System)

BIOSYNTHESIS OF ACETYLCHOLINE

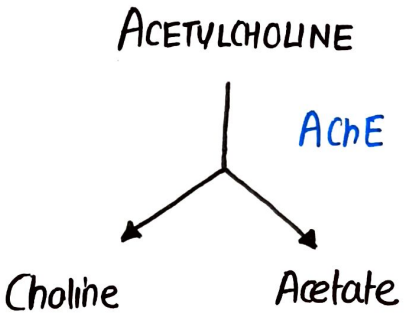
- Biosynthesis of Acetylcholine refers to the biological process by which the neurotransmitter Acetylcholine (ACh) is produced.
- It occurs mainly in the nerve terminals of Cholinergic Neurons.
- The reaction is catalyzed by the enzyme choline acetyltransferase (ChAT)
- Choline (obtained from the diet or recycled from ACh breakdown) combines with Acetyl-CoA (produced in the mitochondria) to form Acetylcholine.
- The reaction is :

$$\boxed{\text{Choline} + \text{Acetyl-CoA} \longrightarrow \text{Acetylcholine} + \text{CoA}}$$



CATABOLISM OF ACETYLCHOLINE

- Catabolism of Acetylcholine refers to the breakdown of Acetylcholine after it has carried out its function at a synapse.
- It mainly happens in the synaptic cleft & involves :
- The enzyme acetylcholinesterase (AChE) rapidly breaks down acetylcholine



- The choline is taken back into the neuron to be reused for making new acetylcholine.
- This breakdown occurs very fast (within miliseconds)

CHOLINERGIC RECEPTORS

- Cholinergic Receptors are specialized proteins located on the surface of cells (mainly neurons, muscles & glands) to which Acetylcholine bind & mediate its effect.
- Cholinergic Receptors are broadly classified into two types:

① Nicotinic Receptors
② Mascarinic Receptors

① MASCARINIC RECEPTORS

- It belongs to G- Protein couple receptors family.
- It is further divided into five subtypes:

(a) M_1 Receptors
(b) M_2 Receptors
(c) M_3 Receptors
(d) M_4 Receptors
(e) M_5 Receptors

② NICOTINIC RECEPTORS

- They are ligand gated ion channels.
- It is of further two types:

