M.Sc., Biochemistry **2018-2020**

Semester III

18BCP304 **DRUG BIOCHEMISTRY** **4H-4C**

Instruction hours / week: L:4 T:0 P:0 **Marks:** Internal: **40** External: **60** Total: **100**

End Semester Exam: 3 Hours

Course objectives

- This paper gives insight knowledge about the emerging themes of drug biochemistry.
- Provides an in depth analysis of specific drug classes, its metabolism and therapeutic approaches.

Course outcomes (CO's)

1. Ensure the widespread visibility and high impact of Drugs, thereby promoting on emerging research, pointing the way for the establishment of new medicines – from the identification of targets, through to the synthesis and evaluation of putative therapeutic entities.
2. Able to understand the adverse effect of drugs in various organs.

UNIT I: Basic concepts of Drugs

Drugs – Introduction, sources and routes of administration, Structural features and pharmacological activity, prodrug concept, Adsorption – factors modifying drug absorption. Distribution, metabolism - phase I, II reactions, action of cytochrome P450 and excretion of drugs.

Drug receptors – Localization, types and subtypes, models and theories. G-protein coupled receptor and ion-channel linked receptors. Examples of drug-receptor interactions. Agonists and antagonists. Bioavailability of drug

UNIT II: Assay of Drug

Drug tolerance and drug dependence. Principles of basic pharmacokinetics. Adversse response to drugs, drug intolerance, pharmacogenetics, drug allergy, tachyphylaxis, drug abuse, vaccination against infection, factors modifying drug action and effect. Assay of drug potency: chemical, bioassay and immunoassay.

UNIT III: Engineered Protein

Genetically engineered protein and peptide agents as drugs, Novel drug delivery systems, anti-AIDS drug development, oncogenes as targets for drugs, multidrug resistance phenotypes, production of secondary metabolites by plant tissue culture. Genome based medicine.

UNIT IV: Mechanism of action of drugs used in therapy

Mechanism of action of drugs used in therapy of Respiratory system – cough, bronchial asthma, pulmonary tuberculosis. Antimicrobial drugs – sulphonamides, trimethoprim, penicillins, aminoglycosides and bacterial resistance, Cancer chemotherapy. Thyroid and antithyroid drugs, insulin and oral antidiabetic drugs, antifertility and ovulation inducing drugs. Pharmacotherapy of gout and rheumatoid arthritis, Immuno therapy – Immunosuppressants and immunostimulants, Enzymes in therapy.

UNIT V: Neurotransmitter Drugs

Brain – Neurotransmitters, encephalins and endorphins; general function of autonomic and somatic nervous system; cholinergic transmission and receptors; adrenergic transmission and receptors; muscarinic receptors. Non steroidal and anti inflammatory drugs; adrenergic blocking drugs; cholinergic blocking drugs; muscatrinic blocking drugs; parkinson's disease; Alzhiemier's disease. Neurodegenerative disorders – Amylotropic, lateral sclerosis, senile dementia, schizophrenia, Huntington's disease.

SUGGESTED READINGS

1. Satoskar, R.S., Bhandarkar, S.D., and Ainapare, S.S., (2003). Pharmacology and Pharmacotherapeutics, Popular Prakasham, Mumbai.

2. Patrick, G., (2002). Medicinal Chemistry Instant notes, Viva books private limited, New Delhi.

3. Chauduri, S.K., (2001). Quintessence of Medical Pharmacology, New central book agency limited, Calcutta.

4. Glick, B.R., Pasternak, J.J., and Patten, C.L., (2009). Molecular Biotechnology, 4th edition, Panima Publishing Corporation, Delhi.

5. Grahame-Smith, D.G., and Aronson, J. K., (2002). Oxford textbook of Clinical Pharmacology and Drug Therapy: 3rd edition. Oxford University Press.

6. Foye, W.O., Lemke, T.L., Williams, D.A., (2012). Principles of Medicinal Chemistry, 7th edition, B.I. Wanerly Pvt. Ltd, New Delhi.

7. Wolf, E.,(1995). Burgers Medicinal Chemistry and Drug Discovery. Principles and Practice, John Wiley and Sons, Manfred.

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DEPARTMENT OF BIOCHEMISTRY

LESSON PLAN

STAFF NAME: Dr. A. RAMAKRISHNAN

SUBJECT NAME: DRUG BIOCHEMISTRY

SUB.CODE: 18BCP304

SEMESTER: III **CLASS: II M.Sc., BIOCHEMISTRY**

S.No	Duration of Period	Topics to be Covered	Books referred with Page No.	Web page referred
UNIT I				
1	1	Introduction, sources and routes of administration, structural features and pharmacological activity	S1: 23-27	
2	1	Pro drug concept, excretion of drugs.		
3	1	Adsorption – factors modifying drug absorption and distribution	S2: 4-6	
4	1	Metabolism - phase I, II reactions, action of cytochrome P450	S1: 16-18	
5	1	Excretion of drugs	S1: 18-20	
6	1	Drug receptors – Localization, types and subtypes, models and theories	S1: 29-31	
7	1	G-protein coupled receptor and ion-channel linked receptors	S1: 31-32	
8	1	Examples of drug-receptor interactions		
9	1	Agonists and antagonists. Bioavailability of drug	S1: 29-30	
Total No. of Hours planned for Unit I : 9 hours				
UNIT II				
1	1	Drug tolerance and drug dependence, principles of basic pharmacokinetics	S1: 29-31	

2	1	Adverse response to drugs, drug intolerance, pharmacogenetics,	S1: 36-37	
3	1	Drug allergy, tachyphylaxis, drug abuse, vaccination against infection,	S1: 37-43, S1: 54-56	
4	1	Factors modifying drug action and effect	S2: 376-378	
5	1	Assay of drug potency:	S1: 56-60	
6		Chemical assay		
7	1	Bioassay		
8	1	Immunoassay		
9	1	Revision and Possible QP discussion		
Total No. of Hours planned for Unit II : 9 hours				
UNIT III				
1	1	Genetically engineered protein	S1: 3-5	
2	1	Peptide agents as drugs, Novel drug delivery systems	S1: 23-24	W1
3	1	Anti-AIDS drug development	S2: 367-371	
4	1	Oncogenes as targets for drugs	S1: 722-724	
5	1	Multidrug resistance phenotypes	S2: 376-378	
6	1	Production of secondary metabolites		W3
7	1	Production of secondary metabolites by plant tissue culture		
8	1	Genome, Genome based medicine.		
9	1	Revision and Possible QP discussion		
Total No. of Hours planned for Unit III : 9 hours				
UNIT IV				
1	1	Mechanism of action of drugs used in therapy of Respiratory system	S1: 340-342	
2	1	Cough, bronchial asthma, pulmonary tuberculosis	S1: 346-350 S1: 735-741	
3	1	Antimicrobial drugs – sulphonamides, Trimethoprim, penicillins	S1: 684-688	
4	1	Aminoglycosides and bacterial resistance		
5	1	Cancer chemotherapy, thyroid and antithyroid drugs	S1: 802-804	
6	1	Insulin and oral antidiabetic drugs	S1: 935-937 S1: 949-952	
7	1	Antifertility and ovulation inducing drugs.	S1: 935-937 S1: 949-952	
8	1	Pharmacotherapy of gout and rheumatoid arthritis	S1: 1016-1019 S1: 1022-1027	
9	1	Immuno therapy – Immunosuppressants and immunostimulants, Enzymes in therapy	S1: 1077-1080 S1: 1048-1050	

Total No. of Hours planned for Unit IV : 9 hours				
UNIT V				
1	1	Brain – Neurotransmitters, encephalins and endorphins; general function of autonomic and somatic nervous system		W1
2	1	Cholinergic transmission and receptors, adrenergic transmission and receptors; muscarinic receptors		
3	1	Non-steroidal and anti-inflammatory drugs, adrenergic blocking drugs	S2: 403-411	
4	1	Cholinergic blocking drugs; muscatrinic blocking drugs	S2: 71-78 S2: 45-48	
5	1	Parkinson's disease		W2
6	1	Alzhiemier's disease		
7	1	Neurodegenerative disorders – Amylotropic, lateral sclerosis		W2
8	1	Senile dementia, schizophrenia, Huntington's disease		
9	1	Revision and Possible QP discussion		
Total No. of Hours planned for Unit V : 9 hours				
Previous year ESE Question Paper Discussion				
1	1	Previous year ESE question paper discussion		
2	1	Objective questions discussion		
3	1	Revision		
Total Hours Planned: 45 + 3 : 48				

SUGGESTED READINGS

1. Satoskar, R.S., Bhandarkar, S.D., and Ainapare, S.S., (2003). Pharmacology and Pharmacotherapeutics, Popular Prakasham, Mumbai.

2. Patrick, G., (2002). Medicinal Chemistry Instant notes, Viva books private limited, New Delhi.

3. Chauduri, S.K., (2001). Quintessence of Medical Pharmacology, New central book agency limited, Calcutta.

4. Glick, B.R., Pasternak, J.J., and Patten, C.L., (2009). Molecular Biotechnology, 4th edition, Panima Publishing Corporation, Delhi.

5. Grahame-Smith, D.G., and Aronson, J. K., (2002). Oxford textbook of Clinical Pharmacology and Drug Therapy: 3rd edition. Oxford University Press.

6. Foye, W.O., Lemke, T.L., Williams, D.A., (2012). Principles of Medicinal Chemistry, 7th edition, B.I. Wanerly Pvt. Ltd, New Delhi.

7. Wolf, E.,(1995). Burgers Medicinal Chemistry and Drug Discovery. Principles and Practice, John Wiley and Sons, Manfred.

W1: http://qjmed.oxfordjournals.org/content/92/1/1

W2: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4058009

UNIT-I

SYLLABUS

Drugs – Introduction, sources and routes of administration, Structural features and pharmacological activity, prodrug concept, Adsorption – factors modifying drug absorption. Distribution, metabolism - phase I, II reactions, action of cytochrome P450 and excretion of drugs. Drug receptors – Localization, types and subtypes, models and theories. G-protein coupled receptor and ion-channel linked receptors. Examples of drug-receptor interactions. Agonists and antagonists. Bioavailability of drug

Route of drug administration

Classification

Routes of administration are usually classified by application location (or exposition). The route or course the active substance takes from application location to the location where it has its target effect is usually rather a matter of pharmacokinetics (concerning the processes of uptake, distribution, and elimination of drugs).

Gastrointestinal/enteral

Administration through the gastrointestinal tract is sometimes termed *enteral or enteric administration* (strictly meaning 'through the intestines'). *Enteral/enteric administration* usually includes *oral* (through the mouth) and *rectal* (into the rectum) administration, in the sense that these are taken up by the intestines. Furthermore, some application locations often classified as *enteral*, such as sublingual (under the tongue) and sublabial or buccal (between the cheek and gums/gingiva), are taken up in the proximal part of the gastrointestinal tract without reaching the intestines.

Many drugs as tablets, capsules, or drops are taken orally. Administration methods directly into the stomach include those by gastric feeding tube or gastrostomy.

Central nervous system

epidural (synonym: peridural) (injection or infusion into the epidural space), e.g. epidural anesthesia

intracerebral (into the cerebrum) direct injection into the brain. Used in experimental research of chemicals and as a treatment for malignancies of the brain.

