

**SCHOOL OF SCIENCE AND TECHNOLOGY**

**APPLIED SCIENCE-II**

**BSN 2306**

**PHARMACOLOGY**



**BANGLADESH OPEN UNIVERSITY  
SCHOOL OF SCIENCE AND TECHNOLOGY**

# APPLIED SCIENCE–II

## BSN 2306

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# BANGLADESH OPEN UNIVERSITY

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## **Preface**

Applied Science-II is one of the foundation courses of health science and is very important component of students in medical disciplines. B.Sc.-in-Nursing students have to learn the course very attentively for their career development. All modules for distance learners have some specificity and specialty in respect of the style or format of presentation. Here lesson begins with learning objectives and ends with exercises. Self-activities are so designed that the learner will have the base at the text and will have to work a little more for a completed answer. Important messages can easily be given the self-activity exercise that has not been totally covered in the short text. In fact learners will get the clue for further reading through the self-assessment questions. Most of the portions of the course are self-illustrating but some identified areas have been recorded for audio-visual aid. The assigned teacher will demonstrate practical portion of the course. This mark will be added at the final examination. This course has been prepared by active participation of the course development team and has been examined by the referee. In spite of it, any suggestion would be highly appreciated regarding further enrichment of the book.

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## Unit 3: Systemic Pharmacology

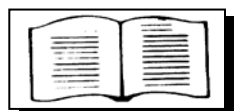
### Lesson 1: Analgesics, Antipyretics and Antiinflammatory Drugs

#### 1.1. Learning Objectives



At the end of this lesson you will be able to-

- ◆ define and classify antipyretics and analgesics
- ◆ differentiate narcotic and non narcotic analgesics
- ◆ describe acetic acid derivatives.



#### 1.2. Definition

Analgesics are group of drugs that reduces pain with or without degree of sedation.

Antipyretics are drugs that reduce body temperature.

Usually analgesics have antipyretic effect and antipyretic has analgesic effect.

#### 1.3. Classification of Analgesics

##### A. Non-narcotic analgesics (*Mild to moderate pain*)

- Aspirin
- Paracetamol (Acetaminophen)
- Phenacetin

##### B. Narcotic analgesics (*Moderate Pain*)

- Pentazocin (Talacen/ Talwin– Tab 50 mg)

##### C. Narcotic analgesics (*severe pain*)

- Codeine phosphate
- Morphine
- Pethidine (Meperidin)

#### 1.4. NSAIDS

- Aspirin
- Diclofenac
- Fenamates
- Fenoprofen



- Ibuprofen
- Indomethacin
- Ketoprofen
- Naproxin
- Piroxicam
- Tolmetin etc.

### **Aspirin (Acetylsalicylic Acid)**

A weak organic acid irreversibly acetylating cyclooxygenase and hence a unique NSAID. Relieves mild to moderate pain, gives symptomatic relief of inflammation and reduces fever. Used in low dose to prevent blood clotting hence used to prevent risk of heart attack, embolism to brain, post-surgery thromboembolism.

1. Aspirin reduces prostaglandin biosynthesis and thus relieves pain and inflammation.
2. Modifies the temperature regulating centre in the brain, dilates blood vessels, increases sweating and relieves fever.
3. Prevents thromboxane in blood platelets and inhibits blood clot formations.

Possible risks of aspirin include irritation of stomach, bleeding and ulceration; hearing loss, decreased numbers of WBC and platelets, hemolytic anemia and respiratory paralysis with respiratory acidosis.

### **1.5. Acetic Acid Derivatives**

(Indomethacin, Diclofenac, Tolmetin, Etodolac, Sulindac, Ketorolac etc.)

Used for effective relief of mild to moderate pain and inflammation. All of them except ketorolac are used for osteoarthritis; all of them except ketorolac and etodolac are used for rheumatoid arthritis.

These drugs are thought to reduce tissue concentration of prostaglandins and related compounds. Thus they reduce pain and inflammation.

Possible risks include GI pain, ulceration and bleeding; liver and kidney damage; fluid retention; bone marrow depression, mental depression, confusion; lung fibrosis pneumonitis (sulindac), aseptic meningitis (diclofenac) and skin reactions.

### **Propionic Acid Derivatives**

(Ibuprofen, naproxen, fenoprofen, Ketoprofen, flurbiprofen, oxaprozin)

Used as antiinflammatory, analgesic and antipyretic agent for chronic treatment of rheumatoid and osteoarthritis.

Well absorbed on oral administration and almost totally albumin bound.

Adverse and side effects include GI problems, headache, tinnitus and dizziness.



**Exercise:** Write short notes on Piroxicam, Mefenamic acid and phenylbutazone.

### Paracetamol (Acetaminophen)

Acts as antipyretic agent with poor antiinflammatory effect and no effect on blood clotting.

Paracetamol inhibits prostaglandin biosynthesis in the CNS and have less effect on cyclooxygenase. Rapidly absorbed from GI tract, a first- pass metabolism occurs in intestinal cells and in the hepatocytes. A portion is metabolized to non-toxic and a part to potentially dangerous quinoneimine that reacts with sulfhydryl groups. Paracetamol is excreted through kidney.

Adverse effects may be skin rash, minor allergic reactions. Renal tubular necrosis and hypoglycaemic coma is rare complications. Hepatic necrosis may happen at larger dose.



**Exercise:** Write short notes on Gold salts, D-Penicillamine, Colchicine, Allopurinol, Sulfinpyrazone.

### Morphine

The major narcotic analgesic drug contained in opium. Used for analgesia, diarrhoea treatment and relief of cough.

- ◆ Morphine causes analgesia by altering CNS perception of pain and also by raising the pain threshold at spinal cord level.
- ◆ It may cause depression of the respiratory center at brain, which may lead to death.
- ◆ It creates a feeling of contention, well- being and euphoria.
- ◆ Morphine causes miosis of pupil.

- ◆ Morphine causes emesis but relieves diarrhoea and dysentery.
- ◆ It causes urticaria, sweating and vasodilatation. Can cause bronchoconstriction, respiratory depression and raised CSF pressure.

Adverse effects include severe respiratory depression, vomiting, dysphoria, and urinary retention and withdrawal responses.



## 1.6. Exercises

### 1.6.1. Multiple Choice Questions

**Tick (✓) the correct answer**

1. A unique NSAID is
  - a. aspirin
  - b. paracetamol
  - c. morphine
  - d. none of the above.
2. Morphine is a
  - a. mild analgesic
  - b. nonnarcotic analgesic
  - c. narcotic analgesic
  - d. none of the above.
3. Paracetamol has
  - a. strong effect on blood clotting
  - b. no effect on blood clotting
  - c. both of the above
  - d. none of the above.

### 1.6.2. Short Questions

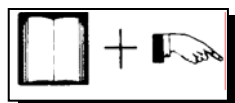
1. Define analgesics and antipyretics.
2. Write down the indications for usage of aspirin.
3. Name some acetic acid derivative among NSAID.
4. What is Paracetamol?

### 1.6.3. Analytical Questions

1. Classify analgesics.
2. Describe how aspirin acts.
3. What do you know about propionic acid derivatives?
4. What do you know about Morphine?

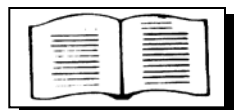
## Lesson 2: Effect of Drugs on Nervous System

### 2.1. Learning Objectives



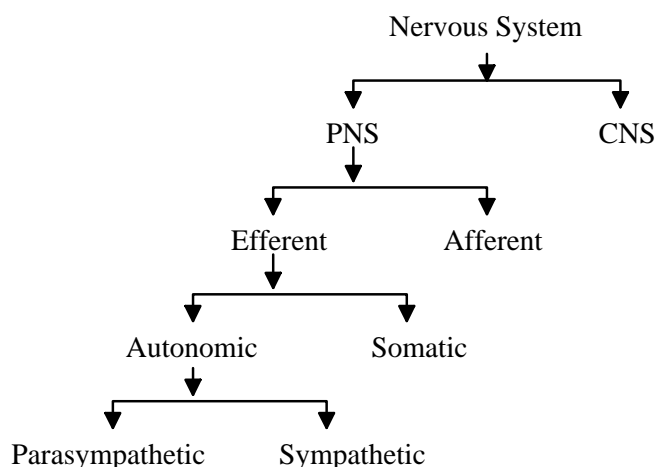
At the end of this lesson you will be able to-

- ◆ know anatomical and functional divisions of nervous system
- ◆ classify autonomic drugs
- ◆ classify drugs affecting CNS.



### 2.2. Nervous System

Nervous system is divided into two anatomical divisions



- i. *Central Nervous System* (CNS) comprising brain and spinal cord.
- ii. *Peripheral Nervous System* (PNS), which includes neurons, located outside brain and spinal cord. PNS has *efferent wing* whose neurons carry signals from CNS to peripheral tissues and *afferent wing* whose neurons carry information from periphery to CNS.

Functionally efferent wing can be divided into *Somatic system* which is involved in voluntary controlled functions such as contraction of skeletal muscles; and *Autonomic system* which controls involuntary functions of the body as per daily need and requirement of the body without conscious participation of mind.

Automatic system is divided into *parasympathetic network*, which maintains essential bodily functions like digestion, excretion, etc., and *sympathetic network*, which adjusts the body at stressful situations like trauma, fear, cold, etc.

### 2.3. Autonomic Drugs

Drugs that produce their effects (therapeutic) by mimicking or altering the function of the autonomic nervous system (ANS) are called autonomic drugs. They may act by stimulating any part of the autonomic nervous system or by blocking the ANS actions. They are discussed sequentially.

#### A. Cholinergic agonist

- Direct acting
- Acetylcholine
- Bethanechol
- Carbachol
- Pilocarpine
- Indirect acting (reversible)
- Edrophonium
- Neostigmin
- Physostigmin
- Pyridostigmine
- Indirect acting (irreversible)
- Echothiophate
- Isoflurophate

#### B. Cholinergic antagonists

- Antimuscarinic agents
- Atropine
- Ipratropium
- Scopolamine
- Ganglionic blockers
- Mecamylamine
- Nicotine
- Trimethaphan
- Neuromuscular blockers
- Succinylcholine

- Tubocurarine
- Doxacurium
- Metocurine
- Mivacurium
- Pancuronium.

C. Adrenergic agonists

- Direct acting
- Clonidine
- Dopamine
- Epinephrine
- Isoproterenol
- Metaproterenol
- Methoxamine
- Norepinephrine
- Terbutaline
- Indirect acting
- Amphetamine
- Tyramine
- Direct and indirect acting (mixed action)
- Ephedrine
- Metaraminol

D. Adrenergic blockers

- *Alpha- blockers*
- Doxazosin
- Phenoxybenzamine
- Phentolamine
- Prazosin
- Terazosin
- *Beta- blockers*

## Systemic Pharmacology

- Acebutolol
- Atenolol
- Labetalol
- Metoprolol
- Nadolol
- Pindolol

### 2.4. Drugs Affecting CNS

#### A. Anxiolytic and hypnotic drugs

- *Benzodiazepines*
    - Alprazolam
    - Chlordiazepoxide
    - Clonazepam
    - Clorazepate
    - Diazepam
    - Lorazepam
  - *Midazolam*
    - Estazolam
    - Flurazepam
    - Triazolam
    - Other anxiolytic drugs
    - Buspirone
    - Hydroxyzine
    - Zolpidem
    - Barbiturates
    - Phenobarbital
    - Pentobarbital
    - Thiopental
  - *Nonbarbiturate sedatives*
- |             |
|-------------|
| Anxiolytics |
| Hypnotic    |

- Antihistamines
- Chloralhydrate
- Ethanol

*B. CNS stimulants*

- Psychomotor stimulants
- Amphetamine
- Caffeine
- Cocaine
- Methylphenidate
- Nicotine
- Theobromine
- Theophylline
- Psychotomimetic drugs
- Lysergic acid diethylamide (LSD)
- Phencyclidine (PCP)
- Tetrahydrocannabinol (THC)

*C. Antidepressant drugs*

- Tricyclic / Polycyclic
- Amitriptyline
- Amoxapine
- Desipramine
- Doxepin
- Imipramine
- Maprotiline
- Nortriptyline
- Trimipramine
- Selective serotonin reuptake inhibitors
- Fluoxetine
- Nefazodone



## Systemic Pharmacology

- Paroxetine
- Sertraline
- Monoamineoxidase inhibitors
- Isocarboxazid
- Phenelzine
- Tranylcypromine
- Drugs used to treat mania
- Lithium salts

### *D. Neuroleptic drugs*

- Phenothiazines
- Chlorpromazine
- Fluphenazine
- Prochlorperazine
- Thioridazine
- Benzisoxazoles
- Risperidone
- Dibenzodiazepines
- Clozapine
- Butyrophenones
- Haloperidol
- Thioxanthenes
- Thiothixene

### *E. Antiepileptics*

- Carbamazepine
- Clonazepam
- Diazepam
- Ethosuximide
- Phenobarbital
- Phenytoin

- Primidone
- Valproic acid

*F. Antiparkinsonian drugs*

- Amantadine
- Antimuscarinic agents
- Bromocriptine
- Carbidopa
- Deprenyl
- Levodopa

*G. Anaesthetics*

- Local Anaesthetics
- Lignocaine
- Procaine
- Tetracaine
- Bupivacaine
- General Anaesthetics
- Halothane
- Isoflurane
- Nitrous oxide
- Enflurane
- Methoxyflurane



## **2.5. Exercises**

### **2.5.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

1. CNS includes
  - a. autonomic nervous system
  - b. sympathetic nervous system
  - c. brain and Spinal cord
  - d. none of the above.
2. Dopamine is
  - a. a directly acting adrenergic agonist
  - b. a direct indirectly acting adrenergic agonist
  - c. an indirectly acting adrenergic agonist
  - d. none of the above.
3. Phenobarbitone is mainly used for
  - a. hypertension
  - b. epilepsy
  - c. depression
  - d. none of the above.