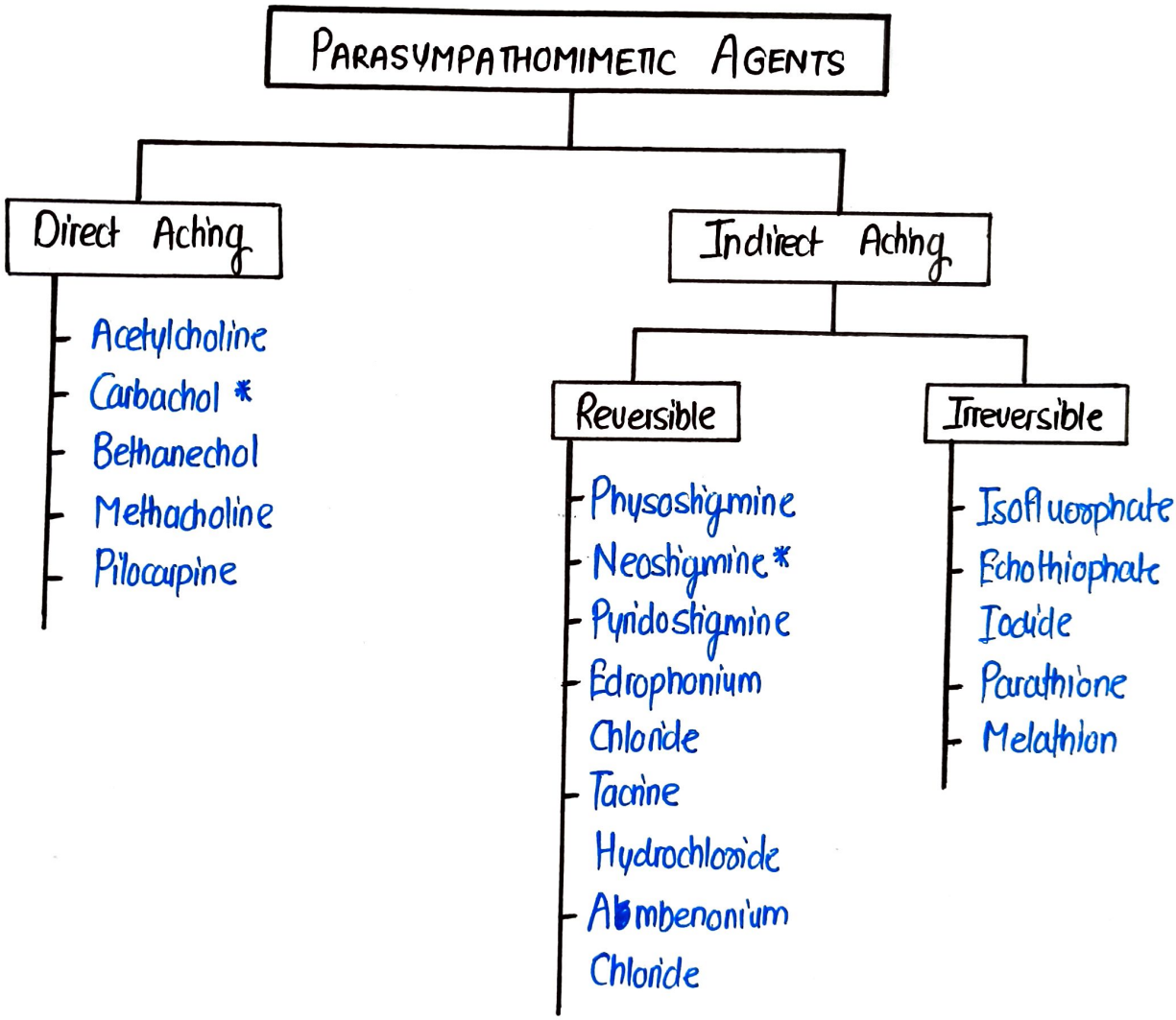
(a) N_M Receptors
(b) N_N Receptors

Distribution Of Cholinergic Receptors

Receptors	G-Protein	Distribution	Function
M_1	Gq	CNS, Autonomic Ganglia Gastric Parietal Cells	Memory Enhancement Gastric Acid Secretion Neuronal Excitation
M_2	Gi	Heart, CNS	Slows Heart Rate Decreases conduction ↓ Neurotransmitter release
M_3	Gq	Smooth Muscles, Exocrine Glands, Eye	Smooth Muscle Contraction, Gland Secretion (saliva tears), pupil constriction
M_4	Gi	CNS	Inhibits Neurotransmitter Release
M_5	Gq	CNS	May Modulate dopamine pathways.
N_N	Ion Channel (Na^+/K^+)	Autonomic Ganglia (Sympathetic & Parasympathetic) Adrenal Medulla	Postganglionic neuron activation, catecholamine release
N_M	Ion Channel (Na^+/K^+)	Skeletal Muscle Neuromuscular Junction	Skeletal Muscle Contraction

PARASYMPATHOMIMETIC AGENTS

Parasympathomimetic Agents are drugs that stimulate or mimic the effect of Parasympathetic Nervous System by either directly activating Cholinergic Receptors (Muscarinic / Nicotinic) or by increasing Acetylcholine levels.



① Direct Acting Parasympathomimetics

MoA

Direct acting Parasympathomimetics bind directly to muscarinic or nicotinic receptors, mimicking the action of acetylcholine

Pharmacokinetics

- Absorption: Quaternary compounds (e.g. bethanechol) are poorly absorbed orally & don't cross BBB, alkaloids (e.g. pilocarpine) are better absorbed.
- Distribution: Depends on lipid solubility, Pilocarpine distributed widely.
- Metabolism: Rapidly broken by cholinesterases.
- Excretion: Mostly excreted via urine.

Uses

- Glaucoma
- Urinary Retention
- Tachycardia

Examples

- Carbachol
- Bethanechol
- Methacholine

Adverse Effect

- Bradycardia
- Dizziness
- Blurred Vision
- Sweating

② Indirect Acting Parasympathomimetics

MOA

Indirect - acting parasympathomimetics inhibit the enzyme Acetylcholinesterase (AChE), which normally breaks down acetylcholine in the synaptic cleft. which leads to :

- increased Ach levels
- Prolonged stimulation of muscarinic & nicotinic receptors.
- Enhanced parasympathetic activity

Pharmacokinetics

- Absorption : Tertiary amines are well absorbed compared to Quaternary.
- Distribution : Tertiary agents distribute in both CNS & PNS. Quaternary restricted to PNS
- Metabolism : Metabolised in liver by hydrolysis & conjugation.
- Excretion : Excreted mainly via kidneys.

Therapeutic Uses

- Myasthenia Gravis
- Alzheimer's Disease
- Glaucoma
- Urinary Retention

Examples

- Physostigmine
- Neostigmine
- Pyridostigmine
- Malathion

Adverse Effect

- Bradycardia, Hypotension
- Nausea, Vomiting, Diarrhoea.

