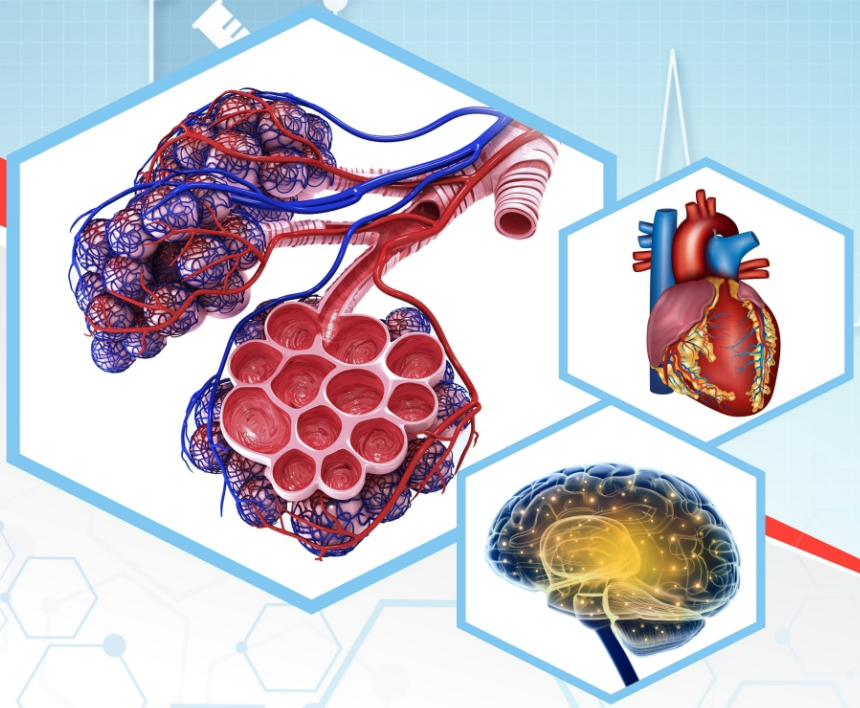
PHARMACY INDIA

PHARMACOLOGY

A COMPETITIVE EXAMINATION BOOK



COMPETITIVE EXAMINATION BOOK FOR

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PHARMACOLOGY

A Competitive Examination Book

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Contents

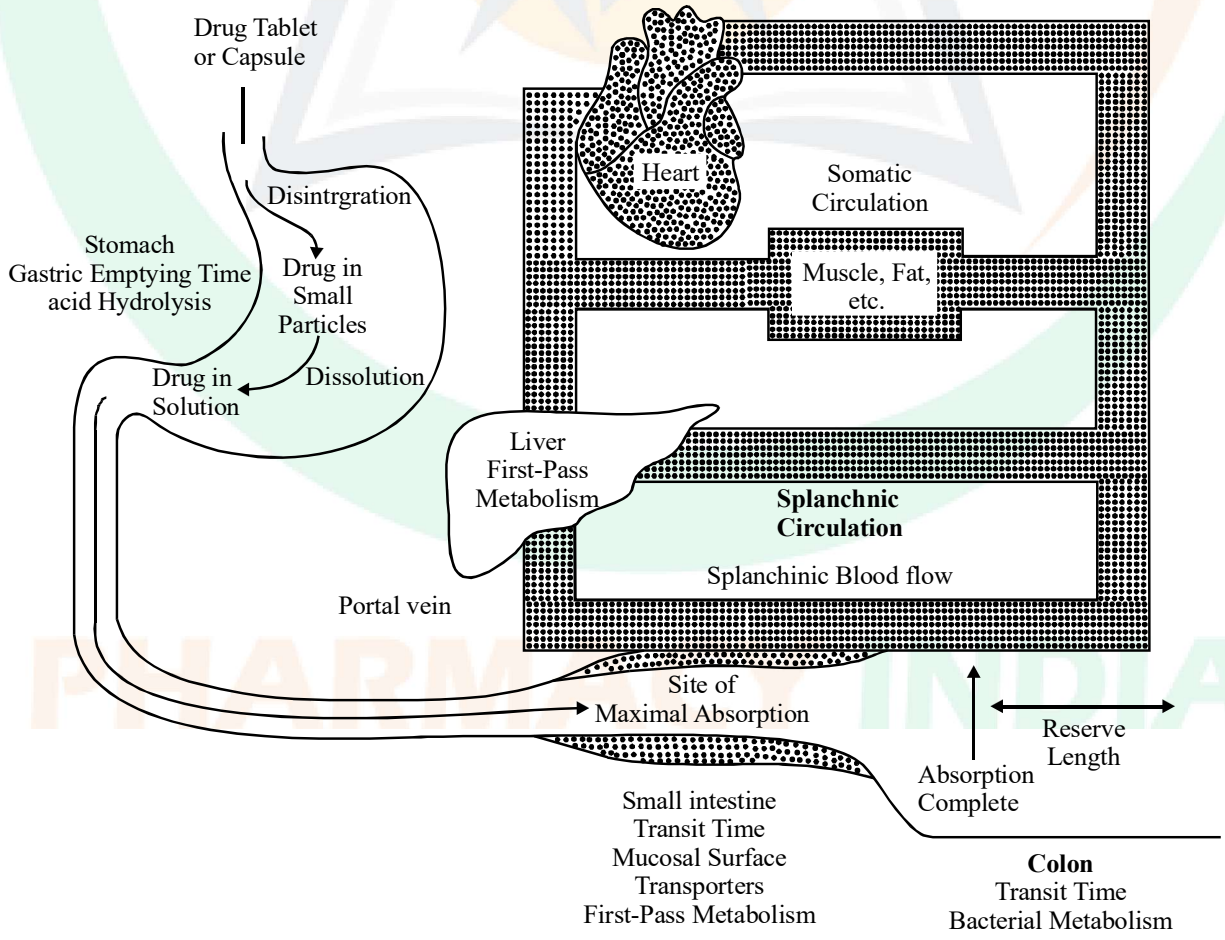
Bioavailability

- It is the fraction of administered drug that reaches the systemic circulation in the unchanged form.
- Intravenous route of drug administration gives 100% bioavailability as its directly into the systemic circulation
- When we administer a drug orally, first it is absorbed into the portal circulation and reaches the liver. Here, some of the drug may be metabolized (first pass metabolism or pre-systemic metabolism) and rest of the drug reaches the systemic circulation. Thus absoprption and first pass metabolism are two important determinants of bioavailability

Factors affecting bioavailability

- **First –pass metabolism (presystemic elimination):-** when drugs are admintered orally ,they have to pass via gut wall → portal vein → liver → systemic circulation. During this passage certain drugs get metabolized and removed or inactivated before they reach the systemic circulartion, this process is known as first pass metabolism.

Low	Intermediate	High	
		Not given orally	High an dose
Phenobarbitone	Aspirin	Isoprenaline	Propranolol
Phenylbutazone	Quinidine	Lidocaine	Alprenolol
Tolbutamide	Desipramide	Hydrocortisone	Verapamil
Theophylline	Nortriptyline	Testosterone	Salbutamol
Pindolol	Chlorpromazine		Glyceryl trinitrate
Isosorbide	Pentazocine		Morphine
Mononitrate	Metoprolol		Pethidine



PRODRUGS

It is an inactive form of a drug which is converted to an active form after metabolism .

Uses of prodrugs (advantages)

- To improve bioavailabilty :- parkinsonism is due to deficiency of dopamine .Dopamine itself cannot be used since it does not cross the blood brain barrier (BBB).So it is given in the form of a prodrug ,levodopa Levodopa crosses the BBB and it is then converted into dopamine .
- To prolong the duration of action :- phenothiazines have a short duration of action whereas esters of phenothiazines (fluphenzine)have a longer of duration of action
- To improve the tatste :- clindamycin has a bitter tate so clindamycin palmitate suspension has been developed for pediatric use to improve the taste .