The intracerebral route can also interrupt the blood brain barrier from holding up against

subsequent routes.

intracerebroventricular (into the cerebral ventricles) administration into the ventricular system of the brain.

Other locations

Epicutaneous (application onto the skin). It can be used both for local effect as in allergy testing and typical local anesthesia, as well as systemic effects when the active substance diffuses through skin in a transdermal route.

Intradermal, (into the skin itself) is used for skin testing some allergens, and also for mantoux test for Tuberculosis

Subcutaneous (under the skin), e.g. insulin. Skin popping is a slang term that includes this method of administration, and is usually used in association with recreational drugs.

Nasal administration (through the nose) can be used for topically acting substances, as well as for insufflation of e.g. decongestant nasal sprays to be taken up along the respiratory tract. Such substances are also called *inhalational*, e.g. inhalational anesthetics.

Intravenous (into a vein), e.g. many drugs, total parenteral nutrition

intraarterial (into an artery), e.g. vasodilator drugs in the treatment of vasospasm and thrombolytic drugs for treatment of embolism

Intramuscular (into a muscle), e.g. many vaccines, antibiotics, and long-term psychoactive agents. Recreationally the colloquial term 'muscling' is used.[8]

intracardiac (into the heart), e.g. adrenaline during cardiopulmonary resuscitation (no longer commonly performed)

intraosseous infusion (into the bone marrow) is, in effect, an indirect intravenous access because the bone marrow drains directly into the venous system. This route is occasionally used for drugs and fluids in emergency medicine and pediatrics when intravenous access is difficult.

intrathecal (into the spinal canal) is most commonly used for spinal anesthesia and chemotherapy

intraperitoneal, (infusion or injection into the peritoneum) e.g. peritoneal dialysis

Intravesical infusion is into the urinary bladder.

intravitreal, through the eye

Intracavernous injection, an injection into the base of the penis

Intravaginal, e.g. topical estrogens, antibacterials

Intrauterine

Extra-amniotic administration, between the endometrium and fetal membranes

Route from application to target

The route or course the active substance takes from application location to the location where it has its target effect is usually rather a matter of pharmacokinetics (concerning the processes of uptake, distribution, and elimination of drugs).

1. Transdermal (diffusion through the intact skin for systemic rather than topical distribution), e.g. transdermal patches such as fentanyl in pain therapy, nicotine patches for treatment of addiction and nitroglycerine for treatment of angina pectoris.

2. Transmucosal (diffusion through a mucous membrane), e.g. insufflation (snorting) of cocaine, sublingual, i.e. under the tongue, sublabial, i.e. between the lips and gingiva, nitroglycerine, vaginal suppositories

Local or systemic effect

Routes of administration can also basically be classified whether the effect is local (in topical administration) or systemic (in enteral or parenteral administration):

1. Topical: local effect, substance is applied directly where its action is desired. Sometimes, however, the term *topical* is defined as applied to a localized area of the body or to the surface of a body part, without necessarily involving target effect of the substance, making the classification rather a variant of the classification based on application location.

Topical

Epicutaneous (application onto the skin), e.g. allergy testing, typical local anesthesia

Inhalational, e.g. asthma medications

E, e.g. contrast media for imaging of the bowel

Eye drops (onto the conjunctiva), e.g. antibiotics for conjunctivitis

Ear drops - such as antibiotics and corticosteroids for otitis externa

Through mucous membranes in the body

Enteral

In this classification system, enteral administration is administration that involves any part of the gastrointestinal tract and has systemic effects:

by mouth (orally), many drugs as tablets, capsules, or drops

by gastric feeding tube, duodenal feeding tube, or gastrostomy, many drugs and enteral nutrition rectally, various drugs in suppository

Parenteral

Intravenous (into a vein), e.g. many drugs, total parenteral nutrition

Intra-arterial (into an artery), e.g. vasodilator drugs in the treatment of vasospasm and thrombolytic drugs for treatment of embolism

intraosseous infusion (into the bone marrow) is, in effect, an indirect intravenous access because the bone marrow drains directly into the venous system. This route is occasionally used for drugs and fluids in emergency medicine and pediatrics when intravenous access is difficult.

Intra-muscular

Advantages and disadvantages

There are advantages and disadvantages to each route of administration

Inhalation

Advantages

Fastest method, 7–10 seconds for the drug to reach the brain

User can titrate (regulate the amount of drug they are receiving

Disadvantages

Typically a more addictive route of administration because it is the fastest, leading to instant gratification. In addition, drugs taken by inhalation do not stay in the bloodstream for as long, causing the user to redose more quickly and intensifying the

Injection

Injection encompasses intravenous (IV), intramuscular (IM), and subcutaneous (subcut)

Disadvantages

Onset of action is quick, hence more risk of addiction when it comes to injecting drugs of abuse

Patients are not typically able to self-administer. Belonephobia, the fear of needles and injection.

If needles are shared, there is risk of HIV and other infectious diseases

It is the most dangerous route of administration because it bypasses most of the body's natural defenses, exposing the user to health problems such as hepatitis, abscesses, infections, and undissolved particles or additives/contaminants

Absorption (pharmacokinetics)

In pharmacology (and more specifically pharmacokinetics), absorption is the movement of a drug into the bloodstream.

Absorption involves several phases. First, the drug needs to be introduced via some route of administration (oral, via the skin, *etc*.) and in a specific dosage form such as a tablet, capsule, and so on.

In other situations, such as intravenous therapy, intramuscular injection, enteral nutrition and others, absorption is even more straight-forward and there is less variability in absorption and bioavailability is often near 100%.

Dissolution

In the most common situation, a tablet is ingested and passes through the esophagus to the stomach. Because the stomach is an aqueous environment, this is the first place where a tablet may dissolve.

The rate of dissolution is a key target for controlling the duration of a drug's effect, and as such, several dosage forms that contain the same active ingredient may be available, differing only in the rate of dissolution. If a drug is supplied in a form that is not readily dissolved, the drug may be released more gradually over time with a longer duration of action. Having a longer duration of action may improve compliance since the medication will not have to be taken as often. Additionally, slow-release dosage forms may maintain concentrations within an acceptable therapeutic range over a long period of time, as opposed to quick-release dosage forms which may result in sharper peaks and troughs in serum concentrations.

The rate of dissolution is described by the Noyes-Whitney equation as shown below:

$$\frac{dW}{dt} = \frac{DA(C_s - C)}{L}$$

Where:

$\frac{dW}{dt}$ is the rate of dissolution.

A is the surface area of the solid.

C is the concentration of the solid in the bulk dissolution medium.

C_s is the concentration of the solid in the diffusion layer surrounding the solid.

D is the diffusion coefficient.

L is the diffusion layer thickness.

Also, coatings on a tablet or a pellet may act as a barrier to reduce the rate of dissolution. Coating may also be used to modify where dissolution takes place. For example, enteric coatings may be applied to a drug, so that the coating only dissolves in the basic environment of the intestines. This will prevent release of the drug before reaching the intestines.

Since solutions are already dissolved, they do not need to undergo dissolution before being absorbed. Lipid-soluble drugs are less absorbed than water-soluble drugs,specially when they are enteral.

Ionization

The gastrointestinal tract is lined with epithelial cells. Drugs must pass or permeate through these cells in order to be absorbed into the circulatory system. One particular cellular barrier that may prevent absorption of a given drug is the cell membrane. Cell membranes are essentially lipid bilayers which form a semipermeable membrane. Pure lipid bilayers are generally permeable only to small, uncharged solutes.

The Henderson-Hasselbalch equation offers a way to determine the proportion of a substance that is ionized at a given pH. In the stomach, drugs that are weak acids (such as aspirin) will be present mainly in their non-ionic form, and weak bases will be in their ionic form. .

Other factors

Other facts that affect absorption include, but are not limited to, bioactivity, resonance, the inductive effect, isosterism, bio-isosterism, and consideration. of physico chemical factors biological factors patient related factors

Distribution (pharmacology)

Distribution in pharmacology is a branch of pharmacokinetics which describes the reversible transfer of drug from one location to another within the body.

The distribution of a drug between tissues is dependent on permeability between tissues (between blood and tissues in particular), blood flow and perfusion rate of the tissue and the ability of the drug to bind plasma proteins and tissue. pH parturition plays a major role as well.

Once a drug enters into systemic circulation by absorption or direct administration, A drug has to be distributed into interstitial and intracellular fluids.The lipid solubility, pH of compartment, extent of binding with plasma protein and tissue proteins, cardiac output, regional blood flow, capillary permeability are associated for distribution of the drug through tissues.The drug is easily distributed in highly perfused organs like liver, heart, kidney etc in large quantities & in small quantities it is distributed in low perfused organs like muscle, fat, peripheral organs etc. The volume of distribution (V_D) of a drug is a property that quantifies the extent of distribution.

Drug metabolism

Drug metabolism is the biochemical modification of pharmaceutical substances by living organisms, usually through specialized enzymatic systems. This is a form of xenobiotic metabolism. Drug metabolism often converts lipophilic chemical compounds into more readily excreted polar products. Its rate is an important determinant of the duration and intensity of the pharmacological action of drugs.

Drug metabolism can result in toxication or detoxication - the activation or deactivation of the chemical. While both occur, the major metabolites of most drugs are detoxication products.

Drugs are almost all xenobiotics. Other commonly used organic chemicals are also xenobiotics, and are metabolized by the same enzymes as drugs. This provides the opportunity for *drug-drug* and *drug-chemical* interactions or reactions.

I reactions can lead either to activation or inactivation of the drug.

Phases

Phase I

Phase I reactions (also termed nonsynthetic reactions) may occur by oxidation, reduction, hydrolysis, cyclization, and decyclization addition of oxygen or removal of hydrogen, carried out by mixed function oxidases, often in the liver. These oxidative reactions typically involve a

cytochrome P450 monooxygenase (often abbreviated CYP), NADPH and oxygen. The classes of pharmaceutical drugs that utilize this method for their metabolism include phenothiazines, paracetamol, and steroids. If the metabolites of phase I reactions are sufficiently polar, they may be readily excreted at this point. However, many phase I products are not eliminated rapidly and undergo a subsequent reaction in which an endogenous substrate combines with the newly incorporated functional group to form a highly polar conjugate.

A common Phase I oxidation involves conversion of a C-H bond to a C-OH. This reaction sometimes converts a pharmacologically inactive compound (a prodrug) to a pharmacologically active one. By the same token, Phase I can turn a nontoxic molecule into a poisonous one ([[toxification>CN. Simple hydrolysis in the stomach transforms. Which are comparatively innocuous. But Phase I metabolism converts acetonitrile to $HOCH_2CN$, which rapidly dissociates into formaldehyde and hydrogen cyanide, both of which are toxic.

Phase I metabolism of drug candidates can be simulated in the laboratory using non-enzyme catalysts.[1] This example of a biomimetic reaction tends to give products that often contains the Phase I metabolites. As an example, the major metabolite of the pharmaceutical trimebutine, desmethyltrimebutine (nor-trimebutine), can be efficiently produced by in vitro oxidation of the commercially available drug. Hydroxylation of an N-methyl group leads to expulsion of a molecule of formaldehyde, while oxidation of the O-methyl groups takes place to a lesser extent.