CHOLINERGIC BLOCKING AGENTS

They are also known as

- Cholinolytic Agents
- Anticholinergic Agents
- Cholinergic Antagonist
- Parasympatholytic Agents
- Antimascarinic Agents

These are those drugs or Agents which inhibit the effect of **Acetylcholine** or **Parasympathomimetic Agents** by blocking the cholinergic receptors.

CLASSIFICATION

Solanaceous Alkaloids

- Atropine Sulphate
- Hyoscyamine Sulphate
- Scopolamine hydrobromide
- Homatropine hydrobromide
- Ipratropium bromide

Synthetic Cholinergic Blockers

- Tropicamide
- Cyclopentolate hydrochloride
- Clidinium bromide
- Dicyclomine hydrochloride
- Glycopyrrolate
- Methantheline bromide
- Propantheline bromide
- Benztropine mesylate
- Orphenadrine citrate
- Biperidine hydrochloride
- Procyclidine hydrochloride
- Trihexyethyl chloride
- Isopropamide iodide
- Ethopropazine hydrochloride

① SOLANACEOUS ALKALOIDS

Solanaceous Alkaloids are naturally occuring anticholinergic compounds found in plants of solanaceae family

MOA

- Solanaceous alkaloids are competitive antagonist at muscarinic acetylcholine receptors.
- They block parasympathetic activity at $M_1 - M_5$ receptors, which leads to :
- Reduced secretions
- Relaxed smooth muscle
- Increased Heart rate
- dilated pupils etc.

PHARMACOKINETICS

- Absorption : Well absorbed orally, parenterally or transdermally
- Distribution : Cross blood brain barrier, widely distributed.
- Metabolism : Primarily hepatic metabolism.
- Excretion : Excreted via urine.

Uses

- Bradycardia
- Motion sickness
- IBS

Examples

- Atropine
- Hyoscyamine
- Scopolamine

ADVERSE EFFECTS

- Mydriasis, Blurred Vision
- Confusion, Tachycardia, Dry Mouth.

② SYNTHETIC CHOLINERGIC BLOCKERS

MOA

- Synthetic Cholinergic blockers are competitive antagonist at muscarinic acetylcholine receptors
- They inhibit parasympathetic nervous system activity leading to effects such as

- Decreased glandular secretion
- Relaxation of smooth muscles
- Increased Heart Rate
- Mydriasis

PHARMACOKINETICS

- Absorption: Well absorbed orally & parenterally
- Distribution: Some drugs cross BBB, causing CNS effect.
- Metabolism: Most undergo hepatic metabolism
- Excretion: Primarily excreted via kidneys.

Uses

- Asthama, COPD
- IBS
- GI spasm

Example

- Tropicamide
- Clinidium Bromide
- Glycopyrrolate
- Cyclopentolate Hydrochloride