1. Inactive form
2. Active metabolite, E.g.:- Codeine to morphine
3. Prodrug to active drug, E.g.:- L-Dopa to Dopamine

PRODRUG	ACTIVE FORM
Levodopa	Dopamine
Enalaprila	Enalaprilat
a-Methyldopa	a-methylnorepinephrine
Dipivefrine	Epinephrine
Proguanil	Cycloguanil
Prednisone	Prednisolone
Clopidogrel	Thiol metabolite
Bacampicillin	Ampicillin
Sulfasalazine	5-Aminosalicylic acid
Cyclophosphamide	Aldophosphamide, phosphoramide mustard, acrolein
Fluorouracil	Fluorouridine monophosphate
Mercaptopurine	Methylmercaptopurine ribonucleotide
Acyclovir	Acyclovir triphosphate

Pathways of Drug Metabolism

Drug metabolic reaction are grouped into two phases .

Phase I metabolism: - Nonsynthetic

REACTION	DEFINITION	EXAMPLES
Oxdation	Addition of oxygen /removal of hydrogen	Phenytoin ,phenobarbitone , pentobarbitone ,propranolol
Reduction	Removal of oxygen/addition of hydrogen	Chloramphenicol ,methadone
Hydrolysis	Break down of compound by addition of water	Esters procaine ,succinylcholine Amides lignocaine , procainaamide
Cyclisation	Conversion of straight chain compound into ring structure	Proguanil to cycloguanil
Decyclisation	Breaking up of the ring st. of the drug	Phenobarbitone & Phenytoin

CLINICAL TRIALS

PHASE	NAME	CONDUCTED ON	PURPOSE
I	Human Pharmacology and safety	Healthy volunteers (20 100)	To know max. Tolerable dose(MTD)
II	Therapeutic exploratory	100 150 Patients (homogenous population	To establish therapeutic efficacy
III	Therapeutic confirmatory	Upto 5000 patients from several centres (heterogenous population)	To confirm therapeutic efficacy
IV	Post marketing surveillance	Large number of patients	To know rare & long terma ADR
0	Microdosing studies	Healthy volunteers (small number)	To know pharmacokinetic

ADVERSE DRUG EFFECTS

INTRODUCTION

- Adverse effect is 'any undesirable or unintended consequence of drug administration'.
- Adverse drug reaction (ADR) has been defined as 'any noxious change which is suspected to be due to a drug, occurs at doses normally used in man, requires treatment or decrease in dose or indicates caution in the future use of the same drug'.
- Another term 'adverse drug event' (ADE) has been used to mean 'any untoward medical occurrence that may present during treatment with a medicine, but which does not necessarily have a causal relationship with the treatment'.
- Adverse effects have been classified in many ways:

1. **Predictable (Type A or Augmented) reactions** (mechanism based adverse reactions):
   - These are based on the pharmacological properties of the drug, which means that they are augmented, but qualitatively normal response to the drug; include side effects, toxic effects and consequences of drug withdrawal.
   - They are more common, dose related and mostly preventable and reversible.
2. **Unpredictable (Type B or Bizarre) reactions:**
   - These are based on peculiarities of the patient and not on drug's known actions; include allergy and idiosyncrasy.
   - They are less common, often non-dose related, generally more serious.
   - Require withdrawal of the drug.

Pharmacovigilance

- Pharmacovigilance has been defined by the WHO (2002) as the 'science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug related problems.'
- Its main purpose is to reduce the risk of drug-related harm to the patient.
- It has an important role in the rational use of medicines, as it provides the basis for assessing safety of medicines.
- The activities involved in pharmacovigilance are:

14. Two drugs having opposite response via action on same receptors are called pharmacological antagonists, e.g. propanolol (causing bradycardia by acting on β1 receptors) is pharmacological antagonist of adrenaline (cause tachycardia by acting on β_1 receptors)
15. Alpha 1 (α1) receptors act by increasing Ca^{2+} whereas β_1 increase cAMP in the cell.
16. **Grapefruit juice** acts as inhibitor of CYP3A4 due to its content of furanocumarins and narigin.
17. **Therapeutic index** is a measure of safety of a drug. It is calculated as **LD50/ED50**
18. **Rifampicin** can result in failure of oral contraceptives due to its enzyme inducing property.
19. **Pharmacogenetics** refers to study dealing with how variations in human genome affect the response to drugs.
20. Most accurate method of calculating drug dosage in children is **body surface area.**
21. **Gastric lavage** is contra-indicated in corrosive [strong acid or strong base] and kerosene poisoning.
22. **Forced alkaline dieresis** is effective for management of acidic drug poisoning like phenobarbitone, aspirin and methotrexate, etc.
23. Drug induced diseases:- These are also called iatrogenic (physician induced) diseases. caused by drugs which persist even after the offending drug has been withdrawn and largely eliminated, e.g.: **Peptic ulcer by salicylates and corticosteroids. Parkinsonism by phenothiazines and other antipsychotics. Hepatitis by isoniazid. DLE by hydralazine.**
24. **Dose-response relationship :-** Dose-response curve is a rectangular hyperbola
25. **Intrinsic activity :-** of a drug is a measure of its ability to induce a functional change in the receptor which could very from 0 to 1 (nil to maximal)

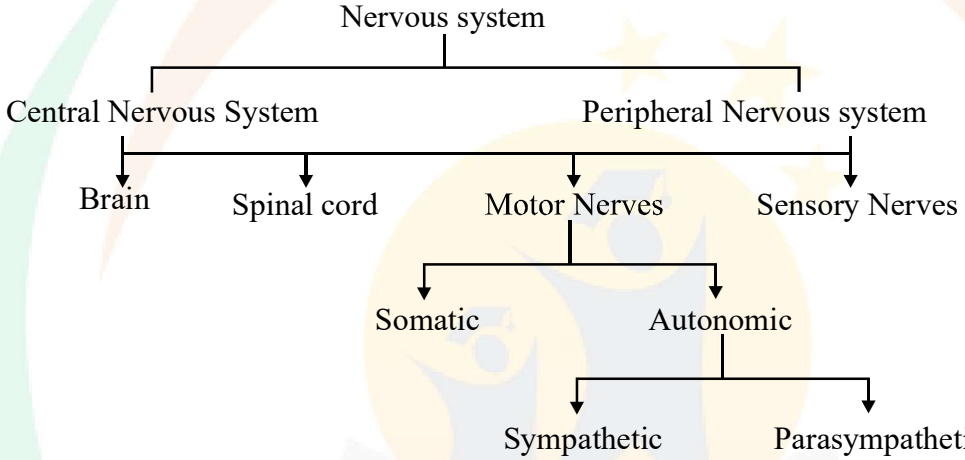
Thalidomide caused **phocomelia** in Germany in 1960s when it was used for treatment of vomiting due to morning sickness.
Vitamin K was isolated from **alfa alfa grass**.

Chapter 2

AUTONOMIC NERVOUS SYSTEM

INTRODUCTION

- The autonomic nervous system (ANS) is the primary moment-to-moment regulator of the internal environment of the organism, regulating specific functions that occur without conscious control.