Oxidation

Cytochrome P450 monooxygenase system

Flavin-containing monooxygenase system

Alcohol dehydrogenase and aldehyde dehydrogenase

Monoamine oxidase

Co-oxidation by peroxidases

Reduction

NADPH-cytochrome P450 reductase

Cytochrome P450 reductase also known as NADPH:ferrihemoprotein oxidoreductase, NADPH:hemoprotein oxidoreductase, NADPH:P450 oxidoreductase, P450 reductase, POR, CPR, CYPOR, is a membrane-bound enzyme required for electron transfer to cytochrome P450 in the

microsome of the eukaryotic cell from a FAD- and FMN-containing enzyme NADPH:cytochrome P450 reductase The general scheme of electron flow in the POR/P450 system is: NADPH → FAD → FMN → P450 → O2

Reduced (ferrous) cytochrome P450

During reduction reactions, a chemical can enter *futile cycling*, in which it gains a free-radical electron, then promptly loses it to oxygen (to form a superoxide anion).

Hydrolysis

Esterases and Amidase

Epoxide hydrolase

Phase II

Phase II reactions - usually known as conjugation reactions (e.g., with glucuronic acid, sulfonates (commonly known as sulfation) , glutathione or amino acids) — are usually detoxication in nature, and involve the interactions of the polar functional groups of phase I metabolites. Sites on drugs where conjugation reactions occur include carboxyl (-COOH), hydroxyl (-OH), amino (NH_2), and sulfhydryl (-SH) groups. Products of conjugation reactions have increased molecular weight and are usually inactive unlike Phase I reactions which often produce active metabolites.

Mechanism	Involved enzyme	Co-factor	Location
Methylation	Methyltransferase	S-adenosyl-L-methionin	Liver, kidney, lung, CNS
Sulphation	Sulfotransferases	3'-phosphoadenosine-5'-phosphosulfate	Liver, kidney, intestine
Acetylation	N-acetyltransferases Bile acid-CoA:amino acid N-acyltransferases	Acetyl coenzyme A	Liver, lung, spleen, gastric mucosa, RBCs, lymphocytes
Glucuronidation	UDP-glucuronosyltransferases	UDP-glucuronic acid	Liver, kidney, intestine, lung, skin, prostate, brain
Glutathione	Glutathione S-transferases	Glutathione	Liver, kidney

conjugation

Sites

Quantitatively, the smooth endoplasmic reticulum of the liver cell is the principal organ of drug metabolism, although every biological tissue has some ability to metabolize drugs. Factors responsible for the liver's contribution to drug metabolism include that it is a large organ, that it is the first organ perfused by chemicals absorbed in the gut, and that there are very high concentrations of most drug-metabolizing enzyme systems relative to other organs. If a drug is taken into the GI tract, where it enters hepatic circulation through the portal vein, it becomes well-metabolized and is said to show the *first pass effect*.

Other sites of drug metabolism include epithelial cells of the gastrointestinal tract, lungs, kidneys, and the skin. These sites are usually responsible for localized toxicity reactions.

Factors that affect drug metabolism

The duration and intensity of pharmacological action of most lipophilic drugs are determined by the rate they are metabolized to inactive products. The Cytochrome P450 monooxygenase system is the most important pathway in this regard. In general, anything that *increases* the rate of metabolism (*e.g.*, enzyme induction) of a pharmacologically active metabolite will *decrease* the duration and intensity of the drug action. The opposite is also true (*e.g.*, enzyme inhibition). However, in cases where an enzyme is responsible for metabolizing a pro-drug into a drug, enzyme induction can speed up this conversion and increase drug levels, potentially causing toxicity.

Various physiological and pathological factors can also affect drug metabolism. Physiological factors that can influence drug metabolism include age, individual variation (*e.g.*, pharmacogenetics), enterohepatic circulation, nutrition, intestinal flora, or sex differences.

In general, drugs are metabolized more slowly in fetal, neonatal and elderly humans and animals than in adults.

Genetic variation (polymorphism) accounts for some of the variability in the effect of drugs. With N-acetyltransferases (involved in *Phase II* reactions), individual variation creates a group of people who acetylate slowly (*slow acetylators*) and those who acetylate quickly, split roughly 50:50 in the population of Canada. This variation may have dramatic consequences, as the slow acetylators

are more prone to dose-dependent toxicity.

Cytochrome P450 monooxygenase system enzymes can also vary across individuals, with deficiencies occurring in 1 - 30% of people, depending on their ethnic background.

Pathological factors can also influence drug metabolism, including liver, kidney, or heart diseases. *In silico* modelling and simulation methods allow drug metabolism to be predicted in virtual patient populations prior to performing clinical studies in human subjects.[3] This can be used to identify individuals most at risk from adverse reaction

Excretion

Excretion is the process by which waste products of metabolism and other non-useful materials are eliminated from an organism.[1] It is an essential process in all forms of life. It contrasts secretion, where the substance may have specific tasks after leaving the cell.

In single-celled organisms, waste products are discharged directly through the surface of the cell. Multicellular organisms utilize more complex excretory methods. Higher plants eliminate gases through the stomata, or pores, on the surface of leaves. Animals have special excretory organs

Clearance

In medicine, the clearance is a measurement of the renal excretion ability. Although clearance may also involve other organs than the kidney, it is almost synonymous with renal clearance or renal plasma clearance. Each substance has a specific clearance that depends on its filtration characteristics. Clearance is a function of glomerular filtration, secretion from the peritubular capillaries to the nephron, and reabsorption from the nephron back to the peritubular capillaries.

When referring to the function of the kidney, clearance is considered to be the amount of liquid filtered out of the blood that gets processed by the kidneys or the amount of blood cleaned per time because it has the units of a volumetric flow rate [volume / time].

Effect of plasma protein binding

For substances that exhibit substantial plasma protein binding, clearance is generally defined as the total concentration (free + protein-bound) and not the free concentration.

Most plasma substances have primarily their free concentrations regulated, which thus remains the same, so extensive protein binding increases total plasma concentration (free + protein-bound).

This gives a decreased clearance than what would have been the case with no protein binding. In other sites than the kidneys, however, where clearance is made by membrane transport proteins rather than filtration, extensive plasma protein binding may increase clearance by keeping concentration of free substance fairly constant throughout the capillary bed, inhibiting a decrease in clearance caused by decreased concentration of free substance through the capillary.

Pro drug

A prodrug is any compound that undergoes biotransformation before exhibiting its pharmacological effects. Prodrugs can thus be viewed as drugs containing specialized non-toxic protective groups used in a transient manner to alter or to eliminate undesirable properties in the parent molecule.

A prodrug is a pharmacological substance (drug) administered in an inactive (or significantly less active) form. Once administered, the prodrug is metabolised in vivo into an active metabolite, a process termed bioactivation. The rationale behind the use of a prodrug is generally for absorption, distribution, metabolism, and excretion (ADME) optimization. Prodrugs are usually designed to improve oral bioavailability, with poor absorption from the gastrointestinal tract usually being the limiting factor.

Additionally, the use of a prodrug strategy increases the selectivity of the drug for its intended target. An example of this can be seen in many chemotherapy treatments, in which the reduction of adverse effects is always of paramount importance. Drugs used to target hypoxic cancer cells, through the use of redox-activation, utilise the large quantities of reductase enzyme present in the hypoxic cell to bioactivate the drug into its cytotoxic form, essentially activating it. As the prodrug has low cytotoxicity prior to this activation, there is a markedly lower chance of it "attacking" healthy, non-cancerous cells which reduces the side-effects associated with these chemotherapeutic agents.

In rational drug design, the knowledge of both chemical properties likely to improve absorption and the major metabolic pathways in the body is used to modify the structure of new chemical entities for improved bioavailability. Conversely, the creation of prodrugs is sometimes unintentional, for example with serendipitous drug discoveries, where the drug is only later identified as a prodrug after extensive drug metabolism studies.

Prodrugs can be classified into two major types, based on their cellular sites of bioactivation into the final active drug form, with Type I being those that are bioactivated intracellularly (e.g., anti-viral nucleoside analogs, lipid-lowering statins,), and Type II being those that are bioactivated extracellularly, especially in digestive fluids or the systemic circulation (e.g., etoposide phosphate, valganciclovir, fosamprenavir, antibody-, gene- or virus-directed enzyme prodrugs [ADEP/GDEP/VDEP] for chemotherapy or immunotherapy). Both types can be further categorized into Subtypes, i.e. Type IA, IB and Type IIA, IIB, and IIC based on whether or not the intracellular bioactivating location is also the site of therapeutic action, or the bioactivation occurs in the gastrointestinal (GI) fluids or systemic circulation.

Type IA prodrugs include many antimicrobial and chemotherapy agents (e.g., 5-flurouracil). Type IB agents rely on metabolic enzymes, especially in hepatic cells, to bioactivate the prodrugs intracellularly to active drugs. Type II prodrugs are bioactivated extracelluarly, either in the milieu of GI fluids (Type IIA), within the systemic circulation and/or other extracellular fluid compartments (Type IIB), or near therapeutic target tissues/cells (Type IIC), relying on common enzymes such as esterases and phosphatases or target directed enzymes. Importantly, prodrugs can belong to multiple subtypes (i.e., Mixed-Type). A Mixed-Type prodrug is one that is bioactivated at multiple sites, either in parallel or sequential steps. For example, a prodrug, which is bioactivated concurrently in both target cells and metabolic tissues, could be designated as a "Type IA/IB" prodrug (e.g., HMG Co-A reductase inhibitors and some chemotherapy agents; note the symbol applied here). When a prodrug is bioactivated sequentially, for example initially in GI fluids then systemically within the target cells, it is designated as a "Type IIA-IA" prodrug (e.g., tenofovir disoproxil fumarate; note the symbol applied here). Many ADEPs, VDEPs, GDEPs and futuristic nanoparticle- or nanocarrier-linked drug moieties can understandably be Sequential Mixed-Type prodrugs. To differentiate these two Subtypes, the symbol dash is used to designate and to indicate sequential steps of bioactivation, and is meant to distinguish from the symbol slash used for the Parallel Mixed-Type prodrugs.

Monoacetylmorphine (6-MAM) is a heroin metabolite which converts into active morphine in vivo.

Carisoprodol is metabolized into meprobamate. Carisoprodol is not a controlled substance in the

United States, but meprobamate is classified as a potentially addictive controlled substance that can produce dangerous and painful withdrawal symptoms upon discontinuation of the drug.

Enalapril is bioactivated by esterase to the active enalaprilat.

Valacyclovir is bioactivated by esterase to the active acyclovir.

Fosamprenavir is hydrolysed to the active amprenavir.

Levodopa is bioactivated by DOPA decarboxylase to the active dopamine.

Chloramphenicol succinate ester is used as an intravenous prodrug of chloramphenicol, because pure chloramphenicol does not dissolve in water.

Psilocybin is dephosphorylated to the active psilocin.

Heroin is deacetylated by esterase to the active morphine.

Molsidomine is metabolized into SIN-1 which decomposes into the active compound nitric oxide.

Paliperidone is an atypical antipsychotic for schizophrenia. It is the active metabolite of risperidone.

Prednisone, a synthetic cortico-steroid drug, is bioactivated by the liver into the active drug prednisolone, which is also a steroid.

Primidone is metabolized by cytochrome P450 enzymes into phenobarbital, which is major, and phenylethylmalonamide, which is minor.

Dipivefrine, given topically as an anti-glaucoma drug, is bioactivated to epinephrine.