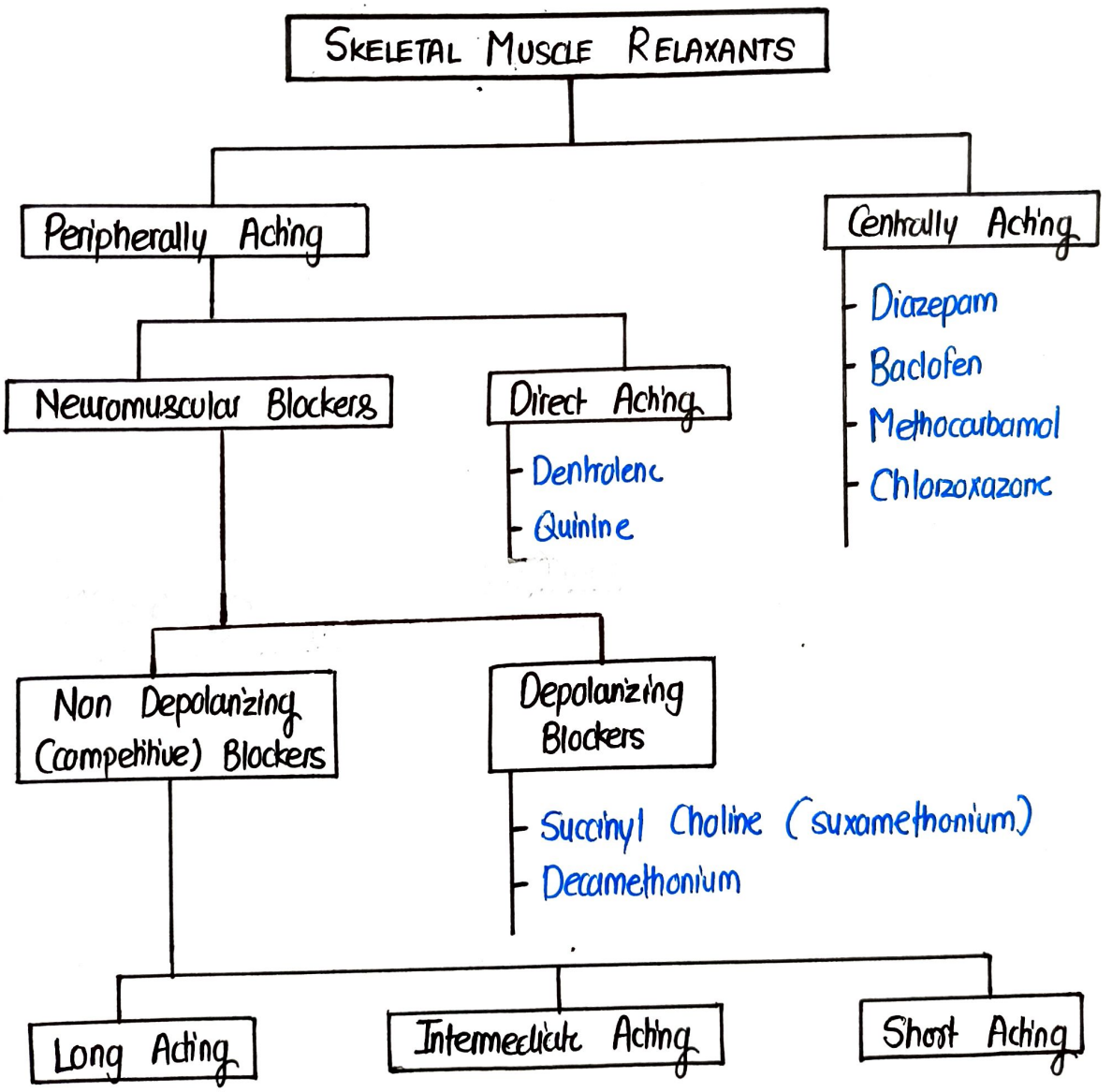
Adverse Effect

- Drowsiness, Blurred Vision
- Tachycardia, Dry Mouth
- Constipation.

SKELETAL MUSCLE RELAXANT

Skeletal Muscle Relaxants are agents that inhibit contraction of skeletal muscle either by :

- Blocking nerve impulse in the CNS.
- Interrupting transmission at neuromuscular junction.



① PERIPHERALLY ACTING SMR

- Peripherally acting Skeletal Muscle Relaxants are drugs that inhibit skeletal muscle contractions by acting at neuromuscular junction or directly on muscle fibres, without involving CNS.
- It is of two types:

ⓐ Neuromuscular Blocking Agents
ⓑ Directly Acting Agents

① NEUROMUSCULAR BLOCKING AGENTS

- Neuromuscular Blocking Agents are drugs that cause temporary paralysis of skeletal muscles by blocking nerve impulse transmission at neuromuscular junction.
- They are primarily used during surgical procedures or mechanical ventilation to produce muscle relaxation.
- They are of two types:

(1) Non Depolarising Blockers
(2) Depolarising Blockers

(1) Non Depolarising Blockers

Non-depolarising blockers are neuromuscular blocking agents that prevent muscle contraction by competitively blocking Acetylcholine at N_M receptors.

MOA:
- ACh normally bind to nicotinic receptors → causes muscle contraction.
- Non depolarising agents bind to same receptors without activating them.
- They block ACh from binding preventing muscle contraction

(2) DEPOLARISING AGENTS

Depolarising blockers are neuromuscular blocking agents that mimic acetylcholine & stimulate nicotinic receptors, causing continuous depolarization, which leads to temporary muscle paralysis

MOA :
- Depolarising agents binds to nicotinic receptors at neuromuscular junction
- It acts like ACh & causes depolarisation, leading to initial muscle fasciculation (twiches)
- However, unlike ACh, it is not rapidly broken down by Acetylcholinesterase
- This causes persistent depolarization, preventing repolarization of muscle membrane
- As a result, further action potential cannot be generated leading to temporary paralysis

Uses

Surgical Procedures
Mechanical Ventilation

(2) DIRECT ACTING AGENTS

Direct acting skeletal muscle relaxants are drugs that act directly on the skeletal muscle fibres to reduce muscle contraction by inhibiting the release of calcium ions from sarcoplasmic reticulum in the skeletal muscles.