- **Example -** Respiration, circulation, digestion, body temperature, metabolism, sweating, and the secretions of certain endocrine glands.
- The autonomic nervous system consists of three main anatomical divisions: sympathetic, parasympathetic and enteric nervous systems. The sympathetic and parasympathetic systems provide a link between the central nervous system and peripheral organs. The enteric nervous system comprises the intrinsic nerve plexuses of the gastrointestinal tract, which are closely interconnected with the sympathetic and parasympathetic systems.
- In the periphery, the ANS consists of nerves, ganglia, and plexuses that innervate the heart, blood vessels, glands, other visceral organs, and smooth muscle in various tissues.

Difference between somatic and autonomic nervous system

	SOMATIC	AUTONOMIC
Organ supplied	Skeletal muscles	All other organs
Distal most synapse	Within CNS	Outside CNS (in ganglia)
Nerve fibres	Myelinated	Preganglia-myelinated Postganglia-non-myelinated
Peripheral plexus formation	Absent	Present
Primary efferent transmitter	Acetylcholine	Acetylcholine, Noradrenaline
Effect of nerve section on organ supplied	Paralysis and atrophy	Activity maintained, no atrophy

Differences between sympathetic and parasympathetic divisions of the autonomic nervous system

Sympathetic Parasympathetic

	SYMPATHETIC	PARASYMPATHETIC
Origin	Dorso-lumbar (T_1 to L_2 or L_3)	Cranio-sacral (III, VII, IX, X; S_2S_4)
Distribution	Wide	Limited to head, neck and trunk
Ganglia	Away from the organs supplied	On or close to the organ supplied
Postgang. fibre	Long	Short
Pre: post ganglionic 0fibre ratio	1: 20 to 1: 100	1: 1 to 1: 2 (except in enteric plexuses)
Neuroeffector transmitter	Major: Noradrenaline Minor: Adenosine triphosphate, Neuropeptide Y, Dopamine, Acetylcholine	Major: Ach Minor: Vasoactive intestinal peptide, Nitric oxide
Stability of transmitter	Noradrenaline stable, diffuses for wideraction	Achrapidly destroyed locally
Important function	Tackling stress and emergency	Assimilation of food, conservation of energy

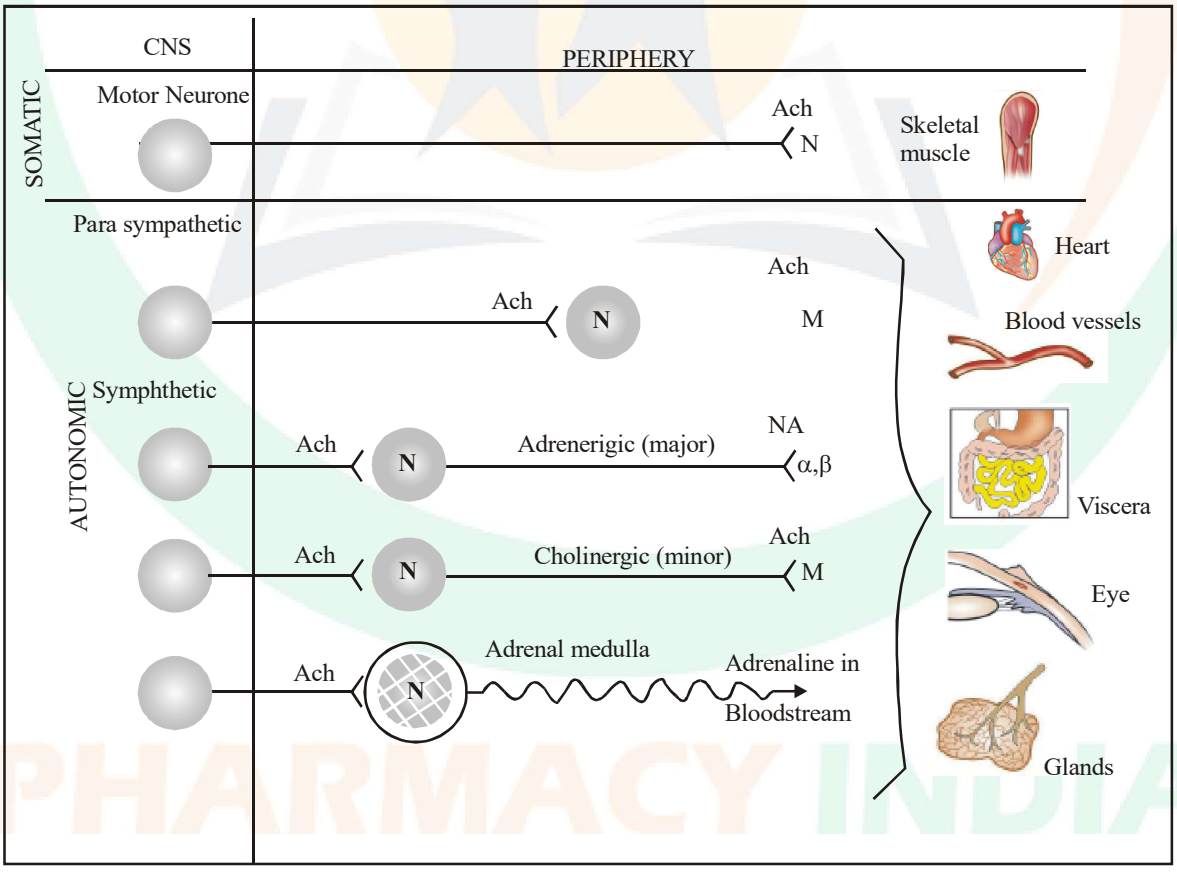
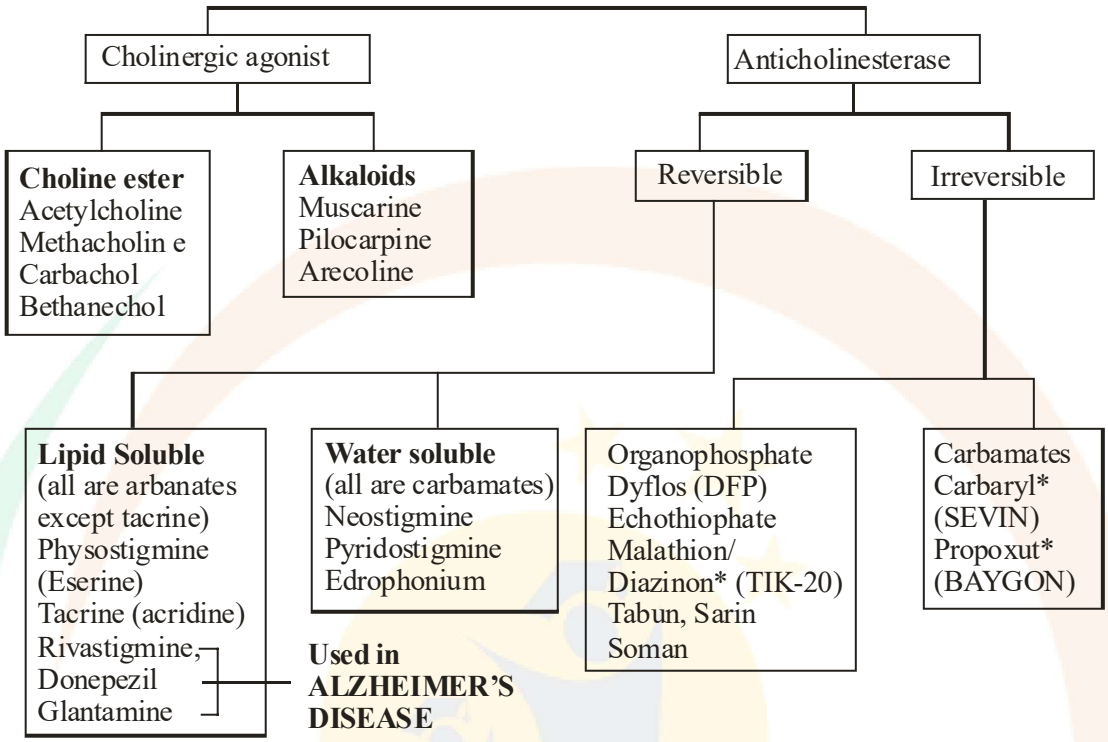


Figure: The general outlay of efferent autonomic nervous system. The transmitter released and the primary postjunctional receptor subtype is shown at each synapse/neuroeffector junction

ACh= Acetylcholine, NA= Noradrenaline, N = Nicotinic, M = Muscarinic, α= α adrenergic, β = β adrenergic

CHOLINERGIC AGENTS



Pharmalogical actions of acetylcholine: - Ach produces muscarinic and nicotinic effect by interacting with respective receptors on the effector cells.