### **2.5.2. Short Questions**

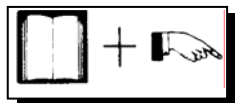
1. Define CNS, PNS, and ANS.
2. Name Antiparkinsonian drugs.
3. Name Antiepileptic drugs.
4. Name local anaesthetics.

### **2.5.3. Analytical Questions**

1. Classify autonomic drugs.
2. Name Psychomotor stimulants.
3. Name Anxiolytics and Hypnotics.

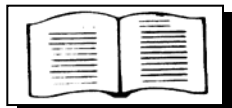
## Lesson 3: Drugs Acting on Cardiovascular System

### 3.1. Learning Objectives



At the end of this lesson you will be able to-

- ◆ classify cardiovascular drugs
- ◆ name drugs effective against hypertension
- ◆ name drugs effective for blood diseases
- ◆ tell about drugs acting against hyperlipidaemia.



### 3.2. Classification of Cardiovascular Drugs

#### A. Cardiac Glycosides

- Digitoxin
- Digoxin

**Exercise:** Describe difference between digoxin and digitoxin. Describe contraindication for usage of digitalis.

#### B. Antiarrhythmic Drugs

*Class I - Blocks Na<sup>+</sup> channel*

- Disopyramide
- Quinidine
- Lignocaine, procainamide
- Phenytoin

*Class II – Blocks sympathetic activity*

- Propranolol
- Metoprolol
- Atenolol

*Class III – Delays polarization (K<sup>+</sup> channel blockers)*

- Bretylium
- Amiodarone

*Class IV – Calcium channel blockers*

- Verapamil
- Nifedipine
- Diltiazem

**3.3. C. Antihypertensive Drugs**

1. Diuretics

- Carbonic anhydrase inhibitors- acetazolamide
- Loop diuretics- Bumetanide, furosemide, Ethacrynic acid
- Thiazides- Chlorothiazide, Hydrochlorothiazide, Chlorthalidone  
K<sup>+</sup>-sparing- Spironolactone, Triamterene, Amiloride.
- Osmotic- Mannitol, Urea.

2. Sympatholytic agents

Acting on CNS- Methyldopa, Clonidine

Autonomic ganglion blockers- Trimethaphan

Acting on postganglionic sympathetic neuron- Guanethidine, Reserpine

Receptor blockers

- Alpha- receptor- Prazocin, Phentolamine, Terazosin
- Beta- receptor- Propranolol, Atenolol, Metoprolol, Acebutalol.

3. Vasodilators

Arterial- Hydralazine, Diazoxide

Calcium antagonist Verapamil, Nifedipine, Diltiazem, Amlodipine

Venular and arteriolar- Prazosin, Nitroprusside

4. Angiotensin Converting Inhibitors Ramipril, Captopril, Enalapril

**D. Antianginal Drug**

**E. Coronary Vasodilators**

*Nitrites and Nitrates*

- Inhalation- Amylnitrite, Sodium nitrite
- Sub-lingual- Nitroglycerin, Glyceryl trinitrate

- Oral - Isosorbide Mono and dinitrate
- Mannitol hexa- nitrate.

*Beta blockers*

- Propranolol
- Oxprenolol

*Papavarine and related drugs*

- Papavarine
- Ethaverine

*Calcium channel blockers*

- Verapamil
- Nifedipine
- Diltiazem

*Newer drugs*

- Dipyridamole, Perhexiline



**Exercise:** Describe mechanism of action of Beta-blockers.

### 3.4. Drugs Affecting on Blood Disorders

#### A. Platelet inhibitors

- Aspirin
- Dipyridamole
- Ticlopidine

#### B. Anticoagulants

- Heparin
- Warfarin
- Enoxaprin

#### C. Antianaemics

- Iron

## Systemic Pharmacology

### Antihyperlipidaemic drugs

- Cholestyramine
  - Clofibrate
  - Gemfibrozil
  - Lovastatin
  - Simvastatin

- Cyanocobalamin (B<sub>12</sub>)
- Folic acid
- Erythropoietin
- Hydroxyurea (sickle cell anaemia)

### D. Antihaemorrhagics

- Vitamin K
- Aminocaproic acid
- Tranexamic acid

### E. Thrombolytics

- Streptokinase
- Urokinase
- Anistreplase
- Alteplase(tpA)

### 3.5. Exercises

#### 3.5.1. Multiple Choice Questions

Tick (✓) the correct answer

1. Lignocaine is a
  - a. class- IV antiarrhythmic drugs
  - b. class- I antiarrhythmic drugs
  - c. cardiac glycosides
  - d. none of the above.
  
2. Furosemide is a
  - a. loop diuretics
  - b. potassium sparing diuretics
  - c. sympathetic agent
  - d. none of the above.
  
3. Streptokinase is a
  - a. thrombolytic drug
  - b. platelet inhibitor
  - c. drug of choice for anaemia
  - d. none of the above.

#### 3.5.2. Short Questions

1. Classify diuretics.
2. Name few coronary vasodilators.
3. Name some antihyperlipidaemic drugs.

#### 3.5.3. Analytical Questions

1. Classify antiarrhythmic drugs.
2. Classify antihypertensive drugs.
3. What are the drugs against blood disease?



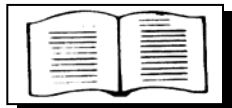
## Lesson 4: Drugs Acting on Gastrointestinal and Respiratory System

### 4.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ describe antacids , purgatives and antiemetics
- ♦ identify drugs used to treat Peptic Ulcer Disease.



### 4.2. Gastric Antacids

Gastric antacids are weak bases that neutralize or lower gastric acidity producing symptomatic relief of pain. pH of antacids are higher so they are not used as intravenous preparations.

**Exercise:** Describe advantages and disadvantages of systemic and non systemic antacids

#### Purgatives

Purgatives are the agents that promote defecation as a result of muscle contraction.

#### Laxatives

Laxatives are the agents that evacuate soft, formed stool without griping and without much loss of water.

#### Cathartics

Cathartics are the agents that evacuate more fluid stool.



**Exercise:** Write down mechanism of action of purgatives.

### 4.3. Antiemetics

Antiemetics are drugs used specifically to prevent or relieve nausea and vomiting.

#### A. Central antiemetics

##### *Specific antiemetics*

- Prochlorperazine

- Chlorpromazine
- Perphenazine

*Nonspecific antiemetics*

- Barbiturates
- Antihistamines
- Promethazine theoclate
- Promethazine hydrochloride
- Diphenhydramine
- Meclizine

*B. Local antiemetics*

Anticholinergic drugs

- Atropine
- Scopolamine
- Bismuth
- Metochlopramide

**4.4. Digestants**

Substances that promote digestion of food are called digestants e.g., Hydrochloric acid, Rennin, Pancreatin, Diastase and Taka diastase.

**4.5. Drugs used to Treat Peptic Ulcer Diseases**

*A. Anticholinergics*

- Hyoscine- N- butylbromide
- Drotavarine
- Oxyphenonium

*B. H<sub>2</sub> receptor blockers*

- Cimetidine
- Ranitidine
- Famotadine

## Systemic Pharmacology

### *C. Prostaglandin analogs*

- Misoprostol

### *D. Proton pump inhibitor*

- Omeprazole
- Lansoprazole

### *E. Antimicrobial agents*

- Amoxicillin
- Bismuth compounds
- Metronidazole
- Tetracycline
- Clarithromycin

Gallstones  
dissolving drugs  
- Chenodeoxy  
cholic acid  
- Ursodeoxycholic  
acid

## **4.6. Antidiarrhoeals**

- Diphenoxylate
- Loperamide
- Kaolin
- Pectin
- Bismuth subsalicylate
- Aspirin
- Indomethacin

## **4.7. Drugs Acting on Respiratory System**

### ***A. Bronchodilators***

Beta adrenergic agonists

- Salbutamol, Terbutaline
- Isoprenaline, Orciprenaline

Alpha agonists

- Adrenaline, Ephedrine
- Corticosteroids
- Cromolyn and nedocromil
- Aminophylline and theophylline

***B. Drugs for Treating Cough***

*Expectorants* are drugs, which increase bronchial secretion or reduce its viscosity and facilitates its removal. *Antitussives* are drugs that act on CNS to raise cough threshold or act peripherally in the respiratory tract to reduce cough impulses or both actions.

*Directly acting expectorants*

- Sodium or Potassium Citrate
- Potassium Iodide
- Guaiacol
- Guaiphenesin

*Reflexly acting expectorants*

- Ipecacuanha
- potassium Iodide
- Ammonium Chloride

*Mucolytic expectorants*

- Bromhexine

*Opiate antitussives*

- Codeine
- Pholcodeine
- Ethylmorphine
- Morphine

*Nonopiate antitussives*

- Noscapine
- Dextromethorphan
- Carbetapentane

***C. Drugs to treat rhinitis***

Alpha - adrenergic agonists

- Phenylephrine
- Oxymetazoline

## Systemic Pharmacology

### Antihistamines (H<sub>1</sub> receptor blockers)

- Chlorpheniramine
- Diphenhydramine
- Loratadine
- Astemizole
- Acrivastine
- Cetirizine Hcl

### Corticosteroids

- Beclomethasone
- Fluticasone
- Triamcelone
- Cromoglycate



#### 4.8. Exercises

##### 4.8.1. Multiple Choice Questions

Tick (✓) the correct answer

1. Antacids are
  - a. strong acids
  - b. weak acids
  - c. weak bases
  - d. none of the above.
2. Omeprazole is a
  - a. proton pump inhibitor
  - b. H<sub>2</sub> receptor blockers
  - c. prostaglandin
  - d. none of the above.
3. Pholcodeine is an
  - a. analgesic
  - b. anticholinergic
  - c. opiate antitussive
  - d. none of the above.

##### 4.8.2. Short Questions

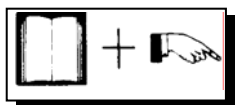
1. Write down name of some antacids.
2. Define Purgative.
3. Name some common antidiarrhoeals.

##### 4.8.3. Analytical Questions

1. Classify anti-emetics.
2. What are the common drugs used to treat Peptic Ulcer Disease?
3. Classify drugs used for different respiratory diseases.

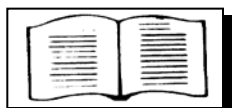
## Lesson 5: Drugs Acting on Endocrine System

### 5.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ classify hypoglycemic drugs
- ♦ define and classify steroids
- ♦ enumerate drugs used for thyroid
- ♦ know about ecbolics and tocolytics.



### 5.2. Hypoglycaemic Agents

Drugs used in the treatment and prevention of Diabetes mellitus and are capable of lowering blood sugar level by different mechanisms.

#### A. *Insulin*

Fast acting (5-12 hours)

- Crystalline/ Regular insulin
- Semilente (Prompt Insulin Zinc suspension)
- Zine Insulin crystal

Intermediate acting (12-24 hours)

- Isophane insulin suspension
- Insulin Zinc suspension (Lente)
- Globulin Zinc Insulin

Long acting (24-36 hours)

- Protamine Zinc Insulin Suspension
- Ultralente Insulin

#### B. *Oral hypoglycaemics*

First generation sulphonylurea derivatives

- Tolbutamide
- Chlorpropamide
- Acetohexamide
- Tolazamide

## Second- generation sulphonylurea derivatives

- Glibenclamide
- Glipizide
- Glicazide
- Glyburide

## Biguanide derivatives

- Phenformin
- Metformin
- Metformin

**5.3. Steroids**

Steroids are water insoluble, fat-soluble organic compounds having cyclopentano phenantherane with various functional groups.