② Centrally Acting Agents

Centrally acting skeletal muscle relaxants are drugs that act on the central nervous system (brain or spinal cord) to reduce muscle tone, without directly affecting the muscles themselves.

MOA

- They depress or inhibit nerve activity in the spinal cord or brain.
- This reduces the signals sent to muscles, leading to relaxation.
- Mostly act by enhancing GABA activity (an inhibitory neurotransmitter)

Example

- Baclofen
- Tizanidine
- Diazepam
- Cyclobenzaprine
- Methocarbamol

LOCAL ANESTHETIC AGENTS

- Local Anesthetics are drugs that temporarily block the sensation of pain in a specific part of the body without affecting conciousness.
- They work by preventing nerves from sending pain signals to the brain.
- They're commonly used during minor surgical procedures, dental treatments, or to relieve localized pain.

CLASSIFICATION

- **Injectible Anesthetic**
  - **Low potency, Short duration**
    - Procaine
    - Chloroprocaine
  - **Intermediate potency and duration**
    - Lidocaine
    - Prilocaine
  - **High potency, Long duration**
    - Tetracaine
    - Bupivacaine
    - Ropivacaine
    - Dibucaine
- **Surface Anesthetic**
  - **Soluble**
    - Cocaine
    - Lidocaine
    - Tetracaine
    - Proparcaine
  - **Insoluble**
    - Benzocaine
    - Oxethazine
    - Butylamino-benzoate

INJECTIBLE ANESTHETICS

- Injectible anesthetics are drugs that are given by injection to cause loss of sensation or unconciousness.
- They are used to prevent pain during medical procedures or surgeries.
- These anesthetics acts quickly and are commonly used to start or maintain anesthesia.

CLASSIFICATION

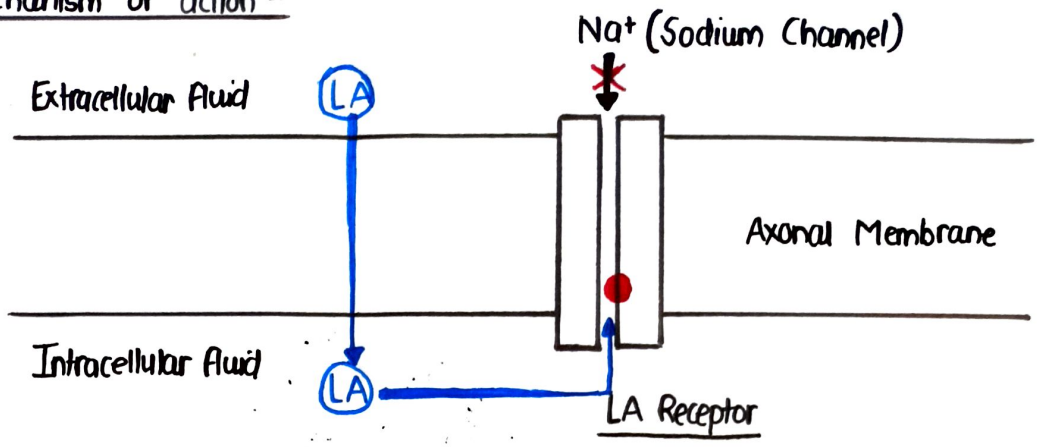
- Injectible Anesthetics
  - Low Potency, Short Duration
    - Procaine
    - Chloroprocaine
  - Intermediate Potency and duration
    - Lidocaine (Lignocaine)
    - Prilocaine
  - High Potency, Long Duration
    - Tetracaine
    - Bupivacaine
    - Ropivacaine
    - Dibucaine

① Low Potency, Short Duration

- They are class of drugs used to primarily for the induction and short-term maintenance of anesthesia.
- They requires higher doses to achieve the desired anesthetic effect compared to high potency agents.
- They rapid onset and rapid clearance from body.

Examples : Procaine , etc.

Mechanism of action -



- Local Anesthetics enters the nerve cells near the area where they are injected or applied.
- They block special sodium gated channels, which helps to carry pain signals to the brain.
- when the channels are blocked, the nerves can't send pain messages. As result, you don't feel pain in that area for a short time.
- The effect is temporary and wears off as the medicine eliminated.

Pharmacokinetics

- **Absorption :** Rapid onset of action due to IV route.
- **Distribution :** Quickly distributed to brain and other organs with high blood flow.
- **Redistribution :** Moves to muscles and fat, causing the anesthetic effect to wear off.
- **Metabolism :** Mainly metabolized in liver (some drugs into plasma).
- **Excretion :** Elimination occurs by kidneys through urine.