[A] Muscuranic action

ORGAN/ PART OF BODY	PHARMACOLOGICAL ACTIONS
Heart	Ach → hyperpolarizes the SA nodal cells and decreases their rate of diastolic depolarization. As a result- • ↓↓ **ses heart rate** (negative chronotropic effect) • ↓↓ ses **force of contraction** (negative ionotropic effect) • ↓↓ ses **AV conduction** (negative dromotropic effect)
Blood vessels	Ach → acts on M_3 receptor of vascular endothelial cells → releases nitric oxide [endothelium dependent relaxing factor (EDRF)] → **vasodilation** → ↓↓ ses **blood pressure**
➢ **Gastrointestinal tract**	Ach acts on M_3 receptor of GIT causes • ↑↑ sed **tone and peristalsis in the gastrointestinal tract** • ↑↑ sed **GIT secretions** • **sphincters relax** - evacuation of bowel **(diarrhoea)**
➢ **Urinary bladder**	Ach → acts on M_3 receptor of urinary bladder • **Detrusor muscle contracts** • trigone and sphincter muscle relaxes - urination
➢ **Bronchi**	Ach → acts on M_3 receptor of bronchi • Bronchial muscles constrict **(bronchospasm)** • asthmatics are highly sensitive bronchospasm, dyspnoea, precipitation of an attack of bronchial asthma. • **Cholinergic drugs are contraindicated in asthmatics**

ANTIMUSCARINIC AGENTS

- **Acetylcholine** (agonist) ’——→ **Muscarinic receptor** ←——**Atropine** (antagonist)
- **Classification –**

1. **Natural alkaloids:** Atropine, Hyoscine (Scopolamine).
2. **Semisynthetic and synthetic derivatives:**

a. For COPD and asthma - Ipratropium bromide, Tiotropium bromide.

b. Mydriatics – Homatropine, Cyclopentolate, Tropicamide, Hyoscin.

c. Antisecretory-antispasmodics:

(i) **Quaternary compounds:** Propantheline, Oxyphenonium, Clidinium, Pipenzolate methyl bromide, Isopropamide, Glycopyrrolate.

(ii) **Tertiary amines:** Dicyclomine, Valethamate, Pirenzepine.

d. For peptic ulcer – Pirenzipine, Propanthaline, Telenzepine.

e. Vasicoselective - Oxybutynin, Flavoxate, Tolterodine.

f. Antiparkinsonian - Trihexyphenidyl (Benzhexol), Procyclidine, Biperiden.

g. Preanaesthetic agent – Glycopyrrolate

PHARMACOLOGICAL ACTIONS OF ATROPINE: -

ORGANS/ PARTS OF BODY	PHARMACOLOGICAL ACTIONS
CNS	• Depresses vestibular excitation and has antimotion sickness property. • Suppresses tremor and rigidity of parkinsonism.
Heart	• Prominent effect of atropine is tachycardia. Initial bradycardia with low dose.
Blood pressure	• Cholinergic impulses are not involved in the maintenance of vascular tone; Atropine does not have any consistent or marked effect on BP. • Tachycardia and vasomotor centre stimulation tend to raise BP. While histamine release and direct vasodilator action • (at high doses) tend to lower BP.
Eye	• Atropine causes mydriasis, abolition of light reflex and cycloplegia lasting 7-10 days. • This results in photophobia and blurring of near vision.
GIT	Atropine causes - • ↓↓ sed **tone and peristalsis in the gastrointestinal tract** • ↓↓ sed **GIT secretions** • **Sphincters contracts constipation**
Urinary bladder	Atropine causes - • **Detrusor muscle relax** • **Trigone and sphincter muscle contracts urinary retention**
Bronchi	Atropine causes - • Bronchial muscles relax **(bronchodilation)**
Glands	Atropine causes - • **Decreased secretion of exocrine glands.** • Decreases sweat, salivary, tracheobronchial and lacrimal secretion (M_3 blockade). • Skin and eyes become dry, talking and swallowing may be difficult.

❒ Differences between α_1 and α_2 receptors

	α_1	α_2
Location	Postjunctional on effector organs	Prejunctional on nerve ending (α_2A), also postjunctional in brain,pancreatic β-cells and extrajunctional in certain blood vessels, platelets
Function	• Genitourinary Smooth muscle contraction • Vasoconstriction • Glandsecretion • Gutrelaxation • Male sex → ejaculation • Heart arrhythmia	• Activation of presynaptic α_2 receptor → inhibition of transmitter release (NA) • Activation of postsynaptic vascular α_2 receptor → Vasoconstriction • Decreased central sympathetic flow • Decreased insulin release • Reduction of aq. Humour secretion • Platelet aggregation
Selective agonist	Phenylephrine, Methoxamine	Clonidine
Selective antagonist	Prazosin	Yohimbine, Rauwolscine
Coupling protein	Gq	Gi/Go
Effector pathway	• IP_3/DAG↑ • Phospholipase A_2 ↑PG release	• cAMP↓ • K^+ channel ↑ • Ca^{2+} channel ↓ or ↑ • IP_3/DAG ↑

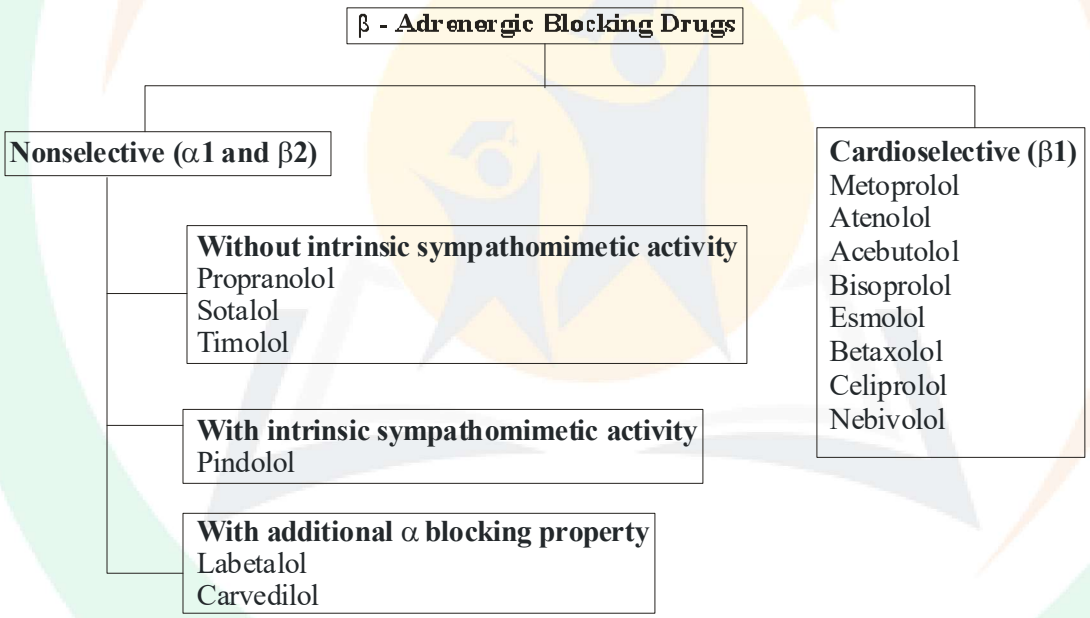
❒ Differences between β_1, β_2 and β_3 receptors