Lisdexamfetamine is metabolized in the small intestine to produce dextroamphetamine at a controlled (slow) rate for the treatment of attention-deficit hyperactivity disorder

Diethylpropion is a diet pill that does not become active as a monoamine releaser or reuptake inhibitor until it has been *N*-dealkylated to ethylpropion.

Fesoterodine is an antimuscarinic that is bioactivated to tolterodine.

Tenofovir disoproxil fumarate is an anti-HIV drug (NtRTI class) that is bioactivated to tenofovir (PMPA).

Drug theories

Receptor theory

Receptor theory is the application of receptor models to explain drug behaviour. John Newport Langley and Paul Ehrlich introduced the concept of a receptor that would mediate drug action at

the beginning of the 20th century. A J Clark was the first to quantify drug-induced biological responses (using an equation described firstly by A V Hill in 1909 and then in 1910) and propose a model to explain drug-mediated receptor activation.

Receptor occupancy model

The receptor occupancy model, which describes agonist and competitive antagonists, was built on the work of Langley, Hill and Clark. It is based on mass-action kinetics and attempts to link the action of a drug to the proportion of receptors occupied by that drug at equilibrium. In particular, the magnitude of the response is directly proportional to the amount of drug bound, and the maximum response would be elicited once all receptors were occupied at equilibrium. He applied mathematical approaches used in enzyme kinetics systematically to the effects of chemicals on tissues. Classic occupational models of receptor activation failed to provide evidence to directly support the idea that receptor occupancy follows a Langmuir curve as the model assumed leading to the development of alternative models to explain drug behaviour.[12]

Competitive inhibition models

The development of the classic theory of drug antagonism by Gaddum, Schild and Arunlakshana built on the work of Langley, Hill and Clark.. Gaddum described a model for the competitive binding of two ligands to the same receptor in short communication to the Physiological Society in 1937. The description referred only to binding, it was not immediately useful for the analysis of experimental measurements of the effects of antagonists on the response to agonists. In Schild regression, the change in the dose ratio, the ratio of the EC_{50} of an agonist alone compared to the EC_{50} in the presence of a competitive antagonist as determined on a dose response curve used to determine the affinity of an antagonist for its receptor.

Agonist models

The flaw in Clark's receptor-occupancy model was that it was insufficient to explain the concept of partial agonist lead to the development of agonist models of drug action by Ariens in

1954 and by Stephenson in 1956 to account for the intrinsic activity (efficacy) of a drug (that is, its ability to induce an effect after binding).[12][13]

Two-state receptor theory

The two-state model is a simple linear model to describe the interaction between a ligand and its receptor, but also the active receptor (R^*). The model uses an equilibrium dissociation constant to describe the interaction between ligand and receptor. It proposes that ligand binding results in a change in receptor state from an inactive to an active state based on the receptor's conformation. A receptor in its active state will ultimately elicit its biological response.

Ternary complex model

The original Ternary complex model was used to describe ligand, receptor, and G-protein interactions. It uses equilibrium dissociation constants for the interactions between the receptor and each ligand (K_a for ligand A; K_b for ligand B), as well as a cooperativity factor (α) that denotes the mutual effect of the two ligands on each other's affinity for the receptor.

Postulates of receptor theory

- Receptors must possess structural and steric specificity.
- Receptors are saturable and finite (limited number of binding sites)
- Receptors must possess high affinity for its endogenous ligand at physiological concentrations
- Once the endogenous ligand binds to the receptor, some early recognizable chemical event must occur

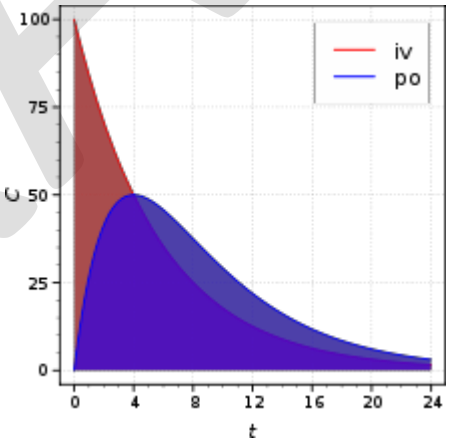
Bioavailability

- In pharmacology, bioavailability (BA) is a subcategory of absorption and is used to describe the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. By definition, when

a medication is administered intravenously, its bioavailability is 100 %.[1] However, when a medication is administered via other routes (such as orally), its bioavailability generally[TH[›]] decreases (due to incomplete absorption and first-pass metabolism) or may vary from patient to patient. Bioavailability is one of the essential tools in pharmacokinetics, as bioavailability must be considered when calculating dosages for non-intravenous routes of administration.

- For dietary supplements, herbs and other nutrients in which the route of administration is nearly always oral, bioavailability generally designates simply the quantity or fraction of the ingested dose that is absorbed.
- Bioavailability is defined slightly differently for drugs as opposed to dietary supplements primarily due to the method of administration and Food and Drug Administration regulations.
- Bio accessibility is a concept related to bioavailability in the context of biodegradation and environmental pollution. A molecule (often a persistent organic pollutant) is said to be bioavailable when is available to cross an organism's cellular membrane from the environment, if the organism has access to the chemical

Absolute bioavailability



- Bioavailabilty is a ratio of areas under the curves

- Absolute bioavailability compares the bioavailability of the active drug in systemic circulation following non-intravenous administration (i.e., after oral, rectal, transdermal, subcutaneous, or sublingual administration), with the bioavailability of the same drug following intravenous administration. It is the fraction of the drug absorbed through non-intravenous administration compared with the corresponding intravenous administration of the same drug. The comparison must be dose normalized (e.g. account for different doses or varying weights of the subjects); consequently, the amount absorbed is corrected by dividing the corresponding dose administered.
- Relative bioavailability and bioequivalence
- In pharmacology, relative bioavailability measures the bioavailability (estimated as the AUC) of a formulation (*A*) of a certain drug when compared with another formulation (*B*) of the same drug, usually an established standard, or through administration via a different route. When the standard consists of intravenously administered drug, this is known as absolute bioavailability (see above).

$$F_{rel} = 100 \cdot \frac{AUC_A \cdot D_B}{AUC_B \cdot D_A}$$

- Relative bioavailability is one of the measures used to assess bioequivalence (BE) between two drug products.

Factors influencing bioavailability

- The absolute bioavailability of a drug, when administered by an extravascular route, is usually less than one (i.e. F <100 %). Various physiological factors reduce the availability of drugs prior to their entry into the systemic circulation. Whether a drug is taken with or without food will also affect absorption, other drugs taken concurrently may alter absorption and first-pass metabolism, intestinal motility alters the dissolution of the drug and may affect the degree of chemical degradation of the drug by intestinal microflora. Disease states affecting liver metabolism or gastrointestinal function will also have an effect.
- Other factors may include, but are not limited to:

- Physical properties of the drug (hydrophobicity, pKa, solubility)
- The drug formulation (immediate release, excipients used, manufacturing methods, modified release – delayed release, extended release, sustained release, etc.)
- Whether the formulation is administered in a fed or fasted state
- Gastric emptying rate
- Circadian differences
- Interactions with other drugs/foods:
- Interactions with other drugs (e.g. antacids, alcohol, nicotine)
- Interactions with other foods (e.g. grapefruit juice, pomello, cranberry juice, brassica vegetables)
- Transporters: Substrate of efflux transporters (e.g. P-glycoprotein)
- Health of the GI tract
- Enzyme induction/inhibition by other drugs/foods:
- Enzyme induction (increased rate of metabolism), e.g. Phenytoin induces CYP1A2, CYP2C9, CYP2C19, and CYP3A4
- Enzyme inhibition (decreased rate of metabolism), e.g. grapefruit juice inhibits CYP3A → higher nifedipine concentrations
- Individual variation in metabolic differences
- Age: In general, drugs are metabolized more slowly in fetal, neonatal, and geriatric populations
- Phenotypic differences, enterohepatic circulation, diet, gender

Disease state

- e.g. hepatic insufficiency, poor renal function
- Each of these factors may vary from patient to patient (inter-individual variation), and indeed in the same patient over time (intra-individual variation). In clinical trials, inter-individual variation is a critical measurement used to assess the bioavailability differences from patient to patient in order to ensure predictable dosing.

POSSIBLE QUESTIONS

UNIT-I

PART-A (20 MARKS)

(Q.NO 1 TO 20 Online Examination)

PART-B (2 MARKS)

1. Write the pharmacological activity of drug?
2. Briefly describe the pro drug and its concept
3. Given account of Agonist and antagonist

PART-C (8 MARKS)

Explain the Distribution of drug

2. What is Receptor? Explain its types
3. Write account of absorption and first pass effect of drugs
4. Given account of elimination of drug in body
5. Briefly explains the G – protein coupled receptor and ion- Channel linked receptors
6. Discuss about Phase I reactions in Metabolism of drug
7. Describe Phase II reactions in metabolism of drug

Questions	opt1	opt2	opt3	opt4	Answer
Pharmacokinetics is:	The study of biological and therapeutic effects	The study of absorption, distribution, metabolism and excretion of drugs	The study of mechanisms of drug action	The study of methods of new drug development	The study of absorption, distribution, metabolism and excretion of drugs
The main mechanism of drugs absorption in	Active transport (carrier-mediated	Filtration (aqueous diffusion)	Endocytosis and exocytosis	Passive diffusion (lipid diffusion)	Passive diffusion (lipid diffusion)
What does the term “bioavailability” mean?	Plasma protein binding degree of substance	Permeability through the brain-blood barrier	Fraction of an uncharged drug reaching the systemic circulation following any route administration	Amount of a substance in urine relative to the initial dose	Fraction of an uncharged drug reaching the systemic circulation following any route administration
Which route of drug administration is most likely to lead to the first-pass	Sublingual	Oral	Intravenous	Intramuscular	Oral
The volume of distribution (Vd) relates:	Single to a daily dose of an administrated	An administrated dose to a body weight	An uncharged drug reaching the systemic circulation	The amount of a drug in the body to the concentration of a drug in plasma	The amount of a drug in the body to the concentration of a drug in plasma
Metabolic transformation (phase 1) is:	Acetylation and methylation of substances	Transformation of substances due to oxidation, reduction or	Glucuronide formation	Binding to plasma proteins	Transformation of substances due to oxidation, reduction or hydrolysis
Which organ involved in first pass	Heart	Kidney	Brain	Liver	Liver
Which one of the following	Intravenous	Oral	Topical	Dissolution	Dissolution

Which of the following processes proceeds in the second phase of biotransformati	Acetylation	Reduction	Oxidation	Hydrolysis	Acetylation
Which enzyme is involved in phase I	Catalase	Polyphenol oxidase	Cytochorome p450 MO	Oxygenase	Cytochorome p450 MO
Cytochorome p450 MO is found mainly	Heart	Liver	Brain	Kidney	Liver
Dichloroisopropylarterenol blocks	Alpha adrenergic	Beta adrenergic receptors	Both alpha and beta receptors	Gamma adrenergic receptors	Beta adrenergic receptors
Half life (t ½) is the time required to:	Change the amount of a drug in	Metabolize a half of an introduced drug into the active	Absorb a half of an introduced drug	Bind a half of an introduced drug to plasma proteins	Change the amount of a drug in plasma by half during elimination
Irreversible interaction of an antagonist with a receptor	Ionic bonds	Hydrogen bonds	Covalent bonds	Sulphur bond	Covalent bonds
The second messenger of G-protein-coupled (metabotropic)	Adenylyl cyclase	Sodium ions	Phospholipase C	cAMP	cAMP
Give the definition for a therapeutical dose:	The amount of a substance to produce the	The amount of a substance to produce effects hazardous for an organism	The amount of a a substance to produce the required effect in most patients	The amount of a substance to accelerate an increase of concentration of medicine in an organism	The amount of a substance to produce the required effect in most patients
The substance which changes the activity of an effector element but doesn’t belong to second	cAMP	cGMP	G–protein	Calcium ions	G–protein