Adverse effects

- Hypotension
- Bradycardia
- Respiratory - depression
- Apnea
- Vomitting
- Laryngospasm etc.

Therapeutic Uses

- Sedation
- Analgesia
- Induction
- Siezures
- Procedures (Surgery)
- Anxiolysis etc.

② Intermediate Potency and duration

- They are anesthetic drugs that have a moderate streng th and ~~potency~~ produce their effects for a moderate amount of time (duration) when given by injection (IV route).
- They works by enhancing inhibitory neurotransmission, leading to temporary loss of conciousness or sedation.

Pharmacokinetics

- Absorption: Rapidly absorbed due to IV administration.
- Distribution: Quickly distributed to highly perfused organs like brain.
- Metabolism: Primarily metabolized in liver.
- Elimination: Excreted through renal pathways, with moderate half-life.
- Duration: last 15-60 minutes depending on drug or dose.

Adverse effects

- Adrenal Suppression
- Bradycardia
- Apnea
- Myoclonus etc.

Therapeutic Uses

- Sedation
- Analgesia
- Burns
- Asthma
- Induction etc.

③ High Potency, Long duration

- They are agents that produce deep and prolonged anesthesia or sedation at low doses due to their strong binding to receptors and slow metabolism or elimination.
- They are also potently enhancing inhibitory neurotransmission, leading to prolonged sedation or anesthesia.

Pharmacokinetics

- **Absorption :** Rapidly absorbed due to IV dose , slower with IM.
- **Distribution :** Widely distributed , including to fat and brain tissue.
- **Metabolism :** Primarily metabolized in liver.
- **Elimination :** Slow elimination via renal pathways.
- **Duration :** Long - acting , effects against for several hours.

Adverse effects

- Arrythmia
- Cardiotoxicity
- Hypotension
- Siezures
- CNS - toxicity
- Nausea etc.

Therapeutic Uses

- Surgery
- Analgesia
- Mayor - trauma
- Burns
- ICU - Sedation
- Intubation etc.

SURFACE ANASTHETICS

- They are topical agents that blocks nerve conduction at the site of application, providing temporary local numbness / sedation without affecting conciousness.

Classification

- Surface Anesthetics
  - Soluble
    - Cocaine
    - Lidocaine
    - Tetracaine
    - Proparacaine
  - Insoluble
    - Benzocaine
    - Oxethazine
    - Butylamino-benzoate

① Soluble Surface Anesthetics

- They are a type of local anesthetic that are water-soluble and used to numb mucous membrane or skin surfaces.
- They work by blocking nerve signals in the area where they are applied, providing temporary pain relief or loss of sensation.

Examples : Cocaine, Lidocaine etc.

Mechanism of Action:

- Soluble surface anesthetics works by blocking sodium channels in nerve endings, preventing nerve signals transmission and causing localized numbness.

Pharmacokinetics

- Absorption: Rapidly absorbed through mucous membranes or damaged skin.
- Distribution: Limited systemic distribution unless applied in large amounts.
- Metabolism: Mostly metabolized in liver.
- Excretion: Excreted by kidneys during urination as metabolites.

Adverse Effects

- Irritation
- Allergy
- Dermatitis
- Tingling
- Burning
- Numbness etc.

Therapeutic Uses

- Dental
- Topical
- Ophthalmic
- Wound treating etc.

② Insoluble Surface Anesthetics

- They are local anesthetics that are poorly soluble in water and are used, only for surface anesthesia, especially on mucous membranes.
- Because they are not water-soluble, they are not suitable for injection or systemic use.

Examples: Benzocaine, Butylaminobenzoate etc.

Mechanism of Action

- They blocks high voltange-gated (Na^+) sodium channels and producing local numbness.

Pharmacokinetics

- Absorption: (fat) Slow absorb through intact skin, faster via mucous membranes.
- Distribution: Limited systemic distribution, mainly staying at the site of applied.
- Metabolism: Typically not metabolized significantly, as they're not absorbed well.
- Excretion: Excreted renally as inactive metabolites.
- Duration: Prolonged local effect due to slow release from lipid stores.

Adverse Effects

- Irritation
- Allergy
- Toxicity
- Burning
- Redness
- Edema etc.

Therapeutic Uses

- Dermatology
- Ophthalmic
- ENT
- Dental Surgery
- Burns
- Teething etc.

Drugs Used In Myasthenia Gravis

Myasthenia Gravis

- Myasthenia gravis is a chronic autoimmune neuromuscular disorder that causes weakness in skeletal muscles.
- It occurs when the immune system produces antibodies abnormally which block or destroy the receptors for acetylcholine at the neuromuscular junction and leads to muscle weakness and fatigue.