	β_1	β_2	β_3
Location	Heart, JG cells in kidney	Bronchi, blood vessels, uterus, liver, skeletal muscles, g.i.t., urinary bladder, radial muscles of eye	Adipose tissue, detrusor muscle of bladder
Functions	• Cardiac stimulation Promote rennin release • ADH secretion from posterior pituitary	Stimulatory effects due to activation of β_2 receptor - • Stimulation of glycogenolysis • Skeletal muscle contraction • Increases aq. Humour secretion • Uptake of K^+ into cells Inhibitory effects due to activation of β_2 receptor - • Relaxation of bronchial, uterine, vascular, bladder smooth muscles Relaxation of GI smooth muscles	Lipolysis

USES OF α BLOCKERS: -

1. **Pheochromocytoma -** Phenoxybenzamine can be used as definitive therapy for inoperable and malignant pheochromocytoma. Prazosin is an alternative.
2. **Hypertension -** phentolamine/phenoxybenzamine
3. **Benign hypertrophy of prostate (BHP) -** α_1 adrenergic blockers (prazosin), 5-α reductase inhibitor (finasteride)
4. **Secondary shock -** Shock due to blood or fluid loss is accompanied by reflex vasoconstriction. Therapy with an α blocker (phenoxybenzamine i.v.)
5. **Peripheral vascular diseases -** Good symptomatic relief is afforded by prazosin or phenoxybenzamine.
6. **Congestive heart failure (CHF) –** Prazosin
7. **Papaverine/Phentolamine Induced Penile Erection (PIPE) therapy for impotence –** Phentolamine.

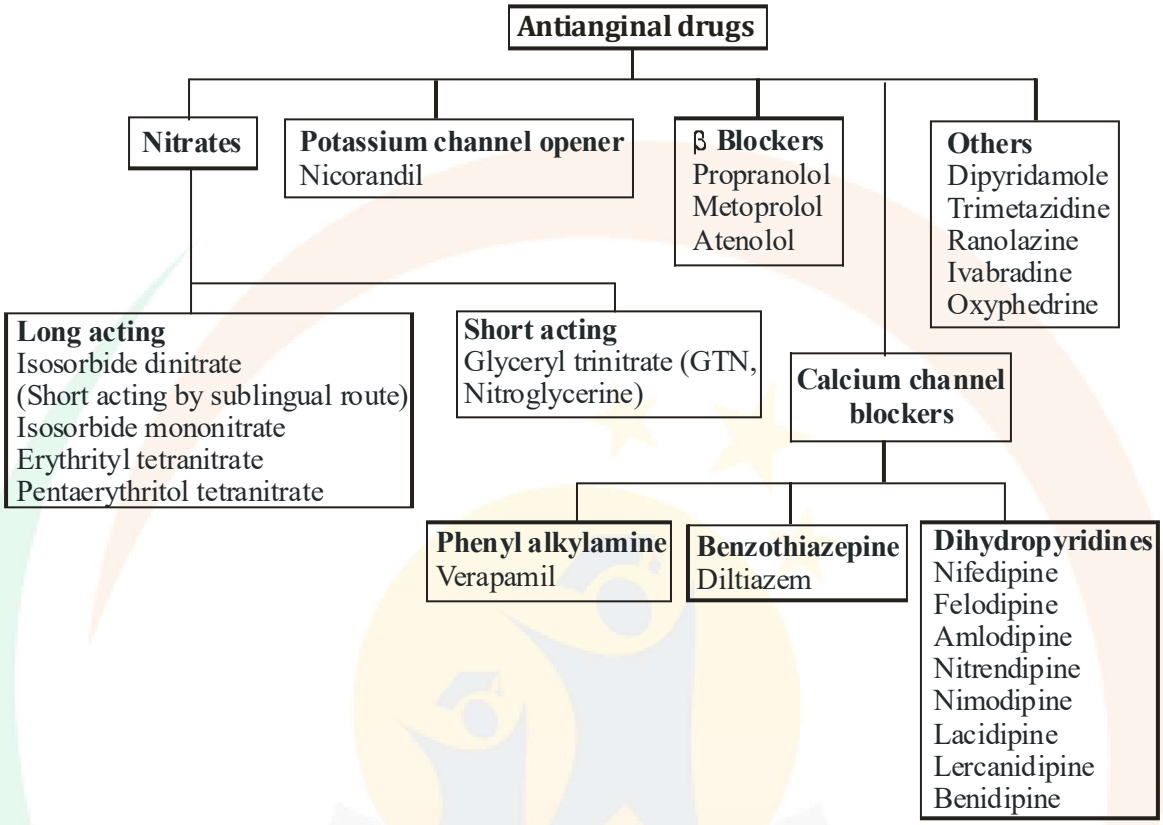
β- ADRENERGIC BLOCKING DRUGS: -



❒ Pharmacological actions of β – blockers: -

ORGAN/ PART OF BODY	PHARMACOLOGICAL ACTIONS
Eye	**Reduces secretion of aqueous humor, i.o.t. is lowered**
Uterus	• Relaxation of uterus in response to isoprenaline selective β2 agonists is blocked by propranolol. • However, normal uterine activity is not significantly affected
Metabolic	• Plasma triglyceride level and LDL/HDL ratio is increased • Blocks adrenergically induced lipolysis • Inhibits glycogenolysis in heart, skeletal muscles and in liver
Blood pressure	**Decreased blood pressure**
Local anaesthetics	Propranolol is as potent a local anaesthetic as lidocaine but → **not clinically used.**

CLASSIFICATION



MECHANISM OF ACTION

Organic nitrates are rapidly denitrated enzymatically in the smooth muscle cell to release the reactive free radical nitric oxide (NO) which activates cytosolic guanylyl cyclise

→ Increased cGMP

→ Causes dephosphorylation of myosin light chain kinase (MLCK) through a cGMP dependent protein kinase .

→ Reduced availability of phosphorylated (active) MLCK interferes with activation of myosin

→ It fails to interact with actin to cause contraction

ACTIONS

- **CVS** :- The most prominent action of Ang II is vasoconstriction—produced directly as well as by enhancing Adr/NA.
  Angiotensin II increase force of contraction by promoting Ca^{+} INFLUX
- **Smooth muscles**:- Ang II contracts many visceral smooth muscles in vitro, but in vivo effects are insignificant.
- **Adrenal cortex**:- They enhance synthesis and release of aldosterone which acts on distal tubule in kidney to promote Na+ reabsorption and K^{+}/H^{+} excretion.
- **Kidney** :- Retention of sodium and water takes place .
- **CNS** :- Activate or induce thirst centre & ADH release
- **Peripheral sympathetic structure** :- Release Adr from adrenal medulla stimulates autonomic ganglia & increase the output NA from adrenergic nerve endings .