An agonist can produce submaximal effects and has moderate efficacy it's	Partial agonist	Antagonist	Agonist-antagonist	Full agonist	Partial agonist
Conjugation is:	Process of drug reduction by	Process of drug oxidation by special	Coupling of a drug with an endogenous substrate	Solubilization in lipids	Coupling of a drug with an endogenous substrate
What is implied by "active transport"?	Transport of drugs trough a membra	Transport without energy consumption	Engulf of drug by a cell membrane with a new vesicle formation	Transport against concentration gradient	Transport against concentration gradient
What kind of substances can't permeate membranes by passive	Lipid-soluble	Non-ionized substances	Hydrophobic substances	Hydrophilic substances	Hydrophilic substances
The reasons determining bioavailability are:	Rheological parameters of blood	Amount of a substance obtained orally and quantity of	Extent of absorption and hepatic first-pass effect	Glomerular filtration rate	Extent of absorption and hepatic first-pass effect
For the calculation of the volume of distribution (Vd) one must take into	Concentration of a substance in plasma	Concentration of substance in urine	Therapeutical width of drug action	A daily dose of drug	Concentration of a substance in plasma
Biotransformation of a medicinal substance	Faster urinary excretion	Slower urinary excretion	Easier distribution in organism	Higher binding to membranes	Faster urinary excretion
The organelle that carry Cytochorome p450 MO is	Endoplasmic reticulam	Golgi complex	Mitochondria	Mitochondria	Endoplasmic reticulam
Conjugation of a drug includes the following EXCEPT:	Glucoronidation	Sulfate formation	Hydrolysis	Methylation	Hydrolysis

The phase II reaction which produce a compound with greater pharmocologic al actvity	Glucoro nic acid conjugati on	Conjugation with amino acid	Methylation	Glutathione conjugation	Methylation
Elimination is expressed as follows:	Rate of renal tubular reabsorpt ion	Clearance speed of some volume of blood from	Time required to decrease the amount of drug in plasma by one-half	Clearance of an organism from a xenobiotic	Clearance of an organism from a xenobiotic
Acidic drug rapidly absorbed at	Stomach	GI tract	Large intestine	Mouth	Stomach
Coenzyme required by Cytochorome p450 MO is	NADH	NADPH	Lipoic acid	TPP	NADPH
Basic drugs are absorbed in	small intestine	stomach	Large intestine	Pancreas	small intestine
Which effect may lead to toxic reactions when a drug is taken continuously or	Refracto riness	Cumulative effect	Tolerance	Tachyphylaxis	Cumulative effect
What term is used to describe a more gradual decrease in responsiveness to a drug, taking days or	Refracto riness	Cumulative effect	Tolerance	Tachyphylaxis	Tolerance
What term is used to describe a decrease in responsiveness to a drug which develops in a	Refracto riness	Cumulative effect	Tolerance	Tachyphylaxis	Tachyphylaxis
Which drug that cross the lipid bilayer	Water soluble drug	lipid soluble drug	ionsoluble drug	Non ionsoluble drug	lipid soluble drug

Science that deals with drug	Pharmacy	pharmacognosy	pharmacodynamics	pharmacology	pharmacology
Inhibition of MAO causses an	decrease in the deaminat	increasse in the deamination	increase in the deamination of noradrenalin	decrease in the deamination of dopamine	decrease in the deamination of noradrenalin
Systemic clearance (CLs) is related with:	Only the concentration of substances in	Only the elimination rate constant	Volume of distribution, half life and elimination rate constant	Bioavailability and half life	Volume of distribution, half life and elimination rate constant
Elimination rate constant (Kelim) is defined by the following	Rate of absorption	Maximal concentration of a substance in plasma	Highest single dose	Half life (t ½)	Half life (t ½)
Half life (t ½) is the time required to:	Change the amount of a drug in	Metabolize a half of an introduced drug into the active	Absorb a half of an introduced drug	Bind a half of an introduced drug to plasma proteins	Change the amount of a drug in plasma by half during elimination
Aspirin is chemically	Sodium salicylate	Acetylsalicylic acid	Salicylamide	Sodium salicylamide	Acetylsalicylic acid
Which is the most appropriate to the term “receptor”	All types of ion channels modulated by a drug	Enzymes of oxidizing-reducing reactions activated by a drug	Active macromolecular components of a cell or an organism which a drug molecule has to combine with in order to elicit its specific effect	Carriers activated by a drug	Active macromolecular components of a cell or an organism which a drug molecule has to combine with in order to elicit its specific effect
What does “affinity” mean?	A measure of how tightly a	A measure of how tightly a drug binds to a receptor	A measure of inhibiting potency of a drug	A measure of bioavailability of a drug	A measure of how tightly a drug binds to a receptor
A measure of bioavailability of a drug	A measure of how tightly a drug	An agonist is a substance that:	Interacts with the receptor without producing any effect	Interacts with the receptor and initiates changes in cell function, producing various effects	Increases concentration of another substance to produce effect

An agonist is a substance that:	Interacts with the receptor without producing any effect	Interacts with the receptor and initiates changes in cell function, producing various	Increases concentration of another substance to produce effect	Interacts with plasma proteins and doesn't produce any effect	Interacts with the receptor and initiates changes in cell function, producing various effects
An antagonist is a substance that:	Binds to the receptors and initiates changes in cell	Binds to the receptors and initiates changes in cell function, producing submaximal	Interacts with plasma proteins and doesn't produce any effect	Binds to the receptors without directly altering their functions	Binds to the receptors without directly altering their functions
A competitive antagonist is a substance that:	Interacts with receptors and produces sub maximal	Binds to the same receptor site and progressively inhibits the agonist	Binds to the nonspecific sites of tissue	Binds to one receptor subtype as an agonist and to another as an antagonist	Binds to the same receptor site and progressively inhibits the agonist response
The substance binding to one receptor subtype as an agonist and to another as an antagonist is	Competitive antagonist	Irreversible antagonist	Agonist-antagonist	Partial agonist	Agonist-antagonist
Irreversible interaction of an antagonist with a receptor	Ionic bonds	Hydrogen bonds	Covalent bonds	Weak bonds	Covalent bonds
Tick the second messenger of G-protein-coupled	Adenylyl cyclase	Sodium ions	Phospholipase C	cAMP	cAMP

What is the type of drug-to-drug interaction which is connected with processes of absorption, biotransformati	Pharmacodynamic interaction	Physical and chemical interaction	Pharmaceutical interaction	Pharmacokinetic interaction	Pharmacokinetic interaction
Chloramphenicol is derived	Streptomyces	Streptomyces griseus	Streptomyces kanamycin	Pencillin	Streptomyces griseus
A hydrophilic medicinal agent has the following property:	Low ability to penetrate through the cell	Penetrate through membranes by means of endocytosis	Easy permeation through the blood-brain barrier	High reabsorption in renal tubules	Low ability to penetrate through the cell membrane lipids
The feature of the sublingual route:	Pretty fast absorption	A drug is exposed to gastric secretion	A drug is exposed more prominent liver metabolism	A drug can be administrated in a variety of doses	Pretty fast absorption
Pick out the parenteral route of medicinal	Rectal	Oral	Sublingual	Inhalation	Inhalation
Parenteral administration:	Cannot be used with unconsciousness patients	Generally results in a less accurate dosage than oral administratio	Usually produces a more rapid response than oral administration	Is too slow for emergency use	Usually produces a more rapid response than oral administration
Volume of distribution (Vd) one must take into _____	Concentration of a substance in	Concentration of substance in urine	Therapeutical width of drug action	A daily dose of drug	Concentration of a substance in plasma
Biotransformation of the drugs is to	Less ionized	More pharmacologically active	More lipid soluble	Less lipid soluble	Less lipid soluble
Tick the drug type for which microsomal oxidation is the most	Lipid soluble	Water soluble	Low molecular weight	High molecular weight	Lipid soluble

UNIT-II

SYLLABUS

Drug tolerance and drug dependence. Principles of basic pharmacokinetics. Adverse response to drugs, drug intolerance, pharmacogenetics, drug allergy, tachyphylaxis, drug abuse, vaccination against infection, factors modifying drug action and effect. Assay of drug potency: chemical, bioassay and immunoassay.

Adverse Drug Reactions

Drug hypersensitivity results from interactions between a pharmacologic agent and the human immune system. These types of reactions constitute only a small subset of all adverse drug reactions. Allergic reactions to medications represent a specific class of drug hypersensitivity reactions mediated by IgE. Immune-mediated drug reactions may be discussed generally in the Gell and Coombs classification system, a widely accepted conceptual framework for understanding complex immune reactions. However, some reactions involve additional, poorly understood mechanisms that are not easily classified. Identifiable risk factors for drug hypersensitivity reactions include age, female gender, concurrent illnesses, and previous hypersensitivity to related drugs. Drug hypersensitivity is a clinical diagnosis based on available data. Laboratory testing may be useful, with skin testing providing the greatest specificity. Treatment is largely supportive and includes discontinuation of the offending medication, symptomatic treatment, and patient education. Patients with penicillin allergy should avoid carbapenems, and caution should be used in prescribing cephalosporins in these patients. Reactions to radiocontrast media can be limited by pretreatment with prednisone, diphenhydramine, and either ephedrine or a histamine H_2-receptor antagonist.

Adverse drug reactions are common. Identifying true drug allergy, however, can be challenging. Complicating factors of drug reactions include the myriad clinical symptoms and multiple mechanisms of drug-host interaction, many of which are poorly understood. In addition, the relative paucity of laboratory testing that is available for drug allergy makes the diagnosis dependent on clinical findings.

Immunologic and Non immunologic Drug Reactions

Type	*Example*
Immunologic	
Type I reaction (IgE-mediated)	Anaphylaxis from β-lactam antibiotic
Type II reaction (cytotoxic)	Hemolytic anemia from penicillin
Type III reaction (immune complex)	Serum sickness from anti-thymocyte globulin
Type IV reaction (delayed, cell-mediated)	Contact dermatitis from topical antihistamine
Specific T-cell activation	Morbilliform rash from sulfonamides
Fas/Fas ligand-induced apoptosis	Stevens-Johnson syndrome
	Toxic epidermal necrolysis
Other	Drug-induced, lupus-like syndrome
	Anticonvulsant hypersensitivity syndrome
Nonimmunologic	
Predictable	
Pharmacologic side effect	Dry mouth from antihistamines
Secondary pharmacologic side effect	Thrush while taking antibiotics
Drug toxicity	Hepatotoxicity from methotrexate
Drug-drug interactions	Seizure from theophylline while taking erythromycin
Drug overdose	Seizure from excessive lidocaine (Xylocaine)
Unpredictable	
Pseudoallergic	Anaphylactoid reaction after radiocontrast media
Idiosyncratic	Hemolytic anemia in a patient with G6PD deficiency after primaquine therapy

Type	*Example*
Intolerance	Tinnitus after a single, small dose of aspirin

Drug Interactions

The effect a drug has on a person may be different than expected because that drug interacts with

- Another drug the person is taking (drug-drug interaction)
- Food, beverages, or supplements the person is consuming (drug-nutrient interaction)
- Another disease the person has (drug-disease interaction).