## Classification of Steroid hormones

## 1. Natural Adrenocorticosteroids

## Glucocorticoids (Zona fasciculata)

- Hydrocortisone
- Cortisone
- Corticosterone

## Mineralocorticoids (Zona granulosa)

- Aldosterone
- 11- desoxycorticosterone

## Sex hormones (Zona reticularis)

- Androgen (male)
- Oestrogen (female)
- Progesterone (female)

## 2. Synthetic steroids

## Glucocorticoids-

Long acting (36-72 hour)

Contraceptive pills

- Combined pill
- Sequential pill
- Mini pill
- Post coital or morning after pill



## Systemic Pharmacology

- Dexamethasone
- Betamethasone

Intermediate acting (12-36 hours)

- Triamcinolone
- Prednisolone
- Methylprednisolone

Short acting (8-12 hours)

- Cortisone
- Cortisol
- Corticosterone

### 5.4. Thyroid Drugs

Thyroid hormones are thyroxine ( $T_3$ ) and triiodothyronine ( $T_4$ ). Antithyroid drugs are substances that inhibit thyroid function, thus reducing synthesis and release of thyroid hormones.

#### A. Thyroxine synthesis inhibitors

Thiourea derivatives

- Propylthiouracil
- Methylthiouracil
- Imidazole derivatives
- Carbimazole
- Methimazole

#### B. Iodine tapping inhibitors

- Thiocyanate
- Potassium perchlorate

#### C. Iodine

- Potassium iodide
- Lugol's iodine

## D. Thyroid tissue destroyers

Hypothalamic and anterior Pituitary hormones

- Corticotrophin (ACTH)
- Radioactive Iodine
- Gonadotropin-releasing hormone
- Luteinizing hormone releasing hormone (LHRH)
- Somatostatin
- Somatotropin (GHIH)

Hormones of the Posterior Pituitary

- Desmopressin
- Oxytocin
- Vasopressin (ADH)



**Exercise: Write short notes on corticosteroids.**

## 5.5. Ecbolics and Tocolytics

*Ecbolics* are agents that cause contraction of gravid uterus and help expulsion of its contents. The term *oxytocic* is better used now for ecbolics.

## Classification of Ecbolics

Usage of uterine relaxants

- Delay or postpone labour
- Threatened abortion
- Dysmenorrhoea

## a. Ergot alkaloids

- Natural ergot alkaloids
- Amine alkaloids-ergometrine
- Aminoacid alkaloids-ergotamine, ergotoxine
- Semisynthetic ergot alkaloids
- Dihydroergotamine (DHE)
- Methylegometrine
- Synthetic ergot alkaloids
- Bromocriptine

b. Prostaglandin



**Exercise:** Write short notes on ergotism.

*Tocolytics* are drugs that decrease uterine motility.

*Classification of Tocolytics*

$\beta_2$ -adrenergic receptor agonist

- Salbutamol, Terbutaline, Ritodrine

Calcium channel blockers

- Nifedipine

Ethyl alcohol

Magnesium sulphate

Progesterone

Prostaglandin synthetase inhibitors

- Aspirin
- Udomethacin

Others

- Oxytocin antagonists
- Atropine



## 5.6. Exercises

### 5.6.1. Multiple Choice questions

Tick (✓) the correct answer

1. Crystalline Insulin action last for
  - a. 03 hour
  - b. 5-12 hour
  - c. 24 hour
  - d. none of the above.
2. Zona Fasciculata releases
  - a. flucocorticoid
  - b. mineralocorticoid
  - c. sex hormone
  - d. all of the above.
3. Tocolytics are used for
  - a. delaying poisoning of labour
  - b. dysmenorrhoea
  - c. threatened abortion.
  - d. none of the above.

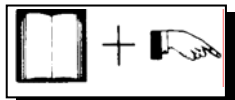
### 5.6.2. Short Questions

1. Define hypoglycaemic agents.
2. What is steroid?
3. Name thyroid hormones.
4. Write down the usage of uterine relaxants.

### 5.6.3. Analytical Questions

1. Classify hypoglycaemics.
2. Classify steroids.
3. How many types of contraceptive pills are there?
4. Classify Ecbolics and Tocolytics.

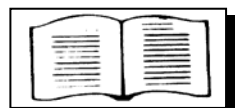
## Lesson 6: Drugs Acting on Systemic Disorders, Pregnancy and Lactation



### 6.1. Learning Objectives

At the end of this lesson you will be able to-

- ◆ describe drugs acting on eye disorders
- ◆ classify drugs acting on cancer disorders
- ◆ enumerate drug affecting pregnancy and lactation.



### 6.2. Drugs Acting on Eye

#### 1. Mydriatics (*cause dilatation of pupil*)

- Adrenaline, Noradrenaline, Amphetamine
- Atropine, Scopolamine
- Homatropine, Cyclopentolate
- Ether, Halothane
- Others Pethidine

#### 2. Myotics (*cause constriction of pupil*)

- Acetylcholine, Carbachol
- Physostigmine
- Pilocarpine
- Ergotamine
- Xylocaine, reserpine
- Opium, Pethidine
- General anaesthetics
- Thiopental Sodium

### 6.3. Anticancer Drugs

#### 1. Antibiotics

- Doxorubicin
- Dactinomycin

- Daunorubicin
  - Bleomycin
  - Plicamycin
2. Alkylating drugs
- Cyclophosphamide
  - Ifosfamide
  - Carmustine
  - Lomustine
3. Antimetabolites
- Methotrexate
  - 5 - Fluorouracil
  - Cytarabine
  - 6 - Mercaptopurine
4. Microtubule inhibitors
- Vincristine
  - Vinblastine
5. Hormones and Antagonists
- Prednisolone
  - Tamoxifen
  - Megestrolacetate
6. Miscellaneous
- Asparaginase
  - Procarbazine
  - Interferon

#### **6.4. Drugs Used in Pregnancy**

No drug is safe in pregnancy; still certain drugs have to be used with caution bearing effects in mind.

## Systemic Pharmacology

*Drugs that probably cause adverse effects when taken during the first trimester*

aminopterin	fluorouracil	opioid analgesics
anticonvulsant	iodides	progestins
antithyroid drugs	isotretinoin	quinine
cytarabine	kanamycin	streptomycin
danazol	mercaptopurine	testosterone
diethylstilbestrol	methotrexate	warfarin
etretinate	misoprostol	

*Drugs that possibly cause adverse effects when taken during the first trimester*

angiotensin converting	lithium	piperazine
enzyme inhibitors	mebendazole	rifampin
busulfan	monoamine oxidase	tetracyclines
chlorambucil	inhibitors	
estrogens	oral contraceptives	

*Drugs that possibly cause adverse effects when taken during the second and third trimesters*

acetazolamide	ethacrynic acid	hydroxyzine
clemastine	fluoroquinolones	promethazine
diphenhydramine	haloperidol	

*Drugs that probably cause adverse effects when taken during the second and third trimesters*

amiodarone	iodides	rifampin
androgens	kanamycin	streptomycin
angiotensin converting	lithium	sulfonamides
enzyme inhibitors	nonsteroidal	sulfonylureas
antithyroid drugs	anti-inflammatory	tetracycline
aspirin	drugs	thiazide diuretics

benzodiazepines	opoid analgesics	tricyclic antidepressants
chloramphenicol	phenothiazines	warfarin
estrogens	progestins	

### 6.5. Drugs Used in Lactation

*Drugs which are contraindicated while nursing; alternatively where nursing must be stopped -*

◆	Radioiodine	◆	Heroin
◆	Anticancer drug	◆	Chloramphenicol
◆	Lithium		

*Drugs to be avoided, there are alternatives*

◆	Diazepam	◆	Nalidixic acid
◆	Barbiturates	◆	Steroids and oral
◆	Tetracycline	◆	Contraceptives
◆	Sulfonamides	◆	Ergot alkaloids

*Drugs with no known risk in normal doses*

◆	Analgesics	◆	Erythromycin
◆	Phenytoin	◆	Antihistamines
◆	Phenothiazides	◆	Digoxin
◆	Penicillins	◆	Heparin
◆	Streptomycin		



**Exercise:** Enumerate the drugs that are used with caution during lactation.





## **6.6. Exercises**

### **6.6.1 Multiple Choice questions**

**Tick (✓) the correct answer**

1. Atropine Causes
  - a. mydriasis
  - b. myosis
  - c. none of above
  - d. all of above.
  
2. Anticancer drug Doxorubicin is an
  - a. antibiotics
  - b. antimetabolite
  - c. both of above
  - d. none of above.
  
3. Thalidomide use in pregnancy is
  - a. safe
  - b. harmful
  - c. non significant
  - d. none of the above.

### **6.6.2. Short Questions**

1. Define myotics and mydriatics.
2. Name some antimetabolites used in cancer therapy.

### **6.6.3. Analytical Questions**

1. Classify drugs acting on eye.
2. Classify anticancer drugs.

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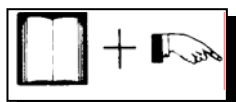


# **PHARMACOLOGY**



# Unit 1: Basics of Pharmacology, Pharmacodynamics and Pharmacokinetics

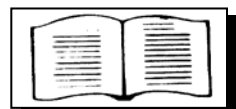
## Lesson 1: Review of Basic Principles of Pharmacology



### 1.1. Learning Objectives

At the end of this lesson you will be able to-

- ♦ define pharmacology and its branches
- ♦ differentiate among drug, medicine and placebo
- ♦ describe about pharmacopoeia.



### 1.2. Definition of Pharmacology

The word pharmacology has been derived from the Greek words - *Pharmakon* meaning a drug and *Logos* meaning science. That is to say, pharmacology is *the science of drug, which deals with detail study of the history, source, chemical nature, route of administration, absorption, biochemical and physiological effect, metabolism, excretion and side effects of drugs in respect to human body.*

In broad spectrum pharmacology may be defined as the branch of science which deals with interactions between living systems and molecules, specially chemical substances introduced from outside the system.

**Medical pharmacology** is the science of materials used for medical purposes as well as the chemical factors in the environment causing disease and the use of certain chemicals as molecular probes for the study of normal biochemistry and pharmacology.

**Clinical pharmacology** is defined as scientific study of drugs in human body.

### Clinical Pharmacology Comprises Two Parts

#### i. Pharmacology

- a. **Pharmacodynamics:** May be defined as the studies of biological and stherapeutic effects of drug i.e. what the drug does to the body.

- b. **Pharmacokinetics:** May be defined as the studies of the absorption, distribution, metabolism and excretion of drugs i.e. what the body does to the drug.

## ii. Therapeutic Evaluations

- a. **Controlled therapeutic trials:** Are studies to find out whether any particular drug is effective in the treatment of disease.
- b. **Therapeutic auditing deals:** with operational research on the use of drugs, evaluation for adverse drug reactions and value analysis for treatment.



**Exercise:** Define clinical pharmacology and therapeutic auditing.

**Toxicology:** is the pharmacology of drugs at higher doses in biological system.

A drug is a small molecule which when introduced into the body interacts at the molecular level and alters body functions

**Pharmacy:** the word has been derived from the Latin word *pharmacia* meaning a drug and is defined as the art or profession of preparing and dispensing drugs and medicines.

**Pharmacotherapeutics:** deals with the practical application of drugs in the treatment and prevention of disease.

**Pharmacogenetics:** deals with the study of genetically mediated variations in drug response.

## 1.3. Drug and Medicine

A drug is any substance or product that is used or intended to be used to modify or explore physiological systems or pathological states for the benefit of the recipient.

A drug is a small molecule which when introduced into the body interacts at the molecular level and alters body functions.

Drugs vary in molecular size. *Smallest is the carbon monoxide and largest are the thrombolytic enzymes.*

*Medicine may be defined as the drug when presented in a final useable form in particular dose pattern and can be used therapeutically. So you can easily utter - all medicines are drugs but all drugs are not medicines.*

All medicines are drugs but all drugs are not medicine.

**Placebo:** the Latin word *placebo* means I will please. Placebo is defined as a harmless, inert chemical, which is given to any person as medicine to satisfy his/ her desire for drug therapy. These inert chemicals may be starch, glucose, sucrose, lactose, etc.

### Usage of Placebo

- i. To prevent habituation and addiction to any drug.
- ii. To satisfy the patient by psychological rather than pharmacological effect of the drug.
- iii. To study and control for scientific evaluation of drug.
- iv. To determine the efficacy of medicines.

### Pharmacopoeia

The word pharmacopoeia has been derived from Greek words *pharmakon* meaning a drug and *poiein* meaning to make and may be defined as an authoritative book containing list, description of drugs and medicinal products, standard method of their identification, production procedure, dispensation, use, etc.