ACE INHIBITORS

- **Teprotide was the first ACE inhibitor to be synthesised taking a lead from the bradykinin potentiating factor found in pit viper venom**
  C = **cough** (reduced by iron supplement & aspirin)**(gpat 2018)**
  A = angioedema
  P= prodrug (except captopril & lisinopril)
  T = Taste disturbance (dysguseia)
  O = Orthostatic hypotension (when combined with diuretics)
  P =Pregnancy contraindicated (foetopathic)
  R= Bilateral Renal artery stenosis (contraindicated)
  I= Increase K+(hyperkalemia)
  L= Lower the formation of Ang 2

❖ **IMPORTENT DIFFERENCE CAPTOPRIL & OTHER ACE s**

- Less potent , fast & short duration of action
- Less absorption in presence of food in GI
- Because of fast & short duration of action it cause postural hypotension .

❖ **ENLAPRILAT**:- I.V route = used in hypertensive emergencies

Uses:-

- Sclerodermacrisis
- Hypertension
- CHF Evolving
- MI Diabetic neuropathy
- Diabetic retinopathy

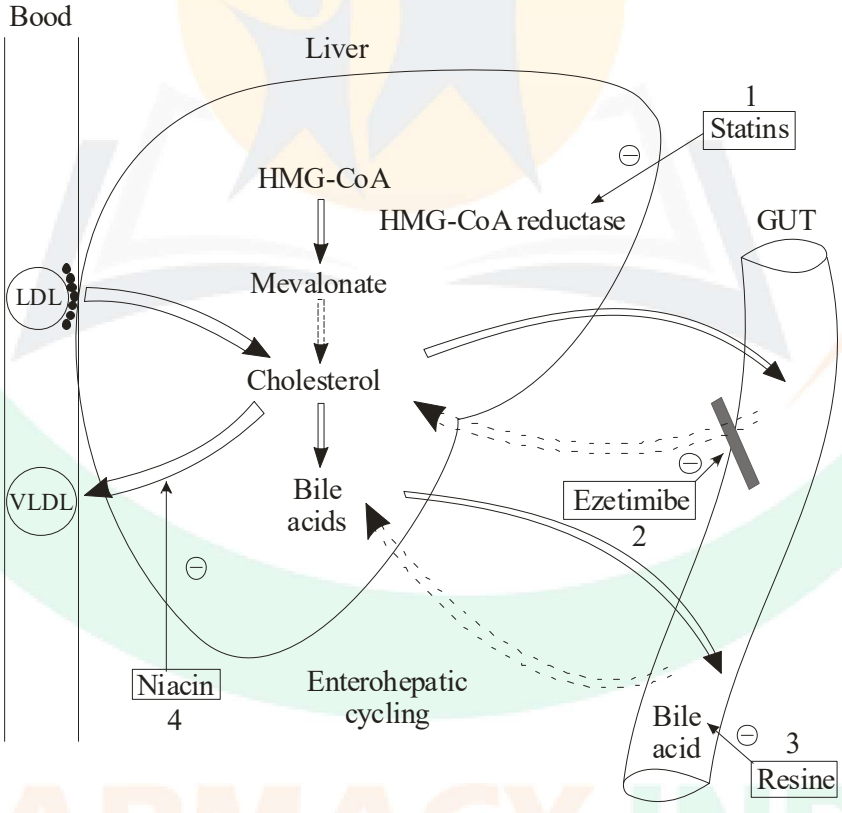
HYPOLIPIDAEMIC DRUGS

Hypolipidaemic drugs are those which lower the level of lipid and lipoproteins in blood

HYPOLIPIDAEMIC DRUGS

HMG-CoA reductase inhibitors (Statins)	Lipoprotein lipase activators (PPARα agonists: Fibrates)	Sterol absorbtion inhibitor
Lovastatin Simvastatin Pravastatin Atorvastatin Rosuvastatin Pitavastatin	Gemfibrozil Bezafibrate Fenofibrate	Ezetimibe

Bile acid sequestrants	Lipolysis and triglyceride synthesis inhibitors
Cholestryramine Colestipol Colesevelam	Nocotinic acid