Pathophysiology

The immune system produces antibodies against the own body's proteins.

↓

These antibodies attack and block (Ach) acetylcholine receptors on muscles.

↓

Due to this acetylcholine not properly sending signals from nerves to muscles

↓

Myasthenia Gravis occurs

↓

As the result:

- Muscle weakness
- Fatigue
- Double vision
- Slurred or Nasal Speech
- Neck weakness etc.

CAUSES

- Stress
- Autoimmunity
- Abnormal antibodies production
- Genetics
- Infection
- Medications
- Thymus Gland abnormalities etc.

SYMPTOMS

- Chewing difficulty
- Limb - weakness
- Head - drop
- Fatigue
- Muscles weakness
- Disphagia etc.

TREATMENT

① **Anticholinesterases** : They are that drug which blocks the enzyme acetylcholinesterase, leading to increased levels of acetylcholine at nerve endings and enhancing nerve signal transmission.
Ex - Pyridostigmine, Neostigmine etc.

- **M.O.A. of Pyridostigmine** : Pyridostigmine works by inhibiting cholinesterase, which increases acetycholine at the neuromuscular junction, improving muscles contraction.

Pharmacokinetics

- Absorption : Moderately absorbed from GIT.
- Distribution: Limited CNS penetration (Poorly crosses blood-brain barrier).
- Metabolism: Partially metabolized in liver.
- Excretion : Excreted mainly through the kidneys.

Adverse Effects

- Cramps
- Diarrhea
- Sweating
- Salivation
- Bradycardia
- Blurred- vision etc.

Therapeutic Uses

- Myasthenia Gravis
- Urinary retention
- Prophylaxis (against nerve agent poisoning)
- Ileus
- Neuromuscular blockade reversal etc.

② **Immunosuppressants** : Immunosuppressants are reduce the activity of immune system to prevent extra immune activity and from attacking the own body's neuro-muscular junctions, helping to improve muscle strength.

Ex- Cyclosporine, Cyclophosphate, Azithoprine etc.

Mechanism of Action: Immunosuppressant works by inhibiting immune cell activity and reducing autoantibody production, thereby decreasing the immune attack on acetycholine receptors in myasthenia gravis.

Pharmacokinetics

- **Absorption:** Well absorbed orally but varies the drug.
- **Distribution:** Widely distributed, some crosses the blood-brain barrier.
- **Metabolism:** Primarily metabolized by liver.
- **Excretion:** Excreted via urine and bile.

Adverse Effects

- Leukopenia
- Infections
- Anemia
- Hepatotoxicity
- Nephrotoxicity
- Hair-loss
- Nausea etc.

Therapeutic Uses

- Myasthenia Gravis
- Arthiritis
- Psoriasis
- IBD
- Lupus
- Nephritis
- Multiple-sclerosis etc.

③ **Corticosteroids:** Corticosteroids are anti-inflammatory drugs that suppress the immune system to reduce to production of antibodies, which attacking the neuromuscular junction, thereby improving muscle strength and symptoms.

Ex.- Hydrocortisone, Beclomethasone, Fluticasone etc.

- **Mechanism of Action:** Corticosteroids works by reducing inflammation and immune system activity, thereby decreasing the production of autoantibodies that attacks on Ach receptors.

Pharmacokinetics

- Absorption: Rapidly well absorbed orally.
- Distribution: Widely distributed and crosses placenta & Blood-brain barrier.
- Metabolism: Metabolized mainly by the liver.
- Excretion: Excreted primarily through urine.

Adverse Effects

- Infection
- Hyperglycemia
- Hypertension
- Osteoprosis
- Weight-gain
- Glaucoma
- Acne etc.

Therapeutic Uses

- Asthma
- Myasthenia Gravis
- Arthiritis
- Allergies
- Autoimmunity etc.

④ Some other treatments :

- Surgery of Thymus Gland.
- Plasma exchange (if needed).

Drugs Used In Glaucoma

Glaucoma

- Glaucoma is group of eye diseases that damage the optic nerves, due to increased pressure inside the eye (intraocular pressure).
- This damage can lead to vision loss or even blindness if not treated.
- It develops slowly and may not cause noticeable symptoms at first, that's regular examinations are important for early detection.

Pathophysiology

Increased intraocular pressure in Eye

↓

Obstruction of Aqueous Humor Outflow

↓

Accumulation of Aqueous Humor

↓

Raised pressure inside the eyes

↓

Compression of Optical Nerve fibres

↓

Reduced blood flow to Optic nerves

↓

Optical Nerves damaged

↓

Glaucoma (Vision loss)

Causes

- Genetics
- Age
- Trauma
- Steroids
- Surgery
- Myopia
- Tumors etc.