Pharmacopoeia is the official publication for pharmacological preparations.

### Name of Some Pharmacopoeia

- ◆ International pharmacopoeia (IP) : Published by WHO
- ◆ British pharmacopoeia (BP)
- ◆ United State of pharmacopoeia (USP)
- ◆ British pharmaceutical codex (BPC)
- ◆ Indian pharmacopoeia (IP)
- ◆ British National Formulary (BNF).



**Exercise:** Write short note on usage of pharmacopoeia.

### 1.4. British National Formulary

The British Medical Association and Royal Pharmaceutical Society of Great Britain publish this book. It describes the drug descriptions, their



mode of action, indications, side effects and other properties. It also includes drug effects during pregnancy and lactating mother.



## **1.5. Exercises**

### **1.5.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

#### **1. Pharmacology is the study of**

- a. plants
- b. drugs
- c. animals
- d. none of the above.

#### **2. Toxicology deals**

- a. only toxic materials
- b. sometimes toxin preparation
- c. toxic effects of drugs
- d. none of the above.

#### **3. Placebo is used to**

- a. increase habituation
- b. increase addiction
- c. prevent addiction
- d. none of the above.

### **1.5.2. Short Questions**

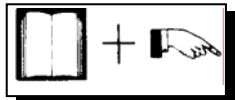
- 1. Define pharmacology.
- 2. Define pharmacodynamics.
- 3. Define pharmacokinetics.
- 4. Define placebo.

### **1.5.3. Analytical Questions**

- 1. Classify clinical pharmacology.
- 2. What is pharmacopoeia? Name five reputed pharmacopoeias in the world.
- 3. Describe usage of placebo.

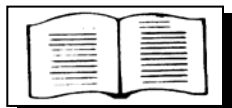
## Lesson 2: Application of Basic Principles of Pharmacology in Nursing Practice

### 2.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ define dose of drugs and posology
- ♦ describe types of dose response relationship
- ♦ differentiate between different dose types.



### 2.2. Introduction

In nursing practice, the first issue of drug that is faced is the dose of medicine and dose-response relationship for any medicine. Hence comprehensive idea about dose is absolutely needed.

Dose is derived from the Greek word *dosis* meaning giving. Dose is defined as the amount of drug, which is taken wholly at a time or in fractional amount within a prescribed time to get biological response.

**Dosage** is defined as giving of medicine in prescribed amount.

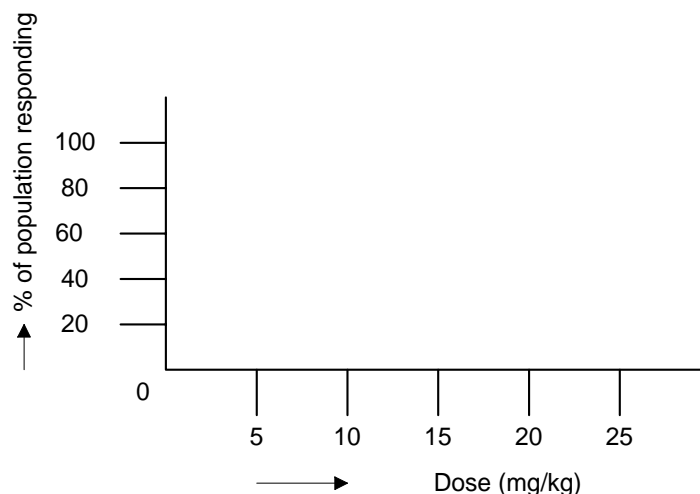
**Posology** is defined as the science dealing with dose for any drug or medicine.

### 2.3. Dose-Response Relationship

Relation between the dose and response of any drug in different concentration is called dose- response relationship. There are two types of relationship-

1. **Graded dose response relationship-** If the dose of any drug is raised gradually, body tissue will respond increasingly up to a certain level making a hyperbolic dose-response curve.

Graded dose-response relationship is important to calculate  $ED_{50}$  and  $LD_{50}$  to display in graph a wide range of drug doses, to compare between agonists and antagonists and also to compare between affinity and efficacy of a drug.



2. **Quantal (All or none) dose response relationship-** Target tissue responds either wholly or not at all to any drug irrespective of the dose. Here responding tissue differs but dose remains same.



**Exercise:** Describe in brief types of dose response relationship.

## 2.4. Different Types of Dose

(ED<sub>50</sub>) - the dose, which produces, specified response in 50% test individuals

(LD<sub>50</sub>) - amount of drug which causes 50% death of the test individuals

1. *Therapeutic (Effective) dose-* commonly used in medical practice, defined as the dose of drug, which produces optimal therapeutic effect.
2. *Median Effective dose (ED<sub>50</sub>)-* the dose, which produces, specified response in 50% test individuals.
3. *Toxic dose-* excess dose that produces toxic effects.
4. *Booster dose-* an additional dose given at a specified time after an initial dose
5. *Test dose-* amount of drug given before main bulk medication to observe the response of the tissue to the drug.
6. *Median Lethal dose (LD<sub>50</sub>)-* amount of drug which causes 50% death of the test individuals.
7. *Minimal dose-* minimum quantity of drug needed for producing desired pharmacological effect.
8. *Maximum dose-* maximum quantity of drug can be given without producing any toxic effect.

**Rough Calculation of Paediatric Dosage**

- # Young's formula (mostly used)-  
Paediatric dose = Adult dose  $\times$  age in year/ (Age + 12)
- # Clerk's rule (most accurate)-  
Paediatric dose = Adult dose  $\times$  (wt. of child in lbs/ 150)
- # Cowling's formula-  
Paediatric = Adult dose  $\times$  (Age on next birth day/ 24)
- # Frid's formula-  
Paediatric dose = Adult dose  $\times$  (Age in months/ 150)

**Pediatric Dosage**

Age	Weight (in kg)	Weight (in lb)	Surface area (m <sup>2</sup> )	% of Adult dose
Birth	3.2	7	0.21	12.5
2 months	4.5	10	0.26	15
4 months	6.5	14	0.34	20
12 months	10	22	0.42	25
18 months	11	24	0.50	30
5 years	18	40	0.68	40
7 years	23	50	0.85	50
10 years	30	66	1.00	60
12 years	40	88	1.28	75
16 years	54	120	1.70	90

**IV Flow Rate/ Infusion Time-****Calculation Formulae-**

$$\text{Flow rate (Drops per minute)} = \frac{\text{Drops in 1 ml} \times \text{total (ml)}}{\text{Total time (min)}}$$

$$\text{Infusion time (h)} = \frac{\text{Total vol. to be delivered}}{\text{ml. being delivered per hour}}$$



## **2.5. Exercises**

### **2.5.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

**1. Dose-response relationship is of**

- a. two type
- b. three type
- c. six type
- d. none of the above.

**2. Commonly used dose in clinical practice**

- a. toxic dose
- b. booster dose
- c. therapeutic dose
- d. all of the above.

**3. Dose depends on**

- a. body weight
- b. body height
- c. purchase capacity
- d. none of the above.

### **2.5.2. Short Questions**

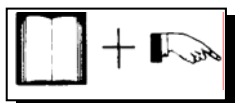
1. Define dose.
2. Define posology.
3. Define medium lethal dose.

### **2.5.3. Analytical Questions**

1. What do you understand by graded dose response relationship?
2. What is the difference between graded and quantal dose response relationship?
3. Define median effective (ED<sub>50</sub>) dose.
5. How you will calculate paediatric dose in nursing practice?

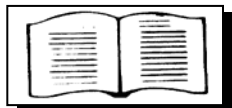
## Lesson 3: Drug Absorption

### 3.1. Learning Objectives



At the end of this lesson you will be able to-

- ◆ define the routes of drug administration
- ◆ discuss the process of absorption
- ◆ identify the factors for drug absorption.



### 3.2. The Route of Administration is Determined by

- ◆ drug properties like solubility, ionization etc.
- ◆ therapeutic objective like slow or rapid onset of drug action
- ◆ need for long term treatment
- ◆ any restriction to local site.

### Routes of Drug Administration

Drugs may be administered in the following routes-

#### A. Enteral

**1. Oral-** Commonest but benefit variable. Several gastrointestinal factors are related to absorption through this route of administration. Though administration is comfortable, first-pass metabolism by the liver and intestine limits efficacy of many drugs when taken orally. Acid in stomach degrades many drugs and thereby effective concentration is not achieved at the target tissue.

**2. Rectal-** About fifty percent of the drainage of the rectal area bypasses the portal circulation; hence biotransformation of drug in liver is reduced. Drugs used rectally can avoid degradation by stomach acid. Patient with nausea or vomiting can use such route of medication safely.

#### B. Parenteral

Preferred for drugs easily degraded by stomach pH, drugs those are poorly absorbed from GI tract, drugs used for unconscious patient and drugs needed to act quickly.

**1. Intravascular (IV)-** Intravenous (IV) is the commonest parenteral route of medication. Best alternative for drugs not absorbed from oral route. In this route drugs avoid GI environment and hence first - pass metabolism by liver. Though drugs administered in this route provides

rapid action but drugs cannot be recalled back by easy steps like enema, emesis, etc. May cause adverse reaction because of allergy, rapid infusion of bolus dose, etc. Intraarterial (IA) route may show similar problems.

2. **Intramuscular (IM)**- Drugs in the form of aqueous solutions or specialized depot preparations and often a suspension of drug in a nonaqueous vehicle are administered through this route. Drugs after injected precipitates at the muscle.
3. **Subcutaneous (SC)**- Absorption of drugs administered in this route is slower than IV route.

#### A. Other Routes

1. **Inhalation**- Provides rapid delivery of drug over a large surface area of respiratory mucosa. Most potent and rapid in action for medications like anaesthetics and drugs used on respiratory tract.
2. **Intranasal**- It is an alternative route for many nasal and systemic conditions. Desmopresin is administered intranasally against Diabetes Insipidus.
3. **Intrathecal/ Intraventricular**- When drugs are needed to introduce directly to CSF.
4. **Topical**- Most dermatological products are used topically. Also this route uses analgesics and ophthalmic preparations.
5. **Transdermal**- Drugs exhibit systemic effect via transdermal patch e.g. Nitroglycerine for Ischemic heart disease.



**Exercise:** Write merits and demerits of IV drug administration.

### 3.3. Process of Absorption

Absorption means passage or entry of drug into the blood stream from its site of administration.

#### Types of Absorption

- A. **Passive transport**- Concentration gradient across a membrane is the driving force for passive transport. No energy and carrier is needed for such drug transport.
1. **Simple diffusion**

- ◆ Unionized drug is lipid soluble and diffusible.
- ◆ Ionized drug is lipid insoluble and non-diffusible.
- ◆ Ionization is pH dependent.

Lipid soluble and unionized drugs dissolve in the lipid of cell membrane and cross the cell membrane from a higher concentration gradient to a lower one. The greater the concentration gradient, the greater the rate of absorption. The larger the absorption surface, the greater the drug flux. Simple diffusion is directly proportional to the magnitude of the concentration gradient across the membrane and lipid: water partition coefficient of the drug.

## 2. Filtration

Low molecular size water-soluble drugs ( $4\text{\AA}^\circ - 40\text{\AA}^\circ$ ) cross the cell membrane through the pores as a result of osmotic or hydrostatic pressure difference across the membrane.

## B. Specialized Transport

### 1. Active Transport (Carrier Medicated Transport)

In this type of transport process the drug binds with a carrier in the cell membrane and forms a drug-carrier complex and this complex move towards the other compartment of the membrane where the drug is released. It is one-way transport process, e.g., Steroids  $\text{Na}^+$ ,  $\text{K}^+$ ,  $\text{Ca}^{+2}$ , and  $\text{Fe}^{+3}$ .

*Criteria of active transport-*

- ◆ Exhibit selectivity
- ◆ Metabolic inhibition
- ◆ Exhibit saturability
- ◆ Carrier mediated
- ◆ Occur against electrochemical conc.gradient
- ◆ Enzyme dependent
- ◆ Competitive inhibition by congeners.

### 2. Facilitated Diffusion (Carrier Mediated)

Type of transport where movement of drug across the membrane is facilitated by a macromolecule e.g. tetracycline. It is a saturable process specific for the chemical structure of the drug but is not an energy dependent process. In this process drug carrier-complex does not move against a concentration gradient and hence still a diffusion process.



### 3. Exchange Diffusion

Some drugs are diffused in exchange of other substances.  $\text{Na}^+$  in distal convoluted tubules of kidney is reabsorbed in exchange of  $\text{H}^+ / \text{K}^+$ .

### 4. Pinocytosis

Process in which membrane engulf droplets of extracellular fluid or substance dissolved in them and transfer across membrane is called pinocytosis e.g. proteins. This process is important for uptake of large molecules.