Adverse effect of HMG-CoA inhibitors

1. Hepatotoxicity
2. Myopathy
3. Gastrointestinal disturbance

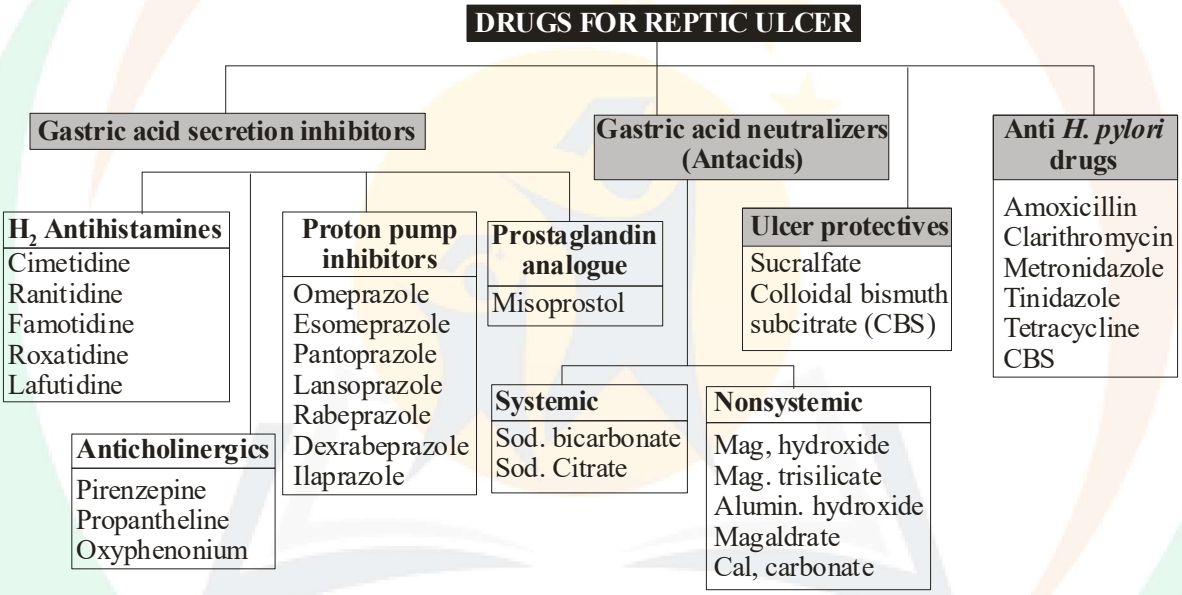
Chapter

11

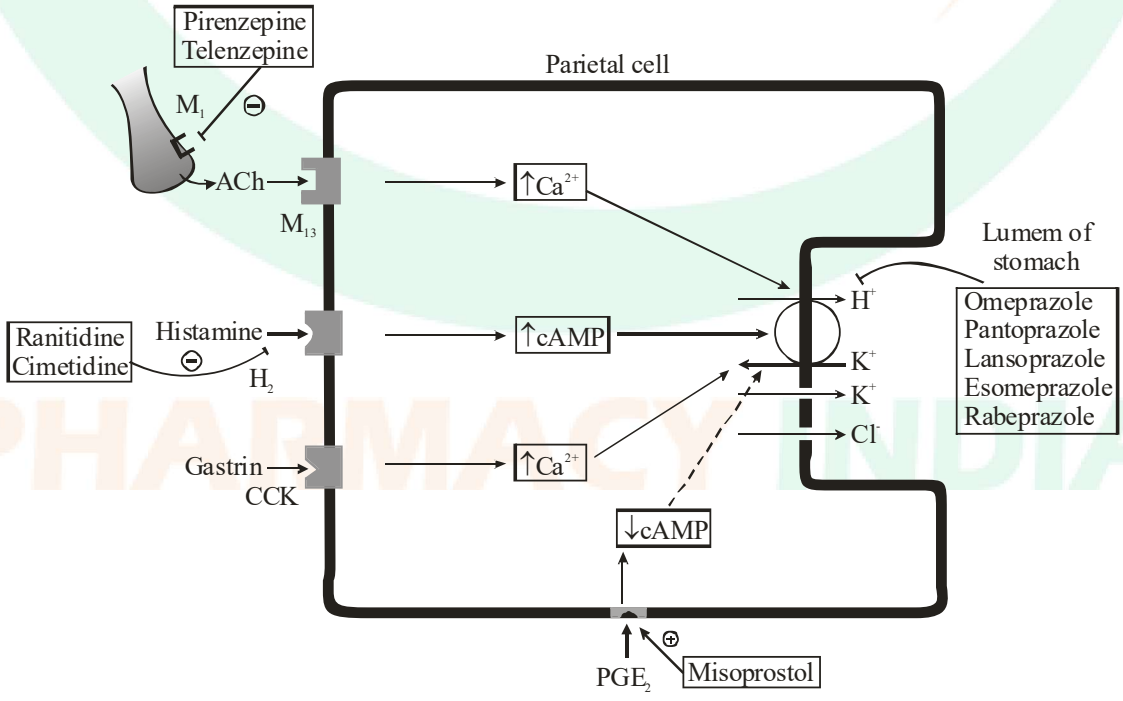
GASTROINTESINAL DRUGS

Peptic ulcers are the result of deterioration of the mucosal lining of the stomach and duodenum that can lead to damage of the gastrointestinal tissue.

Peptic ulcer disease arises from the imbalance between defensive factors (mucus , bicarbonate and mucosal blood flow) and aggressive factors (acid, pepsin, NSAIDs and *Helicobacter pylori)*



MACHANISM OF ACTIION



Chapter 13

CHEMOTHERAPY OF NEOPLASTIC DISEASES

The anticancer drugs either kill cancer cells or modify their growth.

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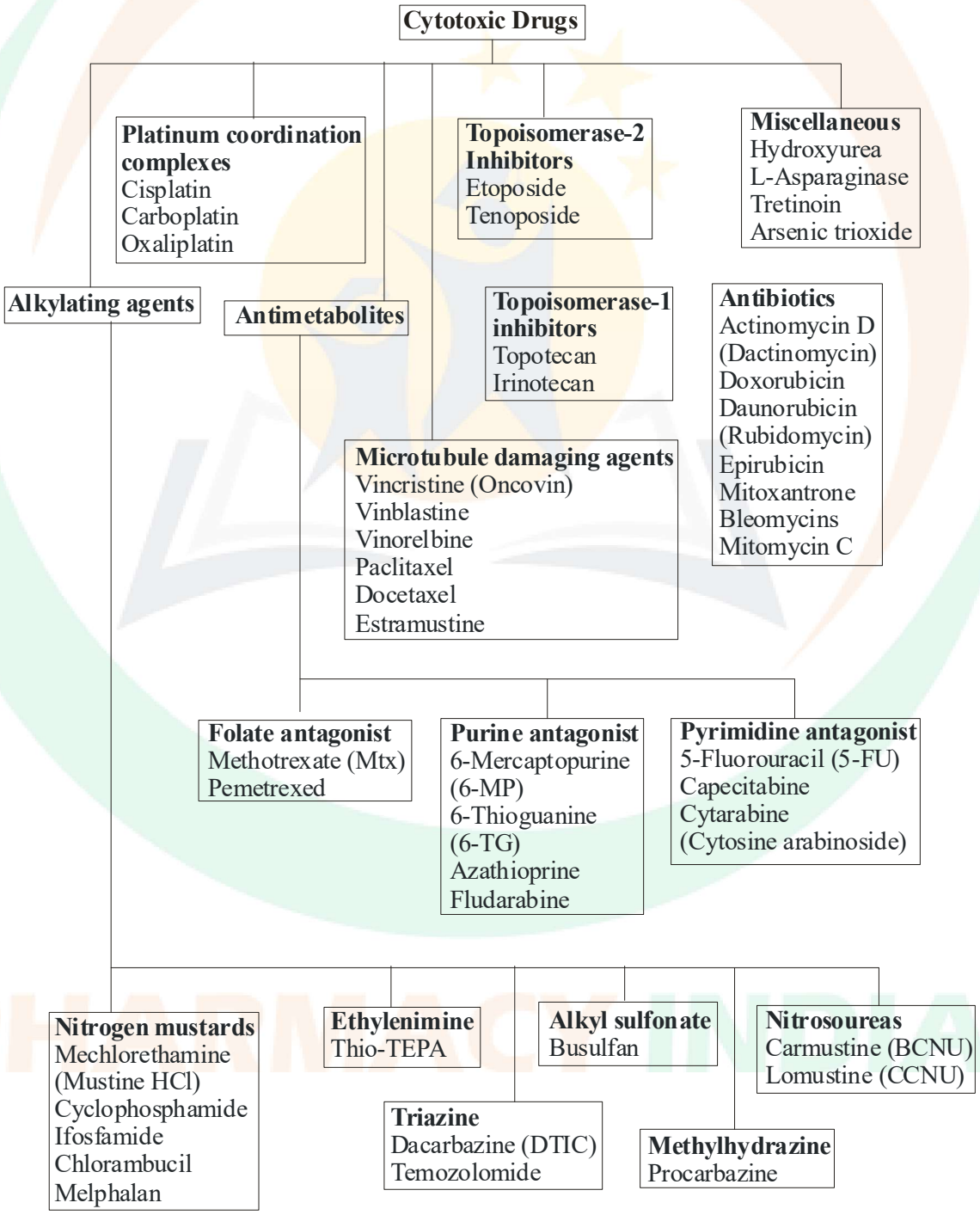


- These can cause delayed neutropenia.
- Dacarbazine primarily affects RNA and protein synthesis unlike alkylating agent.
- Flu like symptoms of dacarbazine can be seen.
- **Streptozocin can destroy beta cells of pancreas, and is thus used for islet cell tumors. It has minimum bone marrow toxicity.**

PLATINUM COMPOUNDS

- These include cisplatin, carboplatin and oxalplatin.
- These **are not alkylating agents** in true sense but are discussed here because of similar mechanism of action.
- Difference is that these use platinum instead of alkyl group to form dimers of DNA.
- Most common adverse effect of these agents is nausea and vomiting (maximum among all anti-cancer drugs).
- **Cisplatin is most nephrotoxic whereas carboplatin is more hematotoxic (bone marrow suppressant).**
- **Cisplatin is always given as slow i.v. infusion (never bolus) to prevent intense nausea and acute rise in serum creatinine.**
- **Cisplatin reduces all ions in serum i.e. causes hypomagnesemia, hypokalemia, hypocalcemia and hypophosphatemia. (Remember, cyclosporine, an immunosuppressive drug cause hyperkalemia).**

METHOTREXATE

- Methotrexate is the **inhibitors of dihydrofolate reductase (DHFRase).**
- This drugs also **inhibit thymidylate synthase (TS)** and the enzymes involved in early purine synthesis.
- Methotrexate has 50000 time more affinity than DHFA . it is **pseudo-reversible with DHFReductase**
- Methotrexate has high plasma protein binding (more than 50% PPB)
- **Methotrexate inhibit DHFReductase which leads to the decrease in level of folic acid , so to avoid this toxicity of methotrexate to normal cells can be reduced by administration of N5 formyl- tetrahydrofolic acid (folinic acid, citrovorum factor or leucovorin).**
- Aspirin & sulphonamides enhance toxicity of methotrexate by decrease its renal tubular secretion
- Kills cells in S- phase
- **Alkalinisation** of urine done on administration of methotrexate to avoid nephrotoxicity
- Uses of methotrexate

  Inhibit – immunosuppressant

  C – Crohn's disease

  A – Abortion

  N – Non Hodgkin Lymphoma

  C – Choriocarcinoma

  E – Ectopic pregnancy

  R – Rheumatoid arthritis & Psoriosis

Methotrexate is the drug of choice for the treatment of chorio carcinoma

PREMETRIXED

- Has **more affinity for thymidylate synthase** and less for DHFReductase
- Side effect :- **Hand & foot syndrome** (erythromatous rashes in hands /foots) **dexamethasone** can used to prevent this → or pre treatment can reduce its incidence **folic acid & Vit B 12.**
- **NSAIDS** not given because affects CL.