Symptoms

- Vision loss (in severe)
- Headache / Pain
- Blurred vision
- Vomiting
- Tearing
- Redness etc.

Treatment

Drugs used in Glaucoma

- **β- Adrenergic blockers**
  - Timolol
  - Betaxolol
  - Carteolol
  - Levobunolol
- **α- Adrenergic blockers**
  - Dipivefrine
  - Apraclonidine
  - Brimonidine
- **Prostaglandin Analogous**
  - Latanoprost
  - Travoprost
- **Carbonic Anhydrase Inhibitors**
  - Acetazolamide
  - Dorzolamide
- **Miotics**
  - Pilocarpine
  - Physiostigmine

① β-ADRENERGIC BLOCKERS :

β - Adrenergic blockers are drugs that blocks beta receptors in the body, mainly in the heart and eyes.

Mechanism of Action : They block beta receptors in the eyes cilliary body, which reduces the production of aqueous humor.

Pharmacokinetics

- Absorption : Rapidly absorbed through eye drop administration.
- Distribution : Distributed locally in eyes tissues.
- Metabolism : Mainly metabolized in liver.
- Excretion : Excreted mostly through the kidneys.

Adverse Effects

- Bronchospasm
- Bradycardia
- Hypotension
- Depression
- Fatigue
- Dryness etc.

Therapeutic Uses

- Glaucoma
- Hypertension
- Angina
- Arrhythmia
- Migraine
- Anxiety etc.

② **α-ADRENERGIC BLOCKERS** : They are medicines that block alpha receptors in the body. They help by relaxing blood vessels or reducing Fluid production in the eye.

Mechanism of Action : They works as block alpha receptors and relaxe the muscles and reduce production of aqeous humor in the eyes.

Pharmacokinetics

- Absorption : Well absorbed after oral or ocular use.
- Distribution : Widely distributed in body tissues.
- Metabolism : Mostly metabolized in the liver.
- Excretion : Excreted through kidneys (urine).

Adverse Effects

- Dizziness
- Headache
- Hypotension
- Fatigue
- Palpitations
- Blurred vision etc.

Therapeutic Uses

- Hypertension
- Glaucoma
- Reynaud's disease
- Pheochromocytoma etc.

③ **PROSTAGLANDIN ANALOGUES**: They are medicines that mimic natural prostaglandins in the body.

Mechanism of Action: They binds to prostaglandin receptors in the eye, which increases the outflow of aqueous humor and lowering intraocular pressure.

Pharmacokinetics

- Absorption : Rapidly absorbed through ocular administration.
- Distribution: Distributed primarily in the eye tissues.
- Metabolism: Metabolized in active forms in the eye and liver.
- Excretion: Excreted through the kidneys and feces.

Adverse Effects

- Iris pigmentation
- Itching
- Dryness
- Blurred vision
- Irritation
- Eyelash growth etc.

Therapeutic Uses

- Glaucoma
- Ocular hypertension
- Eyelash (hypotrichosis) etc.

④ **CARBONIC ANHYDRASE INHIBITORS** : These are medicines that blocks the enzyme carbonic anhydrase.

Mechanism of Action : They block carbonic anhydrase enzyme in the eye, decrease aqeuous humor production and lower intraocular pressure.

Pharmacokinetics

- Absorption : Well absorbed orally and through the eye.
- Distribution : Distributed in eye tissues and body fluids.
- Metabolism : Minimal metabolism
- Excretion : Excreted mainly unchanged in urine.

Adverse Effects

- Fatigue
- Allergy
- kidney stones
- Metallic taste
- Diarrhea
- Tingling etc.

Therapeutic Uses

- Glaucoma
- Epilepsy
- Sickness
- Edema
- Pseudotumor etc.

⑤ **Miotics**: Miotics are medicines that make the pupil smaller by contracting the eye muscles.

Mechanism of Action: They stimulate the eye muscles, causing pupil constriction and opening of the drainage channels, which increases fluid outflow and lower eye pressure.

Pharmacokinetics

- Absorption: Well absorbed through eye drop.
- Distribution: Mainly distributed in eye tissues, minimal systemic absorption.
- Metabolism: Metabolized locally in the eye and liver.
- Excretion: Excreted mainly through kidneys.

Adverse Effects

- Blurred vision
- Headache
- Tearing
- Myopia
- Night blindness
- Allergy etc.

Therapeutic uses

- Glaucoma
- Miosis
- Myasthenia Gravis
- Diagnosis of eye conditions etc.

THANK YOU

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