**Exercise:** Describe criteria for simple diffusion and active transport.

### 3.4. Factors Affecting Drug Absorption

1. *Drug factors* - Size of the drug molecule, nature of drug, structure of the drug, concentration of drug, ionization or pH state of the drug are main factors for absorption.
2. *Blood flow to the absorption site* - Amount of blood flow to the area of absorption is very much important for absorption. Blood flow is directly proportional to the amount of absorption. Local application of heat enhances the rate of drug absorption. Decreased blood flow produced by vasoconstrictor agents, or other disease factors can slow absorption.
3. *Total surface area available for absorption* - Available absorption surface area is directly proportional to the drug absorption.
4. *Contact time at the absorption surface* - The more the contact time, the more is the amount of absorption of any drug. In case of oral administration the presence of food in the stomach also delays drug absorption.



### **3.5. Exercises**

#### **3.5.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

##### **1. Commonest route of drug administration**

- a. oral
- b. intravenous
- c. parenteral
- d. none of the above.

##### **2. Energy dependent mode of absorption**

- a. diffusion
- b. active transport
- c. pinocytosis
- d. all of the above.

##### **3. Amount of blood flow**

- a. reduces drug absorption
- b. increases drug absorption
- c. has no role for drug absorption
- d. none of the above.

#### **3.5.2. Short Questions**

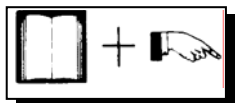
- 1. What is absorption?
- 2. What is active transport?
- 3. What are the factors that affect drug absorption?

#### **3.5.3. Analytical Questions**

- 1. Describe the routes of drug administration.
- 2. What do you know about the process of absorption?

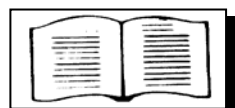
## Lesson 4: Distribution and Excretion of Drug

### 4.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ describe factors for drug distribution
- ♦ write about volume of distribution
- ♦ understand drug metabolism
- ♦ describe elimination of drug from the body.



### 4.2. Drug Distribution

Drug distribution may be defined as the process by which a drug leaves the blood stream and enters the cells of the tissues or extracellular space. It is a reversible process.

#### Factors Affecting Drug Distribution

##### A. Drug Structure

Hydrophobic drugs have uniform electron distribution with no net charge and can dissolve lipid cell membrane permeating to entire cell surface. Hydrophilic drugs with charged ions and nonuniform electron distribution do not readily penetrate cell membrane and must go through slit junctions.

##### B. Regional Distribution

1. *Regional blood flow & tissue perfusion* - The rate of blood flow varies in different parts of the body.
  - a. Liver, Brain, Kidney, Heart, Lungs, Spleen, Thyroids, etc. has more blood flow → more tissue perfusion → rapid distribution.
  - b. Muscle has got medium perfused tissue → less rapid drug distribution.
  - c. Fatty tissue, skin and appendages (nail) have still less blood flowed → slower distribution.
2. *Binding of drugs to proteins*- High protein binding drugs like Digitalis has prolonged action, slows excretion and delayed toxicity. Plasma albumin is the major drug binding protein and may act as a drug reservoir. Reversible binding to plasma proteins sequesters drugs in a

nondiffusible from and slows their transfer out of the vascular compartment.

3. *Blood-brain barrier*- Drugs must pass through endothelial cells of the capillaries of the CNS or by active transport. Lipid soluble drugs readily penetrate into the endothelial cells. Ionized or polar drugs cannot pass through the tight junctions of CNS cells. These juxtaposed cells with tight intercellular junctions form the Blood- Brain Barrier.

### C. Cardiac Out put

Increase cardiac output → improves circulation → rapid redistribution.

### D. Miscellaneous

1. *Capillary structure*- varies in terms of the fraction of basement membrane exposed by slit or tight junctions between endothelial cells.
2. *Pathological states*- disease conditions like congenital heart disease, uraemia, and cirrhosis of liver alter the rate of drug distribution in the body.
3. *Cellular reserve*- Certain drugs have special affinity for certain tissues where they remain in high concentration than in plasma. Heavy metals deport more in hair and nail; nevaquine and mepacrine deport 200 times more than in plasma.



**Exercise:** Describe in 100 words about drug distribution.

### 4.3. Volume of Distribution ( $V_d$ )

The volume of distribution is a hypothetical volume of fluid into which the drug is disseminated. The volume into which drugs are distributed is called the apparent volume of distribution ( $V_d$ ).

$V_d$  = Dose administered in the body/ Plasma conc. of drug. e.g., if 500 mg of a drug is administered i/v to produce a plasma conc. of 25mg/L, the  $V_d$  =  $500/25=20$  liters. High  $V_d$  indicates lipophilicity or many receptors for that particular drug.

#### Apparent volume of distribution of some drugs

Propranolol	-	41 L
Diazepam	-	1.2 L
Salicylates	-	0.15 L

Ampicillin	-	0.3 L
Morphine	-	3.51 L
Digoxin	-	61L.

#### 4.4. Drug Metabolism

Molecular alteration of any drug inside living body by enzymatic actions is called drug metabolism. The liver is the main site for drug metabolism. Other organs like lungs, kidneys, GIT, skin and adrenal glands also metabolize certain drugs. Metabolism usually results in inactivation of drug but some drugs are converted into active drug by metabolism. After metabolism many lipid soluble drugs are transformed to more polar form by conjugation.

#### 4.5. First- Pass metabolism

Means metabolism of a drug during its passage from intestines to systemic circulation. Orally administered drugs are exposed to metabolizing enzymes at the intestine and liver.



**Exercise:** What do you know about factors for drug metabolism?

#### 4.6. Elimination

Drugs eliminated from the body through many routes, the most important of them is through urine via kidney. Bile, intestine, lung or breast milk (of nursing mother) sweat is among other routes. Extra corporeal dialysis may remove small drug molecules.

##### A. Renal Elimination of a Drug

###### 1. Glomerular filtration-

Drugs not bound to albumin flow through the capillary slits into Bowman's space as part of the glomerular filtrate.

###### 2. Proximal tubular secretion-

Drugs not flowing through Bowman's space reach the proximal tubule where secretion occurs by two energy- requiring active transport systems - one for anions and another for actions.

###### 3. Distal tubular reabsorption-

Drugs when move forwards distal convoluted tubules, concentration increases. The uncharged drug may diffuse back to systemic circulation. Changing pH of urine can alter reabsorption of drug. This is known as “ion trapping”.

#### 4. Role of drug metabolism-

A patient with phenobarbital over dose can be given bicarbonate- decreasing reabsorption

In order to reduce reabsorption of lipid soluble drugs from renal tubule, drugs are modified by the body to be more polar using two types of reactions-

**Phase I reaction** involves transfer of drugs into more polar form by introducing a hydroxyl, group or other polar functional group.

**Phase II reaction** involves conjugation of phase 1 reaction drug with sulfate glucuronic acid glutathione, aminoacid or acetate, which are readily excreted from the body.

### B. Quantitative Aspects of Renal Drug Elimination

Plasma clearance is the volume of plasma from which all drugs appear to be removed in a particular time and is expressed as ml/min.

$$\text{Clearance} = \frac{\text{Rate of elimination}}{\text{Plasma drug concentration}}$$

### C. Total Body Clearance (CL<sub>total</sub>)

Sum of the clearances from the various drug metabolizing and drug eliminating organs.

$$\text{CL}_{\text{total}} = \text{CL}_{\text{hepatic}} + \text{CL}_{\text{renal}} + \text{CL}_{\text{pulmonary}} + \text{CL}_{\text{other}}$$

### D. Volume of Distribution (V<sub>d</sub>) and Half-Life of a Drug (t<sub>1/2</sub>)

The larger the volume of distribution, the more amounts of drug is unavailable for excretion by kidney being outside the plasma compartment.

$$t_{1/2} = 0.693V_d / \text{CL}_{\text{total}}$$

### E. Increased Half-Life of Drug in Disease Conditions

Many disease conditions alter half-life of drug. Also usage of concurrent drug may change the drug half-life.



**Exercise:** Describe in brief factors affecting drug elimination.

#### 4.6. Exercises

##### 4.6.1. Multiple Choice Questions

Tick (✓) the correct answer

**1. Which drug is distributed more easily**

- a. hydrophobic
- b. hydrophilic
- c. both of them
- d. none of them.

**2. Most important route for drug excretion**

- a. kidney
- b. perspiration
- c. GI tract
- d. none of them.

**3. Disease conditions**

- a. alters drug half-life
- b. does not alter drug half-life
- c. both of them
- d. none of them.

##### 4.6.2. Short Questions

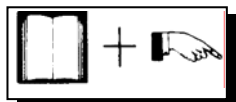
1. Define drug distribution.
1. Define drug metabolism.
2. Define drug elimination.

##### 4.6.3. Analytical Questions

1. Describe factors affecting drug distribution.
2. Describe factors affecting drug excretion from body.
3. What do you know about drug metabolism?

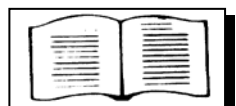
## Lesson 5: Drug Actions

### 5.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ define receptor types
- ♦ differentiate between efficacy and potency
- ♦ write about basic classification of drug action
- ♦ understand about mode of drug action.



### 5.2. Receptor

*Receptor may be defined as the macromolecular lipoprotein component of a cell or organism that interacts with any drug and initiates the series of biochemical events producing pharmacological effect.*

*Receptors largely determine the quantitative relation between dose and concentration of a drug. Receptors are also responsible for selectivity of drug actions.*

Formerly receptors were discussed under the headings - active/membrane receptors, silent/ dead receptors and spare/ reserve receptors. According to location receptors are classified as-

**Type I receptors** are on the external surface of target cells. They interact with drugs that mimic or block the actions of drugs of some class e.g. catecholamine and some peptide hormones.

**Type II receptors** are located in the cytoplasm of target cells. These receptors block or mimic the effect of steroids.

**Type III receptors** are located in the nucleus of some target cells. Nuclear receptors interact with thyroid hormone.

Receptor is responsible for selectivity of drug actions



**Exercise:** Write briefly about specific and non-specific receptors.

### Affinity

May be defined as the tendency of any drug to combine with a particular type of receptor to form a drug-receptor complex and is determined by  $K_1/K_2$ , where  $K_1$  is the association constant and  $K_2$  is the dissociation constant.



### 5.3. Efficacy

May be defined as the capacity of any drug to initiate a series of reactions after binding with receptors to produce pharmacological effect. Aspirin and Morphine produce same pharmacological effect but the level of analgesia differs. This degree of analgesia is the efficacy of the particular drug.

### Potency

May be defined as the dose or concentration of a drug required producing a given effect. Potency depends partly on affinity and partly on efficacy. For clinical reason potency of drug is important to select the dose and is expressed in dosage units.



**Exercise:** What is the difference between efficacy and potency?

### 5.4. Drug Action

Drugs do not impart new functions to any system, organ or cell; they only alter the space of ongoing activity.

#### Basic Types of Drug Action Are

1. *Stimulation*- means increase the activity of specialized cells. e.g., adrenaline stimulates heart cells.
2. *Depression*- means decrease the specialized cell activity. e.g., barbiturate depress CNS.
3. *Irritation*- means drug affects on morphology, nutrition and growth of living tissue. Example, bitters increase salivary and gastric secretion. Strong irritation may result inflammation, corrosion, necrosis and morphological change.
4. *Replacement*- means use of natural metabolized hormones or their congeners in deficiency states. Example- Insulin in Diabetes mellitus.
5. *Antiinfective agents*- act specifically on the causative organism to prevent, arrest and eradicate infection. Example antibiotics.
6. *Cytotoxicity*- means selectivity of invading parasites and cancer cells attenuating them without significantly affecting the host cells. Example- Mebendazole, cyclophosphomides.

7. *Modification of immune status*- some drugs act by enhancing or depressing the immune status e.g., vaccines.

### 5.5. Mechanism of drug action

#### 1. *Specific mechanism*

##### 1.1. Receptor mechanism

- a. Receptor occupational theory by clerk
- b. Rate limiting/ Paton's theory.

##### 1.2. Enzyme mechanism

- a. Enzyme stimulation
- b. Specific enzyme inhibition.

#### 2. *Non specific mechanism*

##### 2.1. By altering physiochemical properties of cells.

##### 2.2. By direct chemical interaction

- a. Neutralization e.g., antacid
- b. Chelation- e.g., antacid chelates tetracycline
- c. Anticoagulation- e.g., citrate of Na and K.

##### 2.3. By physical means

- a. By osmosis- e.g., diuretics, osmotic purgative
- b. By adsorption- e.g., ultracarbon
- c. By emollient and demulcent action - e.g., Magnesium trisilicate
- d. Radioactivity-
- e. Radioopacity- e.g., contrast medium
- f. Mass of drug- e.g., bulk laxative.