PURINE ANALOGS

- **6-mercaptopurine (6-MP) and 6-thioguanine (6-TG)** are the purine antimetabolites that are activated by hypoxanthine-guanine phosphoribosyl transferase (HGPRTase).
- 6-MP is metabolized by **xanthine oxidase** , so when administered along with **allopurinol (xanthineoxidase inhibitor), the dose of 6-MP (and also azathioprine) should be reduced to 1/ 4th of the original dose.**
- Use of 6MP /6TG → acute lymphatic leukemia in children.
- **Hyperurecemia** can occur ,reduced by allopurinol.

AZATHIOPRINE

- Suppress cell mediated immunity (CMI)
- It is vevry potent immunosupressent
- It convert into 6MP
- Used in auto immune disese → rheumatoid arthritis
  - → Ulcerative colitis
  - → Organ transplantation

PYRIMIDINE ANTAGONIST

- **5- fluorouracil** convert into **5 flouro deoxy guinosine monophosphate which inhibit thymidylate synthase**
- **Cisplatin ,oxalipaltin & leucovorin enhance the efficacy of 5-FU**
- A 1% topical solution has good result in superficial basal cell carcinoma & in actinic kerotosis(growth in skin)
- Fludarabine is drug of choice for chronic lymphocytic leukemia (CLL).
- Capecitabine and doxyfluridine is oral prodrug of 5FU cause hyperbilirubinemia

MICROTUBULE DAMAGING AGENTS

MOA:- Vincristine, vinblastine and vinorelbine are the vinca alkaloids that **act by inhibiting polymerization of microtubules (tubilin protein).**

- These are effective in M-phase of cell cycle.
- Side effects of **vincristine is alopecia & peripheral neuropathy**
- Vincristine with glucocorticoids is the treatment of choice for inducing remission in childhood leukemias.
- It can also be used for pediatric solid tumors (Wilm's tumor, neuroblastoma and rhabdomyosarcoma) and lymphomas.

VINBLASTIN

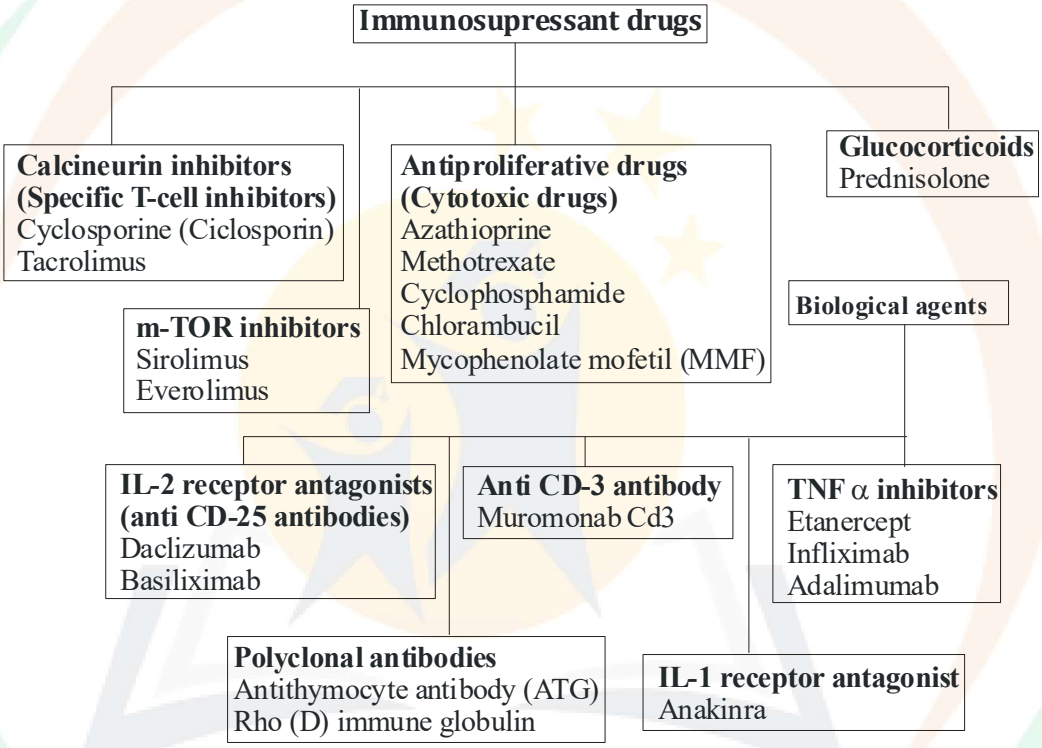
- **Bone marrow is more prominent**
- **Alopecia is less than vincristene**

Chapter

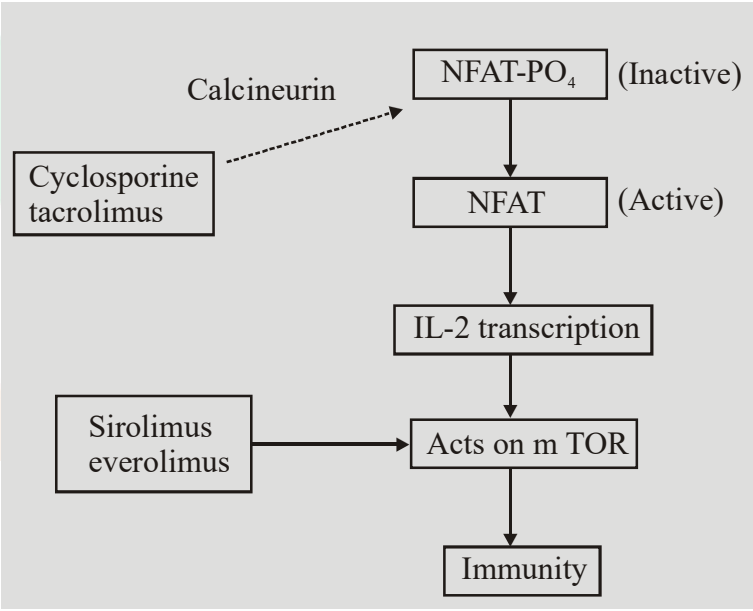
14

IMMUNOSUPPRESSANT DRUG

Immunosuppressants are drugs which inhibit cellular/humoral or both types of immune responses.



CALCINEURIN INHIBITORS



- Continuous administration of glucocorticoids can increase the catabolism of IgG.
- Theseare used as first line immunosuppressive drugs for solid organ as well as hematological stem cell transplant recipients.
- These are also used for the treatment of graft rejection and graft versus host disease (GVHD), treatment of ITP, rheumatoid arthritis and bronchial asthma.
- Cyclosporine can cause nephrotoxicity, hepatotoxicity, hypertension, hyperkalemia, hyperlipidemia, hyperuricemia, hyperglycemia, hirsutism, gum hyperplasia and neurotoxicity (tremor, headache, motor disturbance and seizures).