The effects of drug interactions are usually unwanted and sometimes harmful. Interactions may increase or decrease the actions of one or more drugs, resulting in side effects or failed treatment.

DRUG-DRUG INTERACTIONS

Drug-drug interactions can involve prescription or nonprescription (over-the-counter) drugs. Types of drug-drug interactions include duplication, opposition (antagonism), and alteration of what the body does to one or both drugs.

Drug intolerance

Drug intolerance or drug sensitivity is a lower threshold to the normal pharmacologic action of a drug. It is not to be confused with drug allergy. Drug intolerance is uncommon and idiopathic, thus extremely difficult to predict except in persons with a prior history or a family history of intolerance to that specific drug. Some drug intolerances are known to result from genetic variants of drug metabolism.

Examples

• Tinnitus after a normal dose of aspirin

• Liver failure (possibly also kidney failure) after a normal dose of acetaminophen

• Fatal poisoning in a breastfed newborn baby due to normal use of codeine by the mother.

Analgesic intolerance

Intolerance to analgesics, particularly NSAIDs, is relatively common. Its cause is believed to be variation in the metabolism of arachidonic acid. Symptoms include chronic rhinosinusitis with nasal polyps, asthma, gastrointestinal ulcers, angioedema, and urticaria.

Idiosyncratic drug reaction

Idiosyncratic drug reactions, also known as type B reactions, are drug reactions which occur rarely and unpredictably amongst the population. This is not to be mistaken with idiopathic which implies that the cause is not known. They frequently occur with exposure to new drugs, as they have not been fully tested and the full range of possible side effects have not been discovered; they may also be listed as an adverse drug reaction with a drug, but be extremely rare.

Some patients have multiple-drug intolerance. Patients who have multiple idiopathic effects that are nonspecific are more likely to have anxiety and depression. Idiosyncratic drug reactions appear to not be concentration dependent. A minimal amount of drug will cause an immune response, but it is suspected that at a low enough concentration, a drug will be less likely to initiate an immune response.

Mechanism

In adverse drug reactions involving overdoses, the toxic effect is simply an extension of the pharmacological effect (Type A adverse drug reactions). On the other hand, clinical symptoms of idiosyncratic drug reactions (Type B adverse drug reactions) are different than the pharmacological effect of the drug. The proposed mechanism of most idiosyncratic drug reactions is immune mediated toxicity. To create an immune response, you must have a foreign molecule that antibodies can bind to (ie. the antigen) and you must have cellular damage. Very often, drugs will not be immunogenic because they are too small to bind antibodies. However, a drug can cause an immune response if the drug binds a larger molecule. Some unaltered drugs such as penicillin will bind avidly to proteins. Others must be bioactivated into a toxic compound that will in turn bind to proteins. The second criteria of cellular damage can come either from a toxic drug/drug metabolite or it may come from an injury or infection. These will sensitize the immune system to the drug and cause a response. Idiosyncratic reactions fall conventionally under toxicology

Drug allergy

A drug allergy is an allergy to a drug, most commonly a medication. Medical attention should be

sought immediately if an allergic reaction is suspected. An allergic reaction will not occur on the first exposure to a substance. The first exposure allows the body to create antibodies and memory lymphocyte cells for the antigen. However, drugs often contain many different substances, including dyes, which could cause allergic reactions. This can cause an allergic reaction on the first administration of a drug. For example, a person who developed an allergy to a red dye will be allergic to any new drug which contains that red dye. A drug allergy is different from an intolerance. A drug intolerance, which is often a milder, non-immune-mediated reaction, does not depend on prior exposure. Most people who believe they are allergic to aspirin are actually suffering from a drug intolerance. Risk factors a drug allergy is more likely to develop with large doses and extended exposure. Common drug allergens when a medication causes an allergic reaction, it is called an allergen. The following is a short list of the most common drug allergens:

- Antibiotics
- Penicillin
- Sulfa drugs
- Tetracycline
- Analgesics
- Codeine
- Non-steroidal anti-inflammatory drugs (NSAIDs)
- Antiseizure
- Phenytoin
- Carbamazepine.

Tachyphylaxis

Tachyphylaxis is a medical term describing a decrease in the response to a drug due to previous exposure to that drug. Increasing the dose of the drug may be able to restore the original response. In this context tachyphylaxis is a synonym for drug tolerance. This can sometimes be caused by depletion or marked reduction of the amount of neurotransmitter responsible for creating the drug's effect, or by the depletion of receptors available for the drug or neurotransmitter to bind to. This depletion is caused by the cell's reducing the number of receptors in response to their saturation. Examples: Amphetamine, ephedrine, MDMA (indirectly acting drugs) Tachyphylaxis is

characterized by the rate sensitivity: The response of the system depends on the rate with which a stimulus is presented. To be specific, a high-intensity prolonged stimulus or often-repeated stimulus may bring about a diminished response also known as desensitization. In biological sciences, molecular interactions are the physical bases of the operation of the system. The control of the operation, in general, involves interaction of a stimulus molecule with a receptor/enzyme subsystem by, typically, binding to the macromolecule A and causing an activation or an inhibition of the subsystem by forming an activated form of the macromolecule B. The following schematic represents the activity:

A --------> B

Where p is the activation rate coefficient. It is customary that p is called a rate constant, but, since the p stands for

measure of the intensity of the stimulus causing the activation, p may be variable (non-constant). The above scheme is only the necessary condition for the rate sensitivity phenomenon, and other pathways of deactivation of B may be considered, with the subsequent return to the inactive form of the receptor/enzyme A. Examples offer particular use of such (mathematical) models in endocrinology, physiology and pharmacology.

Examples

Examples of tachyphylaxes are the following:

• Calcitonin demonstrates tachyphylaxis in 2–3 days when being used to treat hypercalcemia of malignancy. This

reaction is anticipated and calcitonin is given along with biphosphonates, which have their maximum effect in 2–3 days.

• Nitroglycerine demonstrates tachyphylaxis, requiring drug-free intervals when administered transdermally

• Repeated doses of ephedrine may display tachyphylaxis, since it is an indirectly acting sympathomimetic amine, which will deplete noradrenaline from the nerve terminal. Thus, repeated doses result in less noradrenaline released than the initial dose.

• Nicotine may also show tachyphylaxis over the course of a day, although the mechanism of this action is unclear.

• Hydralazine displays tachyphylaxis if given as a monotherapy for antihypertensive treatment. It is administered with a beta-blocker with or without a diuretic.

• Metoclopramide is another example.

• Dobutamine, a direct-acting beta agonist used in congestive heart failure, also demonstrates tachyphylaxis.

• Desmopressin used in the treatment of type 1 von Willebrand disease is, in general, given every 12–24 hours in limited numbers due to its tachyphylactic properties.

• Hormone replacement when used in menopausal women in the form of estrogen and progesterone implants is cited as having potential to lead to tachyphylaxis, but that citation is based on a single study done in 1990 and no followup research is available to support this interpretation. Tachyphylaxis 2

• Psychedelics such as LSD-25 and psilocybin-containing mushrooms demonstrate very rapid tachyphylaxis. In other words, one may be unable to 'trip' two days in a row. Some people are able to 'trip' by taking up to three times the dosage, yet some users may not be able to negate tachyphylaxis at all until a period of days has gone by In a patient fully withdrawn from centrally-acting analgesics, viz. opioids, going back to an intermittent schedule or maintenance dosing protocol, a fraction of the old tolerance level will rapidly develop, usually starting two days after opioid therapy is resumed and, in general, leveling off after day 7. Whether this is caused directly by opioid receptors modified in the past or effecting a change in some metabolic set-point is unclear. Increasing the dose will usually restore efficacy; relatively rapid opioid rotation may also be of use if the increase in tolerance continues.

Drug abuse

Drug abuse also known as drug abuse, refers to a maladaptive pattern of use of a substance that is not considered dependent. The term "drug abuse" does not exclude dependency, but is otherwise used in a similar manner in nonmedical contexts. The terms have a huge range of definitions related to taking a psychoactive drug or performance enhancing drug for a non-therapeutic or non-medical effect. All of these definitions imply a negative judgment of the drug use in question (compare with the term responsible drug use for alternative views). Some of the drugs most often associated with this term include alcohol, amphetamines, barbiturates,

benzodiazepines (particularly temazepam, nimetazepam, and flunitrazepam), cocaine, methaqualone, and opioids. Use of these drugs may lead to criminal penalty in addition to possible physical, social, and psychological harm, both strongly depending on local jurisdiction Other definitions of drug abuse fall into four main categories: public health definitions, mass communication and vernacular usage, medical definitions, and political and criminal justice definitions. Substance abuse is a form of substance-related disorder.

Drug misuse

Drug misuse is a term used commonly for prescription medications with clinical efficacy but abuse potential and known adverse effects linked to improper use, such as psychiatric medications with sedative, anxiolytic, analgesic, or stimulant properties. Prescription misuse has been variably and inconsistently defined based on drug prescription status, the uses that occur without a prescription, intentional use to achieve intoxicating effects, route of administration, co-ingestion with alcohol, and the presence or absence of abuse or dependence symptoms.

Multiple drug resistance

Multiple drug resistance or Multidrug resistance is a condition enabling a disease-causing organism to resist distinct drugs or chemicals of a wide variety of structure and function targeted at eradicating the organism. Organisms that display multidrug resistance can be pathologic cells, including bacterial and neoplastic (tumor) cells.

Common MultiDrug-Resistant Organisms (MDROs)

• Vancomycin Resistant Enterococci (VRE)

• Methicillin Resistant *Staphylococcus aureus* (MRSA)

• Extended spectrum ß-lactamse (ESBLs) producing Gram-negative bacteria

• *Klebsiella pneumoniae* carbapenemase (KPC) producing Gram-negatives

• Imipenem resistant or MultiDrug Resistant Organisms *Acinetobacter baumannii*

• Imipenem resistant or MultiDrug Resistant Organisms *Pseudomonas aerginosa*

Bacterial resistance to antibiotics

Various microorganisms have survived for thousands of years by their being able to adapt to antimicrobial agents. They do so via spontaneous mutation or by DNA transfer. This process enables some bacteria to oppose the assault of certain antibiotics, rendering the antibiotics

ineffective. These microorganisms employ several mechanisms in attaining multidrug resistance:

• No longer relying on a glycoprotein cell wall

• Enzymatic deactivation of antibiotics

• Decreased cell wall permeability to antibiotics

• Altered target sites of antibiotic

• Efflux mechanisms to remove antibiotics

• Increased mutation rate as a stress response

Neoplastic resistance

Cancer cells also have the ability to become resistant to multiple different drugs, and share many of the same mechanisms:

• **Increased efflux of drug** (as by P-glycoprotein, multidrug resistance-associated protein, lung resistance-related protein, and breast cancer resistance protein & reproductive cancer resistance protein)

• Enzymatic deactivation (i.e., glutathione conjugation)

• Decreased permeability (drugs cannot enter the cell)

• Altered binding-sites

• Alternate metabolic pathways (the cancer compensates for the effect of the drug).