##### 2.4. Biological mechanism

- a. Inhibition of metabolic process- e. g., sulfonamide
- b. Cytotoxic action- e.g., nitrogen mustard
- c. Uncoupling- e. g., thyroxin.

## **Types of Combined Action**

### **1. Additives or Summation**

When two drugs are administered together, the combined effect of them is equal in magnitude to the sum of the individual drug effect given alone the process is called summation.

### **2. Synergism**

When the combined effect of two drugs administered together is greater in magnitude than the sum of individual drug action then the mechanism is called synergism.

### **3. Potentiation**

When the drug lacks the effect of its own but stimulates activation of a second drug.

### **4. Antagonism**

Antagonism is the interference of one drug with the action of another drug. An antagonistic drug is often desirable as an antidote.



## 5.6. Exercises

### 5.6.1. Multiple Choice Questions

Tick (✓) the correct answer

#### 1. Receptors are

- a. lipoproteins
- b. vitamins
- c. minerals
- d. all of the above.

#### 2. Drugs do not impart new functions to body

- a. true
- b. false
- c. sometimes
- d. occasionally.

#### 3. Antagonists

- a. retard agonist action
- b. enhance agonist action
- c. partially enhance agonist action
- d. none of the above.

### 5.6.2. Short Questions

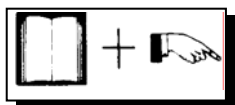
- 1. Define receptor.
- 2. Define affinity, efficacy and potency.
- 3. What do you mean by drug action?
- 4. Define cytotoxicity.

### 5.6.3. Analytical Questions

- 1. Discuss about receptor types and classification.
- 2. Describe the mechanism of drug action.

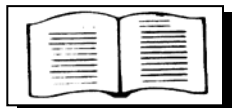
## Lesson 6: Drug Agonist, Antagonist and Synergists

### 6.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ define drug agonists - partial and full
- ♦ describe antagonists
- ♦ define synergists.



### 6.2. Agonist

*Agonist may be defined as any drug, which has affinity for receptor and also efficacy.* Agonists interact with receptor and elicit response e.g. noradrenaline is  $\alpha$  receptor agonist, salbutamol is  $\beta$ -receptor agonist. Agonists are drugs, which have greater rate of dissociation.

*Agonists* can be divided into 02 classes-

1. *Partial agonist* has affinity for receptor and some efficacy but may antagonise other drug with higher efficacy e.g., Nalorphine is partial agonist for Morphine. They are also called *dualists*. Partial agonists are drugs, which have moderate rate of dissociation.
2. *Full agonists* produce full efficacy at full receptor occupancy and better response than partial agonists.

### 6.3. Antagonist

May be defined as the drug, which has affinity for receptor but has no efficacy. It opposes the action of agonist e.g., atropine antagonise the effect of acetylcholine. Antagonists are those drugs, which have very slow rate of dissociation.

#### Types of Antagonism

##### 1. Chemical antagonism

Two drugs react chemically and neutralize each other to produce an inactive substance e.g.

- a. Antacid + Gastric HCl  $\rightarrow$  Neutralization
- b. Mercury poisoning + Dimercaprol (BAL)  $\rightarrow$  Chelation.

##### 2. Physiological antagonism

Two drugs influence physiological system in opposite direction acting independently on separate receptors e.g.

Sympathetic drug (CNS stimulant) + Parasympathetic drug (CNS depressant) → No CNS effect.

### 3. Pharmacological antagonism

Two drugs compete for the same receptor site and one drug prevents access to the other drug. It is of two types -

- 3.1. *Competitive (Reversible)* - here two drugs act on the same receptor but action of one drug can be reversed by raising concentration. e.g.  
Histamine and antihistamine → histamine receptor.  
Ach. + Atropine → muscarinic receptor.
- 3.2. *Noncompetitive (Irreversible)* - here antagonist alters the receptor properties and abolishes agonist action e.g., Organophosphorus + AChE

Substrate or Metabolite is a metabolic or Chemical product with definite structural configuration on which enzyme acts e.g. Folic Acid



### 4. Pharmacokinetic antagonism

One drug reduces the potency of another drug by-

- a. modifying absorption from GI tract e.g., milk and antacid.
- b. affecting plasma protein binding.
- c. influencing renal excretion e.g., increased renal excretion of weakly acidic substrates in an alkaline urine.
- d. altering drug metabolism.

**Exercise:** Write in brief importance of drug antagonism.

### 6.4. Synergist

Synergist may be defined as a drug, which enhances the effect of other drug when given combinedly. In this case the combined effect of two drugs is greater than the sum of the effect of each drug given alone e.g., sulfamethoxazole and trimethoprim. Individually they are bacteriostatic but combinedly they are bactericidal.



## **6.5. Exercises**

### **6.5.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

#### **1. Agonists have**

- a. affinity and efficacy
- b. only affinity
- c. only efficacy
- d. none of the above.

#### **2. Antagonists have**

- a. both affinity and efficacy
- b. affinity but no efficacy
- c. only efficacy
- d. none of the above.

#### **3. Synergists are**

- a. full agonists
- b. chemical antagonists
- c. competitive antagonists
- d. none of the above.

### **6.5.2. Short Questions**

- 1. Define agonist, partial agonist, and full agonist.
- 2. Define synergist.
- 3. Define antagonist.
- 4. Define substrate or metabolite.

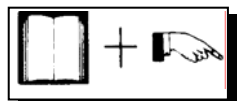
### **6.5.3. Analytical Questions**

- 1. Differentiate between full agonist and partial agonist.
- 2. Describe with example different types of antagonist.

## Unit 2: Drug Classes and Microbial Sensitivity

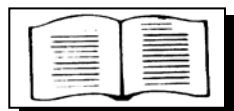
### Lesson 1: Classification of Drugs

#### 1.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ understand importance of drug classification
- ♦ classify drugs in different ways.



#### 1.2. Drug Classification

Classification of drugs means to put drug in order so that they are discussed or represented in peer groups. Classification is the basic issue for any scientific study and analysis. Drugs are thousands in number and varieties. It would be very difficult to describe or discuss individually detail of each drug in relation to the origin, structure, mode of application, route of administration, nature of biotransformation, excretion etc. For this purpose classification or group distribution of drugs are important. Again discussion of group agonists or antagonists are more convenient than discussion of the individual drug. Classification can be done depending on different variables.

Because of wide number of variables, a homogeneous and uniform classification is very difficult to find out. If anatomy is taken into Consideration, pharmacology gets drops. If use is concerned, molecular structure gets lost. Drugs are categorized according to the user's benefits. Clinicians, pharmacologists use different types of classification. A more accepted classification would be -

**1. Therapeutic use-** e.g., antimicrobials, antidiabetic, analgesics, tranquilizer etc.

#### **2. Mode or site of action**

2.1. Molecular interaction- e.g., receptor blockers, enzyme inhibitors.

2.2. Cellular site- e.g., loops diuretic, catecholamine uptake inhibitor (imipramine).

2.3. Physiological system- e.g.



## Drug Classes and Microbial Sensitivity

- vasodilator
- hypolipidaemic
- anticoagulant.

### 3. Molecular structure

- barbiturate
- glycoside
- alkaloid
- steroid.

### 4. Disease condition

- anticancer
- antidiabetic
- antithyroid
- anthelmintics.

There are many other ways of drug classification. Drugs are often used for three types of actions-

#### **Preventive**

To prevent any disease process or physio-pathological changes certain group of drugs is used e.g.

- vaccine
- contraceptives
- antimalarials

#### **Suppressive**

To suppress diseases or symptoms. Usually the OTC products or certain specialist medicines to continue physical well being and healthful living e.g.,

- analgesic
- antipyretic
- antihypertensive
- antidiabetic
- antitussive etc.

#### **Curative**

To cure any pathological conditions e.g.

- antibiotics
- antiparasitic

Also there are group of drugs used as auxiliary therapy e.g.

- anaesthetics.
- ergometrine
- oxytocin

Drugs are again classified according to their behaviour with the receptors e.g.

- agonist
- antagonist
- synergist

These are few of the ways of classification of drugs.

**Exercise:** Briefly discuss suppressive mechanism of drug action.



## **1.4. Exercises**

### **1.4.1. Multiple Choice Questions**

**Tick (✓) the correct answer**

1. Pharmacology is the study of
  - a. plants
  - b. drugs
  - c. animals
  - d. none of the above.
2. Toxicology deals
  - a. only toxic materials
  - b. sometimes toxin preparation
  - c. toxic effects of chemicals
  - d. none of the above.
3. Placebo
  - a. increase habituation
  - b. increase addiction
  - c. prevent addiction
  - d. none of the above.

### **1.4.2. Short Questions**

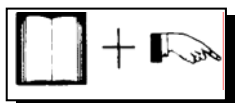
1. Describe importance of drug classification.
2. Describe the class of drug, which acts by mode, or site of action.

### **1.4.3. Analytical Question**

1. Classify drugs clinically.

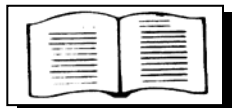
## Lesson 2: Antibiotics-I

### 2.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ define and classify antimicrobials
- ♦ describe different classes of antibiotics
- ♦ write about penicillin's.



### 2.2. Antimicrobials

Antimicrobials are drugs, which are used against microbes. They may be classified according to the mechanism of action as follows-

#### 1. Inhibitors of metabolism

- Sulfonamides
- Trimethoprim

#### 2. Inhibitors of cell wall synthesis

- Penicillins
- Cephalosporins

#### 3. Inhibitors of protein synthesis

- Tetracycline
- Aminoglycosides
- Macrolides
- Chloramphenicol
- Clindamycin

#### 4. Inhibitors of nucleic acid function or synthesis

- Fluroquinolones
- Rifampicin
- alidixic Acid

**Chemotherapeutics** are usually synthetic drugs used to combat parasitic infections without affecting the host tissue e.g., Sulphonamides.

**Sulfonamide** is an antimicrobial agent having sulphanilamide group ( $-\text{SO}_2\text{NH}_2$ ) in it. It is a white crystalline powder mainly acidic in nature.

### Mechanism of Action of Sulphonamides

Sulfonamides act by competitive antagonism against Para-aminobenzoic acid (PABA). PABA helps for endogenous synthesis of folic acid essential for growth of bacteria.

As sulfonamide has structural similarity to PABA, they competed each other and sulfonamide enters bacterial cell instead of PABA to form nonfunctioning analogue of folic acid. As a result no thymidine is formed → No DNA is synthesized → No further growth of bacteria → Death.



**Exercise:** Classify Sulfonamides.

### Adverse effect of sulfonamides

#### 1. On Urinary tract

- Renal irritation, crystalluria, albuminuria, hematuria, oliguria, anuria.

#### 2. On haemopoietic system

- Bone marrow depression
- Aplastic and haemolytic anaemia
- Thrombocytopenia.

#### 3. On G.I.T

- Anorexia, Nausea, Vomiting, Diarrhoea.

#### 4. Allergic symptoms

- Rashes, exfoliative dermatitis
- Stevens- Johnson syndrome (fever, malaise erythema multiforme and mucus membrane ulceration)
- Photosensitivity, conjunctivitis
- Hepatitis, Jaundice
- Peripheral neuritis.

Contraindication of sulfonamides (Priority basis)

- Pregnancy
- Premature infant
- Renal impairment
- Dehydration
- P/H/O reaction

## 5. Others

- Goiter, hypothyroidism
- Arthritis



**Exercise:** Write indications of Sulfonamides.

## 2.3. Antibiotics

Antibiotics are substances obtained from various species of microorganisms (bacteria, fungi, actinomycetes) that suppress the growth of other microorganisms and eventually may destroy them without affecting the host cells.

### Criteria for an Ideal Antibiotic

1. It should be bactericidal other than bacteriostatic
2. It should act against wide range of microbes
3. Microbes should not be able to develop resistance against it
4. Internal body components or conditions should not affect its anti-microbial activity
5. It should exert effective and selective activity
6. It should have a specific pattern of absorption, distribution, fate and excretion
7. It should be nontoxic to the body.

### Classification of Antibiotics

Antibiotics can be classified in a number of ways-

#### A. According to Chemical Structure

##### 1. Beta- Lactams (*Containing a $\beta$ -Lactam ring*)

- Penicillins
- Cephalosporins

##### 2. Aminoglycosides (*Contain an amine-sugar and a glycoside*)

- Streptomycin
- Neomycin

## Drug Classes and Microbial Sensitivity

- Kanamycin
- Gentamycin
- Amikacin (Semi-synthetic)

### 3. Tetracyclines

### 4. Macrolides (*Contain a macrocyclic lactose ring*)

- Erythromycin
- Spiromycin

### 5. Imidazoles (*Contain an imidazole ring*)

- Metronidazole

### 6. Polypeptides (*Contain peptide linked amino acids*)

- Bacitracin
- Polymixin B
- Gramicidine

## B. According to Mechanism of Action

### 1. Antibiotics that Inhibit Cell Wall Synthesis

- Penicillins
- Cephalosporins

### 2. Antibiotics that Inhibit Protein Synthesis

- Tetracyclines
- Erythromycin
- Chloramphenicol

### 3. Antibiotics that Inhibit Neuclic Acid Synthesis

- Rifampicin
- Quinolones

### 4. Antibiotics Interfering with Transport Through Cell Membrane

- Polymixin antibiotics
- Polyene antibiotics

### C. According to Spectrum of Activity

#### 1. Broad spectrum antibiotics that have wide range of antibacterial activity (gram+ve, gram- ve)

- Ampicillin
- Amoxicilin

#### 2. Narrow spectrum antibiotics that have narrow range of antibacterial activity

- Benzylpenicillin
- Cloxacillin

### D. According to Mode of Action

#### 1. Bactericidal Antibiotics

- Penicillins
- Aminoglycosides

#### 2. Bacteriostatic Antibiotics

- Tetracyclines
- Chloramphenicol

### 2.4. Penicillin

Discovered by Sir Alexander Fleming in 1928 and derived from *Penicillium chrysogenum* (previously from *Penicillium notatum*).

#### Mechanism of Action

**M/A:** The cell walls of bacteria are essential for their normal growth and development. Penicillin inhibits the enzyme transpeptidase, which is responsible for the synthesis of bacterial cell wall. As a result, bacterial cell wall cannot be synthesized and thereby causing death of bacteria.

Moreover Penicillin activates an autolytic enzyme which causes breakdown of the bacterial cell wall and thereby causing death of the bacteria.

#### Adverse Reactions of Penicillin

1. Anaphylactic shock- characterized by bronchospasm, hypotension, shock, angioneurotic oedema, arthralgia
2. Delayed allergic reactions- Maculo- papular rashes



## Drug Classes and Microbial Sensitivity

- a. Local effect viz pain, thrombophlebitis
  - b. GIT effect- Nausea, Vomiting
  - c. CNS effect- Delirium, convulsion.
3. Super Infection.

## Treatment of Penicillin Hypersensitivity

### A. General

1. *Stop* the drug immediately
2. Keep patient in supine position - legs elevated
3. Maintain *clear airway* by endotracheal tube

### B. Specific

1. Inj. adrenaline (1:1000) 0.5 to 1 ml s.c. or i.m. may be repeated after 3 minute.

Or

if adrenaline is not available -

Inj. Hydrocortisone hemi- succinate 100 - 250mg i/v slowly followed by oral Prednisolone 5 mg 6 hourly

2. Inj. Antihistamine (Promethazine) 10 mg i/v
3. Fluid administration
4. Other supportive measures e.g.
  - Oxygen inhalation
  - Maintenance of body temperature
  - Loosening of the dress and shoes.



**Exercise:** Briefly describe the indications of Penicillin.



## 2.5. Exercises

### 2.5.1. Multiple Choice Questions

Tick (✓) the correct answer

1. **Antimicrobials are drugs which**
  - a. promote bacterial activity
  - b. retards bacterial activity
  - c. has no role on bacterial activity
  - d. none of the above.
  
2. **Penicillin has been discovered by**
  - a. alexander glen
  - b. alexander graham bell
  - c. alexander fleming
  - d. none of the above.
  
3. **In Penicillin hypersensitivity**
  - a. adrenaline has no role
  - b. adrenaline is not encouraged
  - c. adrenaline is immediately given
  - d. none of the above.

### 2.5.2. Short Questions

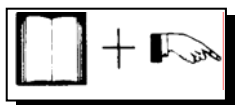
1. Define antimicrobials.
2. Define antibiotics.
3. Whats is sulfonamide?

### 2.5.3. Analytical Questions

1. Describe mechanism of action of sulphonamides.
2. Describe mechanism of action of penicillin.
3. Describe treatment of penicillin hypersensitivity.

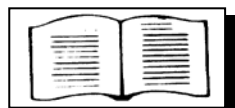
## Lesson 3: Antibiotic-II

### 3.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ describe about beta- lactams antibiotics
- ♦ understand about tetracycline
- ♦ about aminoglycosides
- ♦ write about macrolids and quionolones.



### 3.2. Ampicillin

A semisynthetic, broad-spectrum penicillin effective against gram positive and gram-negative organism.



**Exercise:** Write down differences between Ampicillin and Amoxycillin.

### Cephalosporins

Broad-spectrum  $\beta$ -lactam antibiotics obtained originally from a Cephalosporium mold. They are bactericidal and have some mechanism of action as Penicillin.

### Classification of Cephalosporins

Classification by generations is based on general features of antimicrobial activity.

#### 1. First Generation

- a. Oral- Cephalexin, Cephadrine
- b. Parental- Cephalothin, Cefazoline, Cephaloridine

#### 2. Second Generation

- a. Oral- Cefaclor
- b. Parenteral- Cefuroxime, Cefoxitin.

#### 3. Third Generation

Parenteral- Cefotaxime, Ceftriaxone,  
Ceftazidime, Ceftizoxime.

#### 4. Forth Generation

- cefepime

### 3.3. Tetracycline

Polycyclic *naphthalene carboxamide* derivative. Naphthalene nucleus is made up by fusion of 4 partially unsaturated “*Cyclohexane radicals*”. So is the name Tetracycline.

#### Mechanism of Action

Tetracycline enters the susceptible bacterial cell partly by passive diffusion and partly by an energy-dependent process of active transport. Then it combines to receptor on ribosome subunit (30S) and ultimately inhibits protein synthesis resulting in inhibition of bacterial growth and multiplication.

#### Adverse Effect

1. Allergic reaction
2. Toxic effect on G.I.tract
  - Nausea, vomiting, Diarrhoea
  - Abdominal discomfort, Epigastric pain
  - Enterocolitis, Anal pruritis
  - Fatty changes in liver Jaundice.
3. Effect on teeth
  - Yellow brown discolouration, enamel dysplasia
4. Effect on bone.
  - Depression of bone growth
5. Vestibular reaction
  - Dizziness, Vertigo
6. Superinfection
7. Fanconi’s syndrome
8. Miscellaneous
  - Thrombophlebitis
  - Renal damage, Azotaemia.



**Exercise:** Describe about Fanconi’s syndrome.

--

### Chloramphenicol

Chloramphenicol inhibits protein synthesis in bacteria. The drug readily penetrates bacterial cells, probably by facilitated diffusion. Chloramphenicol acts primarily by binding reversibly to the 50s ribosomal subunit. It appears to prevent the binding of the amino-acid-containing end of the aminoacyl tRNA to the acceptor site on the 50s ribosomal subunit. The interaction between peptidyl transferase and its amino acid substrate cannot occur, and peptide bond formation is inhibited.

Thus chloramphenicol prevents growth and multiplication of bacteria.



**Exercise:** Write short notes on Grey Baby Syndrome and Chloramphenicol induced aplastic anaemia.

### 3.4. Aminoglycosides

Systemic-streptomycin, Gentamycin, Kanamycin, Amikacin, Tobramycin etc.

Topical- Neomycin, Framycetin, Paromomycin.

Members contain two or more amino sugars joined through glucosidic linkage to the central hexose nucleus.

#### Properties

1. All are used as sulphate salts, highly water-soluble.
2. Ionize in solution, are not absorbed orally, do not penetrate Blood Brain Barrier or Cerebro Spinal Fluid.
3. All are bactericidal and more active in alkaline pH.
4. Act by interfering bacterial protein synthesis.
5. Are excreted unchanged in urine by glomerular filtration.
6. All exhibit ototoxicity and nephrotoxicity.
7. Have narrow margin between therapeutic dose and toxic dose.
8. Active against gram-negative bacilli with different spectra.
9. Bacterial killing is concentration dependent.



**Exercise:** Write down the differences between Streptomycin and

Gentamicin.

### 3.5. Macrolides

Group of antibiotics with a macrocyclic lactone structure. Erythromycin (first used one), Clarithromycin and Azithromycin are the members. Erythromycin is used in patients allergic to penicillins.

Macrolides bind irreversibly to a site on the 50s ribosome sub unit, inhibiting the translocation steps of protein synthesis. Generally considered bacteriostatic but may be bactericidal at higher doses.

#### A. Erythromycin- Effective against

- i. *Chlamydial* infections as alternative to tetracycline specially during pregnancy,
- ii. *Mycoplasma pneumonia*
- iii. *Ureaplasma urealyticum* causing urethritis in male
- iv. GTI in female as major cause of foetal death, miscarriage and low birth weight
- v. Syphilis
- vi. *Corynebacterium diphtheriae* to eliminate at carrier state and
- vii. Legionnaire's disease.

#### B. Clarithromycin- More active than erythromycin against *Haemophilus influenzae*, *chlamydia*, *Legionella*, *Ureaplasma*.

#### C. Azithromycin- Less active than erythromycin against strepto and staphylococci, far more active against *Haemophilus influenzae*, *Moraxella catarrhalis*, *Chlamydia trachomatis*, *Mycoplasma pneumoniae*. Also used in AIDS patient with disseminated infections in case of *Mycobacterium avium* intracellulare.



**Exercise:** Describe in brief adverse effects of Macrolids.

### Quinolones

Synthetic bactericidal drugs.

A. Nalidixic Acid (effective against gm-ve bacteria but can adversely affect liver if used more than 2 week)

#### B. Fluroquinolones

**Ciprofloxacin-** is effective against *pseudomona*, *Enterobacteraceae*, *GIT infections*, *resistant resp. tract infections*, *Gonorrhoea*, *UTI*.

**Cinoxacin-** Complicated and uncomplicated UTI, prostatitis.

**Lomefloxacin-** Primarily used in Prostatitis, STD (except Syphilis), skin and Lower resp. tract disinfection.

**Norfloxacin-** (first member)

**Ofloxacin-** UTI and bronchitis. Not effective against *pseudomona* bacteraemia.

Fluroquinolones enter the cell by passive diffusion. They (intracellularly) inhibit the replication of bacterial DNA. Cause bacterial cell death by inducing cleavage of the DNA.



**Exercise:** Write down the pharmacokinetics and adverse effects of quinolones.

### Antimycobacterial Agents

#### *Drugs used for Leprosy*

- Clofazimine
- Dapsone

#### *Drugs used for Tuberculosis*

##### *First-line anti TB drugs*

Drug	Action	Min.Dose mg/kg/day	Min. and Max. Dose for MDR-TB

INH	Bactericidal	5	
Rifampin	Bactericidal	10	
Pyrazinamide	Bactericidal	15	1200-1600
Ethambutol	Bacteriostatic	15	1000-1200
Streptomycin	Bactericidal	15	750-1000

***Second-line anti TB drugs***

<b>Drug</b>		<b>Action</b>	<b>Dose mg/kg/day</b>
Aminoglycosides	Kanamycin Amikacin Capreomycin	Bactericidal	750-1000
Ethionamide		Bactericidal	500-750
Prothionamide			1200-1600
PAS		Bacteriostatic	10,000-12,000
Quinolones	Ciprofloxacin	Weakly bactericidal	1000-1500 (80-90%) bioavailability)
	Ofloxacin		600-800 (90-98% bioavailability)
Cycloserine Terizidone		Bacteriostatic	500-750
Macrolides	Azithromycin Clarithromycin	Active against atypical mycobacteria	
Clofazimine		Not recommended by WHO for MDR-TB	
Amoxiclav		Investigational	
Rifabutin Rifapentine		Bactericidal	Long acting weekly dose





**Exercise:** Write adverse effects of anti- TB drugs.



### 3.6. Exercises

#### 3.6.1. Multiple Choice Questions

Tick (✓) the correct answer

**1. Cephalosporins are**

- a. beta-Lactam antibiotics
- b. sulphonamides
- c. aminoglycosides
- d. none of the above.

**2. Tetracycline is a**

- a. bactericidal drug
- b. bacteriostatic drug
- c. both of the above
- d. none of the above.

**3. Quinolones include**

- a. ampicillin, cephalosporins
- b. streptomycin, gentamicin
- c. ciprofloxacin, ofloxacin
- d. none of the above.

#### 3.6.2. Short Questions

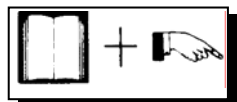
1. Name second generation Cephalosporins.
2. Why is the name Tetracycline?
3. What is the mechanism of action of Chloramphenicol?
4. Classify Quinolones.