Dose-response relationship

Semi-log plots of two agonists with different Kd. The **dose-response relationship**, or **exposure-response relationship**, describes the change in effect on an organism caused by differing levels of exposure (or doses) to a stressor (usually a chemical) after a certain exposure time. This may apply to individuals (e.g.: a small amount has no significant effect, a large amount is fatal), or to populations (e.g.: how many people or organisms are affected at different levels of exposure). Studying dose response, and developing

Dose response models, is central to determining "safe" and "hazardous" levels and dosages for drugs, potential pollutants, and other substances to which humans or other organisms are exposed. These conclusions are often the basis for public policy. The U.S.Environmental Protection Agency has developed extensive guidance and reports on dose-response modeling and assessment, as well as software it should be realized that dose-response relationships will generally depend on the

exposure time and exposure route

(e.g., inhalation, dietary intake); quantifying the response after a different exposure time or for a different route leads to a different relationship and possibly different conclusions on the effects of the stressor under consideration. This limitation is caused by the complexity of biological systems and the often unknown biological processes operating between the external exposure and the adverse cellular or tissue response.

Assay of Drug

Bioassay (commonly used shorthand for biological assay), or biological standardization is a type of scientific experiment. Bioassays are typically conducted to measure the effects of a substance on a living organism and are essential in the development of new drugs and in monitoring environmental pollutants. Both are procedures by which the potency (pharmacology) or the nature of a substance is estimated by studying its effects on living matter. Response that it produces. Quantitative bioassays are typically analyzed using the methods of biostatistics.

Types

- Chemicl assay
- Bio assay
- Immuno assay

POSSIBLE QUESTIONS

UNIT-II

PART-A (20 MARKS)

(Q.NO 1 TO 20 Online Examination)

PART-B (2 MARKS)

1. Write account of receptor interaction
2. Given account on drug allergy
3. Explain the adverse response of drugs
4. Write short notes on tachyphylaxis
5. Briefly discuss the drug tolerance

PART-C (8 MARKS)

1. Explain the drug abuse
2. Discuss about drug-intolerance
3. Describe the multidrug resistance phenotypes
4. What are the different factors that modify the effect of drug?
5. Write the assay of drug potency

Questions	opt1	opt2	opt3	opt4	Answer
Cell surface receptors are	C protein coupled receptors	G-protein coupled receptors	Protein A tyrosine kinases	Protein A B tyrosine kinase	G-protein coupled receptors
The receptor serves as	Recognition molecule	Non recognition molecule	Target sites	Active sites	Recognition molecule
Which one of the following not bound to membrane?	Tyrosine linked receptors	Steroid receptors	ion channel linked receptors	G- protein coupled receptors	steroid receptors
When the person remains well only when he is taking the drug is termed as the State of	psychic dependence	physical dependence	withdrawal syndrome	Non Psychic dependence	physical dependence
If the abusing drug is withdrawn the person	Abstinence	physical dependence	Tolerance	psychic dependence	Abstinence
If a greaster dose of the drug is required to elicit the normal pharmachological Effect the state is known as	dependence	abstinence	tolerance	intolerance	tolerance
Th 1 cells	enhance CMI	enhance humoral immunity	inhibit CMI	inhibit humoral immunity	enhance CMI
If the drug is A repeated	cytotoxic	cell	psychic immune	drug	pharmaco

A state where some changes develop in the tissue leading to less pharmacological Effect of the drug is known as	pharmacokinetic tolerance	pharmacodynamic tolerance	psychic tolerance	drug intolerance	pharmacodynamic tolerance
Best example of psychic dependence is	cigarette smoking	barbiturates	sulphonamides	salicylates	cigarette smoking
The state when the person seeks drugs purely for psychological pleasure is	drug dependence	physical dependence	psychic dependence	pathological equilibrium	psychic dependence
bstances like lead can remain deposited in bones without producing toxic effects Which is called	passive immunization	additive effect	antagonism	synergism	passive immunization
Inflammatory reactions initiated by mononuclear lymphocytes and not by Antibody alone are called	type I hypersensitivity	type II hypersensitivity	delayed hypersensitivity	type III hypersensitivity	delayed hypersensitivity

Methadone is	agonist of opioid receptors	antagonist of opioid receptors	agonist of µ receptors	antagonist of µ receptors	agonist of opioid receptors
Opioids used for abusing are by themselves	CNS stimulants	CNS depressants	CVS stimulants	CVS depressants	CNS depressants
The drug naltrexone is	agonist of opioid receptors	antagonist of opioid receptors	agonist of µ receptors	antagonist of µ receptors	antagonist of opioid receptors
The drugs used to treat abusing of opioids is	Ibu brufen	methadone	Diclofenac	Analgesic	methadone
If the opioid abusers are doctors,nurses and other health workers The choice of drug used for treatment is	methadone	methadyl acetate	naltrexone	pethidine	pethidine
Amphetamine is an	antifatigue agent	fatigue agent	nausea inducer	heroin	antifatigue agent
Polydrug abuse common in USA is	cocaine and heroin	heroin and amphetamine	amphetamine and cocaine	nicotine	cocaine and heroin
The half life of cocaine is	2 hrs	3 hrs	15 hrs	1hr	1hr
Drug used for the treatment of acute cocaine overdose is	Naproxen	amphetamine	diazepam	Ibu brufen	diazepam

The mechanism of action of labetalol used for acute cocaine overdose is	blocking of Ca^{2+} channel	blocking of α and β receptor	blocking of K^{+} channel	blocking of P^{+} channel	blocking of α and β receptor
The mechanism of action of nifedipine used for acute cocaine overdose is	blocking of Ca^{2+} channel	blocking of α and β receptor	blocking of K^{+} channel	blocking of P^{+} channel	blocking of Ca^{2+} channel
The drug of choice for CNS complications due to acute cocaine overdose is	labetalol	nifedipine	diazepam	sulphonamides	diazepam
The craving of cocaine is reduced by	labetalol	nifedipine	desipramine	diazepam	desipramine
LSD causes ---------- of seratoninergic neurons	hyper activity	hypo activity	normal activity	less activity	hypo activity
The half life of LSD is	1 hr	2 hrs	3 hrs	4 hrs	3 hrs
The active principle of cannabis is	diazepam	nifedipine	cannabinol	Ibu brufen	cannabinol

A repeated injection of egg albumin in such an animal causes a violent reaction called	Cytotoxic type reaction	Cell mediated reaction	Immune complex mediated reaction	Anaphylaxis	Anaphylaxis
The drug naltrexone is	Agonist of opioid receptors	Antagonist of opioid receptors	Agonist of morphine receptors	Antagonist of morphine receptors	Antagonist of opioid receptors
The average dose of drug is mentioned	mg per kg body weight	µg per kg body weight	kg per kg body weight	Cal per kg body weight	mg per kg body weight
The pharmacokinetics of drug changes with	sex	height	weight	age	age
The body surface area is calculated from	height and age	height and weight	weight and age	weight alone	height and weight
What type of drugs should be avoided during menstruatio	drugs likely to produce pelvic congestion	drugs which may stimulate uterine smooth muscle	nephrotoxic drugs	neurotoxic drugs	drugs likely to produce pelvic congestion
Consumption of alcohol enhances the effect of	CNS depressants	CNS stimulants	PNS depressants	PNS stimulants	CNS depressants

The chances of drug toxicity is enhanced by administration of drug through	IV route	orally	IM route	Rectal route	IV route
Aspirin reduces body temperature only in the presence of	pyrexia	angina pectoris	bronchial asthma	congestive cardiac failure	pyrexia
The vasoconstrictor effect of noradrenaline is reduced in the presence of	metabolic ketosis	metabolic acidosis	myxedema	pyrexia	metabolic acidosis
In myxedema, morphine acts for a much longer time because of the low rate of	acylation	reduction	oxidation	hydration	oxidation
Both tobacco smoke and alcohol consumption induce	renal enzymes	cardiac enzymes	liver enzymes	Kidney enzymes	liver enzymes

The phenomenon of the total pharmacological action of two or more drugs Administered together is equivalent to the sum of their individual Pharmacological actions is termed as	an synergism	an antagonism	a drug intolerance	an addictive effect	an addictive effect
Facilitation of a pharmacological response by the concomitant use of two or more Drugs is called	antagonism	synergism	additive effect	drug intolerance	synergism
The phenomenon of opposing actions of two drugs on the same physiological System is termed as	drug antagonism	synergism	additive effect	drug intolerance	drug antagonism

The phenomenon of an unusually large dose of a drug is required to elicit an Effect ordinarily producedby the normal therapeutic dose of the drug is termed as drug	tolerance	drug tolerance	antagonism	synergism	drug tolerance
The development of tolerance is confined to certain effects or to certain systems is called	cross tolerance	racial tolerance	tissue tolerance	species tolerance	tissue tolerance
Functional tolerance is otherwise known as	pharmacodynamic tolerance	pharmacogenetic tolerance	acquired tolerance	tachyphylaxis	pharmacodynamic tolerance

If drugs like ephedrine, tyramine etc are administered repeatedly as very short Intervals, the pharmacological response elicited decrease progressively, this Phenomenon is known as	true tolerance	functional tolerance	antagonism	tachyphylaxis	tachyphylaxis
chyphylaxis is otherwise known as	acquired tolerance	acute tolerance	tissue tolerance	true tolerance	acute tolerance
Determination of the amount of biological activity in a unit quantity of the Preparation is known as	chemical assay	immunological assay	bioassay	Radioassay	bioassay
Radio immuno assay is	physico-chemical assay	chemical assay	biological assay	Radioassay	physico-chemical assay
ELISA	Enzyme linked Immunosorbent assay	Enzyme linked innate assay	Enzyme linked immune assay	Enzyme linked immune soluble assay	Enzyme linked Immunosorbent assay

Any response to a drug that is noxious and unintended and that occurs at doses Used in man for prophylaxis, diagnosis or therapy is called an	adverse drug reactions	drug intolerance	drug allergy	idiosyncracy	adverse drug reactions
Inability of the individuals to tolerate a drug is called	Idiosyncracy	drug intolerance	adverse drug reactions	drug allergy	drug intolerance
Qualitative intolerance due to other than immune mechanism	tachyphylaxis	drug intolerance	adverse effects	idiosyncracy	idiosyncracy
The innate immune system are	macrophages and NKcells	lymphocytes	macrophages and lymphocytes	NKcells and mast cells	macrophages and NKcells
Origin of T-lymphocytes is	bursa of fabricus	thymus	thyroid	T cells	Thymus
What type of T-cells are mainly responsible for the helper function	T-cells bearing on CD_4 antigen	T-cells bearing on CD_8 antigen	B cells	K cells	T-cells bearing on CD_4 antigen

When does tachyphylaxis occur	When there is a decreased receptor mediated response to a drug	When there is an increased risk of side effect occurring	When smaller doses cause an increased response to a drug	When the drug causes a faster heart rate	When there is a decreased receptor mediated response to a drug
What term is used to describe a decrease in responsiveness to a drug which develops in a few minutes?	Refractoriness	Cumulative effect	Tolerance	Tachyphylaxis	Tachyphylaxis
If two drugs with the same effect, taken together, produce an effect that is equal in magnitude to the sum of the effects of the drugs given individually, it is called as:	Antagonism	Potentiation	Additive effect	Agonism	Additive effect
What phenomenon can occur in case of using a combination of drugs?	Tolerance	Tachyphylaxis	Accumulation	Synergism	Synergism