#### 3.6.3. Analytical Questions

1. Classify Cephalosporins.
2. Write down properties of Aminoglycosides.
3. What do you know about Ciprofloxacin?

## Lesson 4: Antivirals

### 4.1. Learning Objectives

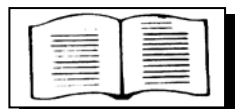


At the end of this lesson you will be able to-

- ♦ classify antivirals
- ♦ describe about Amantadin, Ribavirin
- ♦ describe about Acyclovir
- ♦ understand about anti-HIV drugs
- ♦ know about interferon.

### 4.2. Antivirals

Antivirals are those agents that must inhibit virus direct specific replicative events or preferentially inhibit virus directed rather than host-cell-directed nucleic acid or protein synthesis.



#### Classification of Antivirals

##### A. Antiherpes and Anticytomegalo Virus Agents

1. Acyclovir
2. Famciclovir
3. Ganciclovir
4. Foscarnet

##### B. Antiretroviral Agents

1. Zidovudine (AZT)
2. Didanosine (ddI)
3. Zalcitabine (ddC)
4. Lamivudine (3TC)

##### C. Anti-influenza Agents

1. Amantadine
2. Rimantadine
3. Zanamivir
4. Oseltamivir
5. Ribavirin

## **D. Hepatitis, Leukaemia and Kaposi Sarcoma**

1. Interferon-  $\alpha$
2. Interferon-  $\beta$

### **4.3. Amantadine (Symadine 100 mg Cap) and Rimantadine**

Effective in preventing influenza A infections (also used in Parkinsonism). They block viral membrane matrix M<sub>2</sub> protein, which functions as an ion channel. These drugs may also interfere with the release of new virions. These drugs are 70-90% effective in preventing infection if treatment is begun at the time of exposure to the virus. While already infected, both drugs reduce duration and severity of systemic symptoms if started within the first 48 hours after exposure.

#### **Side Effect**

Side effects include nervousness, nausea, loss of appetite insomnia, dizziness, ataxia may be hallucinations, seizures and congestive cardiac failure.

#### **Ribavirin**

A synthetic guanosine analogue effective against a broad spectrum of RNA and DNA viruses. It is used to treat infants and young children infected with severe RSV infections. Responses for treating hepatitis A and influenza A and B have also been reported.

### **4.4. Acyclovir (Zovirax 200mg)**

A guanosine analogue that lacks a true sugar moiety. Thymidine kinase coded by viral genome phosphorylates acyclovir very faster. Phosphorylation is catalyzed by the enzymes of the host cells, ultimately resulting incorporation of acyclo-GMP from acyclo-GTP into the growing strand of viral DNA leading to chain termination.

Acyclovir is active against herpes simplex Virus- 1 (HSV-1), HSV-2, varicella-zoster virus and some Epstein-Barr virus. CMV is resistant. Acyclovir is the treatment of choice for herpes simplex encephalitis. It is commonly used against genital herpes infections.

### Side Effect

Side effects include local irritation (topical application), headache, diarrhoea, nausea, vomiting (Oral administration), and transient renal dysfunction at high dose (i.v route).



**Exercise:** Write short notes on Ganciclovir, famciclovir, vidarabine and foscarnet.

### 4.5. Trifluridine

Used in the topical treatment of keratoconjunctivitis due to herpes simplex viruses. This drug, being pyrimidine analog incorporated into the viral and cellular DNA and thereby prevents viral DNA synthesis.

### Zidovudine (3-Azido-3- Deoxythymidine, AZT)

(Retrovir-Cap 100 mg, Inj. 10 mg/ml, Sy 50 mg/5ml.)

*AZT should not  
be taken with -*  
- Paracetamol  
- Indomethacin  
- Cimetidine  
- Lorazepam

One of the most effective drugs approved for treatment of HIV infection and AIDS. Used to treat selected patients with AIDS or AIDS related complex (ARC) caused by HIV. Also used to treat Kaposi's sarcoma, hairy leukoplakia in the mouth; prevent HIV to exposed workers and may increase AIDS related low platelet count. This drug works by interfering with essential enzyme system in virus. Limits severity and extent of HIV infection by preventing growth and reproduction of HIV particles within the cells.

### Side Effect

AZT is toxic to bone marrow causing severe anaemia and leukopenia if given in high dose. Headache and nausea are common. Seizures, confusion, tremors, emesis, insomnia, and myalgia may occur.

### Didanosine (ddI)

(Videx - Tab chewable/ dispersible- 25 mg. 50 mg, 100 mg, 150 mg; Oral solution - 10 mg/ ml).

Used to treat HIV infections in adults and children (6 month of age or older) with advanced disease who cannot tolerate AZT or showed significant deterioration during AZT treatment. Acts by interfering enzyme systems in virus. The resulting product ddATP is incorporated

into DNA chain causing termination of chain elongation and hence viral growth is prevented.

### Side Effect

ddI may cause drug induced pancreatitis, peripheral neuritis, seizures and hepatotoxicity.

### Zalcitabine (ddC)

(Hivid- Tab 0.375 mg, 0.75mg)

Commonly used in combination with AZT for advanced (CD4 cell count less than or equal to 300 cell/ cu.mm) HIV infection. This drug may not prevent risk of disease transmission. May have role in paediatric AIDS.

### Side Effect

Peripheral neuritis is the major adverse effect. Other toxicities may be pancreatitis, oesophageal ulcers, cardiomyopathy, CCF and arthritis.



**Exercise:** Write short notes on Stavudine, Lamivudine.

## 4.6. Interferon

(Intermax– Alpha 3 million unit/ ml, Intron- A 3million unit/ ml).

- |  |
|--|
| Indications                              |
| ◆ Interferon – $\alpha$                  |
| ◆ Chronic hepatitis B and C              |
| ◆ Genital warts by Papilloma virus       |
| ◆ Hairy- cell leukemia,                  |
| ◆ Kaposi sarcoma                         |
| ◆ Interferon – $\beta$                   |
| ◆ Relapsing remitting multiple sclerosis |
| ◆ Interferon – $\gamma$                  |
| ◆ Chronic granulomatous diseases         |

Naturally occurring inducible glycoproteins that interfere with the viral ability for infection. There are, at least, three types of interferon -  $\alpha$ ,  $\beta$  and  $\gamma$ . Interferon  $\alpha$  - 2b has been approved for treatment of hepatitis, hairy cell leukemia and kaposi's sarcoma. Interferon involves induction of host cell enzymes (e.g., a protein kinase, 2'-5'-oligoadenylate synthase and a phosphodiesterase) that inhibit viral RNA translation leading to degradation of viral mRNA and tRNA.

### Side Effect

May cause fever, lethargy, marrow depression, CCF and acute allergic reactions. Hepatic failure and pulmonary infiltrates are rare.



## 4.7. Exercises

### 4.7.1. Multiple Choice Questions

Tick (✓) the correct answer

1. **AZT is the main drug to treat**
  - a. hepatitis B infection
  - b. severe Rotavirus diarrhoea
  - c. influenza A infection
  - d. none of the above.
2. **Interferon- $\alpha$  is used to treat**
  - a. AIDS
  - b. HSV-1 infection
  - c. hepatitis B and C
  - d. none of the above.
3. **Pancreatitis is the main side effect of**
  - a. didanosine
  - b. interferon- $\beta$
  - c. interferon- $\alpha$
  - d. none of the above.

### 4.7.2. Short Questions

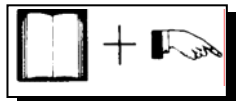
1. Write short note on amantadine.
2. Write adverse effects of acyclovir.
3. What are uses the didanosine?
4. What are main adverse effects of ddC?

### 4.7.3. Analytical Questions

1. Classify antivirals.
2. Write in brief about AZT.
3. Describe indications of interferons.

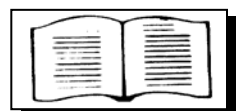
## Lesson 5: Antifungals, Antiprotozoals and Anthelmintics

### 5.1. Learning Objectives



At the end of this lesson you will be able to-

- ♦ classify antifungals
- ♦ describe drugs against superficial and deep mycosis
- ♦ define and classify antiprotozoal drugs
- ♦ classify anthelmintics.



### 5.2. Clotrimazole

Used to treat superficial candida, tinea and related infections.

This drug damages fungal cell walls, blocks essential enzymes, inhibits fungal cell growth and reproduction. It is also fungicidal at high concentration.

Possible risks include skin irritation and nausea, vomiting, stomach cramp when swallowed.

### 5.3. Miconazole

Topically active drug against candida, tinea and other topical fungal infections.

It damages cell wall, impairs critical cell enzymes and thus inhibits fungal growth and reproduction.

### Griseofulvin

Used for treatment of tinea infections like *tinea barbae*, *tinea capitis*, *tinea corporis*, *tinea cruris*, *tinea pedis* and *tinea unguium*. Also used in *Herpes Zoster* to relieve pain.

Griseofulvin acts by disrupting fungal reproduction and thus preventing growth and multiplication of the susceptible fungi. This drug is deposited in the skin, nail and hair.

Adverse effects include hepatitis (rare), headache, lethargy, fatigue, and peripheral neuritis and decreased white blood cell count.



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**Exercise:** Describe in brief about Nystatin.

### Amphotericin- B

A naturally occurring polyene macrolide used to treat systemic mycoses sometimes in combination with flucytosine. Effective against *Candida albicans*, Histoplasma, Cryptococcus, coccidioides and many strains of Aspergillus.

This drug disrupts the fungal cell wall causing leakage of potassium and small molecules from cell as a result of bondage of the drug and ergosterol present in fungal cell wall.

Adverse effects include anaphylaxis, fever and chills, nephrotoxicity, hypertension, anaemia, neurological effects and even thrombophlebitis.



**Exercise:** Write notes on Flucytosine.

### Fluconazole

Clinically important because it lacks endocrine side effects and its excellent entry into CSF. Effective against *cryptococcus neoformans*, candidemia and coccidioidomycosis. Also effective against blastomycosis, candidiasis and histoplasmosis.

Interacts with a cytochrome P-450 enzyme to inhibit synthesis of fungal membrane ergosterol and thus disrupts the membrane function ultimately and increases permeability.

Adverse effects are allergic reactions, liver toxicity, abnormally low blood platelet count, headache, nausea, vomiting, stomach cramp and diarrhoea.



**Exercise:** Describe in brief about ketoconazole.

## 5.4. Antiprotozoal Drugs

Protozoal infection is common in underdeveloped tropical and subtropical countries with poor hygienic or sanitary practices and inadequate vector control. Antiprotozoal drugs are many in-groups and different in mechanism. A clinical classification of them is given here –



**A. Treatment of Amoebiasis**

- Metronidazole
- Secnidazole
- Tinidazole
- Emetine
- Dehydroemetine
- Diloxanide Furoate
- Paramomycin
- Chloroquine

**B. Treatment of Giardiasis**

- Quinacrine
- Metronidazole

**C. Treatment of Malaria**

- Quinine / Qunidine
- Chloroquine
- Mefloquine
- Primaquine
- Pyrimethamine

**D. Treatment of Leishmaniasis**

- Sodium Stibogluconate

**E. Treatment of Trypanosomiasis**

- Melarsoprol
- Pentamidine
- Suramin
- Nifurlimox

**F. Treatment of Toxoplasmosis**

- Pyrimethamin

**5.5. Drugs used to Treat Helmintic Disease**

**A. Treatment of Nematodes**

- Levamisole
- Mebendazole
- Albendazole
- Thiabendazole (Trichinosis)
- Pyrantal Pamoate (Hook worm)
- Diethyl Carbamazine (filariasis)
- Ivermectin (onchocerciasis)

**B. Treatment of Trematodes**

- Praziquantel

**C. Treatment of Cestodes**

- Niclosamide  
(Yomesan - Tab 500mg)



## **5.6. Exercises**

### **5.6.1 Multiple Choice Questions**

**Tick (✓) the correct answer**

- 1. Clotrimazole is used to treat**
  - a. helminthic disease
  - b. systemic fungal diseases
  - c. superficial fungal diseases
  - d. none of the above.
  
- 2. Fluconazole is important clinically because**
  - a. it is cheap and easily available
  - b. it is given in single dose
  - c. it lacks endocrine effects
  - d. none of the above.
  
- 3. Metronidazole is the drug of choice**
  - a. for complicated malaria
  - b. for AIDS
  - c. for amoebiasis
  - d. none of the above.

### **5.6.2. Short Questions**

1. Write short note on Clotrimazole.
2. How Griseofulvin acts?
3. What are the adverse effects of Fluconazole?

### **5.6.3. Analytical Questions**

1. Classify antifungals.
2. Write about Amphotericin- B.
3. Classify antiprotozoal drugs.
4. Name the anthelmintics.