Inflammatory reactions initiated by mononuclear lymphocytes and not by Antibody alone are called	Type I hypersensitivity	Type II hypersensitivity	Delayed hypersensitivity	Type III hypersensitivity	Delayed hypersensitivity
What type of drugs should be avoided during menstruation?	Drugs likely to produce pelvic congestion	Drugs which may stimulate uterine smooth muscle	Nephrotoxic drugs	Neurotoxic drugs	Drugs likely to produce pelvic congestion
The development of tolerance is confined to certain effects or to certain systems is called	Cross tolerance	Racial tolerance	Tissue tolerance	Species tolerance	Tissue tolerance
Enzymes used in ELISA are	Acid phosphatase and penicillinase	Acid phosphatase and peptidase	Alkaline phosphatase and penicillanase	Zinc phosphate	Alkaline phosphatase and penicillanase
Cells of the innate immune system are	Macrophages and NK cells	Lymphocytes	Macrophages and lymphocytes	NK cells and mast cells	Macrophages and NK cells
Origin of T-lymphocytes is	Bursa of fabricus	Thymus	Thyroid	T cells	Thymus

Idiosyncratic reaction of a drug is:	A type of hypersensitivity reaction	A type of drug antagonism	Unpredictable, inherent, qualitatively abnormal reaction to a drug	Quantitatively exaggerated response	Unpredictable, inherent, qualitatively abnormal reaction to a drug
Tachyphylaxis is:	A drug interaction between two similar types of drugs	Very rapidly developing tolerance	A decrease in responsiveness to a drug, taking days or weeks to develop	A drug interaction between similar types of drugs	Very rapidly developing tolerance
What type of T-cells is mainly responsible for the helper function?	T-cells bearing on CD_4 antigen	T-cells bearing on CD_8 antigen	B cells bearing on CD_8 antigen	NK cells	T-cells bearing on CD_4 antigen
Radio immuno assay is	Physico-chemical assay	Chemical assay	Biological assay	Radioassay	Physico-chemical assay
The drugs used to treat abusing of opioids is	Ibu brufen	Methadone	Diclofenac	Analgesic	Methadone
The average dose of drug is mentioned	mg per kg body weight	µg per kg body weight	kg per kg body weight	cal per kg body weight	mg per kg body weight
Consumption of alcohol enhances the effect of	CNS depressants	CNS stimulants	CSF depressants	CSF stimulants	CNS depressants

The phenomenon of an unusually large dose of a drug is required to elicit an effect ordinarily produced by the normal therapeutic dose of the drug is termed as drug	Tolerance	Drug tolerance	Antagonism	Synergism	Drug tolerance

UNIT-III

SYLLABUS

Genetically engineered protein and peptide agents as drugs, Novel drug delivery systems, anti-AIDS drug development, oncogenes as targets for drugs, multidrug resistance phenotypes, production of secondary metabolites by plant tissue culture. Genome based medicine.

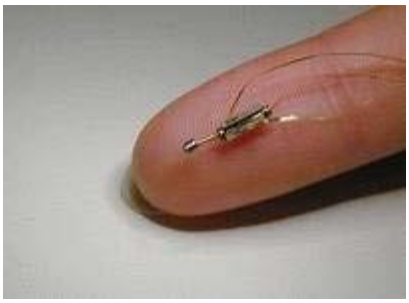
Genetically engineered drugs and their application

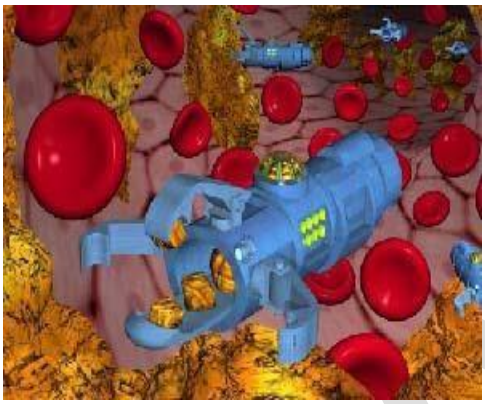
Over the past two decades, many genetically engineered drugs have been developed and approved for the treatment of patients. Typically, these drugs are characterized by a high and specific activity in the presence of optimal safety. They include hormones, enzymes, growth and coagulation factors, antibodies as well as vaccines. All these proteins are generated using recombinant DNA technology. An expression vector with the gene encoding for the protein of interest is introduced into an appropriate microorganism or cell line. The biochemical machinery of the host cell then translates the genetic information into the corresponding protein. Large scale production of the recombinant drugs uses biotechnological processes. The genetically modified organisms are grown in bioreactors from which the desired protein is finally isolated and purified. This review focuses on the production and clinical application of recombinant erythropoietin in the areas of nephrology, hemato-oncology and elective surgery.

Novel drug delivery system

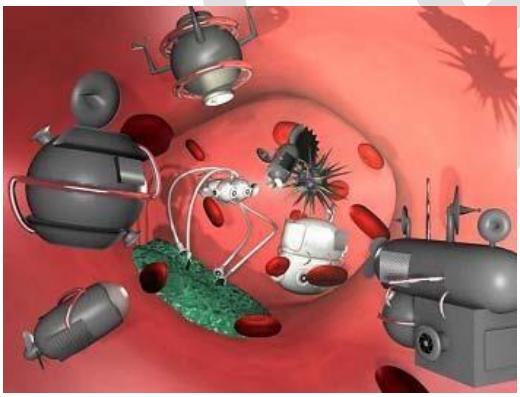
Drug Delivery System

Nanobots are robots that carry out a very specific function and are just several nanometers wide. They can be used very effectively for drug delivery. Normally, drugs work through the entire body before they reach the diseaseaffected area. Using nanotechnology, the drug can be targeted to a precise location which would make the drug much more effective and reduce the chances of possible side-effects.





Nanobots



Miniature Cameras Inside
Blood Vessels

Non conventional routes of administration

The enhancement of oral bioavailability of poorly water-soluble drugs remains one of the most challenging aspects of drug development. The solid dispersions have attracted considerable interest as an efficient means of improving the dissolution rate and thereby the bioavailability of poorly soluble therapeutic substances which were otherwise to be formulated through nanomiling or prodrug formation. This review compiles historical background, definitions as well as rationale and scope of the various solid dispersion systems, the formulation aspects along with different carriers and preparation methods, drug release mechanisms, characterization, advantages and limitations. The present article also addresses some alternative approaches to overcome certain limitations of solid dispersion technology which are responsible for its little commercialization.

Novel Approach for anti AIDS drug development.

Novel Approach for anti AIDS drug development. A peptide that kills HIV infected cells before they produce HIV virus.

HIV infection and AIDS is one of the major causes of worry in front of every nation today as this disease is spreading very fast, and so far there is no lifesaving treatment available for this disease. The anti-retroviral drugs available today do extended the life and do enhance quality of life, but there are causes of worry when the virus develops a drug resistance and the drugs in the regimen do not lower the viral load to the required level. So far the anti-retroviral drugs available work by inhibiting multiplication of HIV virus. HIV virus infect and integrates its own DNA in to Human T–Lymphocytic cells there cells Even if we are successful in killing all the HIV viruses in the body of a HIV virus infected person, later on the T-Lymphocytic cells which are part of our body, automatically starts producing HIV viruses as and when these cells undergo a metabolic process and protein synthesis. Serves as factories of HIV virus.
When these T-Cells are producing required proteins for our body, the DNA in them is also producing HIV virus genetic material as well as proteins and enzymes which after words come together and to form a new HIV virus. Thus a new HIV virus is always arising from Human cells itself, and not directly from HIV virus, unlike bacteria's and other viruses.

Our body cells themselves are now working for HIV virus multiplication. And the drugs available so far till today's date are not able to destroy these infected T-cells.

To make a person free from HIV virus will thus requires that, the whole T cells are required to be replaced with one which do not contain the HIV virus genetic material incorporated in them (Provirus).

This makes it very difficult but it is not impossible we can do this by engineering infected T-Lymphocytes genetically.

Oncogenes as targets for drugs

The universal deregulation of c-*myc* gene expression in tumor cells suggests that this oncogene represents an attractive target for cancer therapeutic purposes. The same applies to the N-*myc* gene, which has a more restricted tissue specificity.

Translocation (e.g., c-*myc* in Burkitt's lymphoma), or amplification (e.g., N-*myc* in neuroblastoma) of *myc* genes has been causally linked to tumor formation. Furthermore, the c-*myc* promoter integrates diverse mitogenic signalling cascades, which are constitutively activated in tumor cells, and translates them into expression of the c-MYC transcription factor, which promotes cell proliferation by regulating the expression of numerous target genes. Recent experimental data suggest, that even a brief inhibition of c-*myc* expression may be sufficient to permanently stop tumor growth and induce regression of tumors. Attempts to identify specific inhibitors of c-MYC/MAX dimerization have yielded promising results. In addition, downstreamtarget genes of c-MYC represent attractive targets for tumor therapy. Tumor cells expressing c-MYC at elevated levels are sensitized to treatment with DNA-damaging drugs. In mice and presumably also in human patients, the successful treatment of c-*myc*-induced tumors with conventional chemotherapy depends on the presence of functional p53. Therefore, restoration of this pathway, which is commonly lost in cancer cells, may enhance therapy of c-*myc*-induced tumors. These and other recent developments, which address the use of *myc* genes as therapeutic targets for cancer treatment.

Cancer chemotherapy

Chemotherapy (sometimes cancer chemotherapy) is the treatment of cancer with an antineoplastic drug or with a combination of such drugs into a standardized treatment regimen. Most commonly, chemotherapy acts by killing cells that divide rapidly, one of the main properties of most cancer

cells. This means that it also harms cells that divide rapidly under normal circumstances: cells in the bone marrow, digestive tract and hair follicles; this results in the most common side effects of chemotherapy: myelosuppression (decreased production of blood cells, hence also immunosuppression), mucositis (inflammation of the lining of the digestive tract), and alopecia (hair loss).

Newer anticancer drugs act directly against abnormal proteins in cancer cells; this is termed targeted therapy and is technically not chemotherapy.

Cancer is the uncontrolled growth of cells coupled with malignant behavior: invasion and metastasis. Cancer is thought to be caused by the interaction between genetic susceptibility and environmental toxins.

In the broad sense, most chemotherapeutic drugs work by impairing mitosis (cell division), effectively targeting fast-dividing cells. As these drugs cause damage to cells they are termed *cytotoxic*. Some drugs cause cells to undergo apoptosis (so-called "self-programmed cell death").

POSSIBLE QUESTIONS

UNIT-III

PART-A (20 MARKS)

(Q.NO 1 TO 20 Online Examination)

PART-B (2 MARKS)

1. Explain genetically engineered protein
2. Write any peptide agents used as drugs

PART-C (8 MARKS)

1. 1. Discuss novel drug delivery systems
2. What are the non-conventional routes of drug administration
3. Describe the anti-AIDS drug
4. Write notes on Oncogenes as targets for drugs?
5. Discuss about cancer chemotherapy?

Questions	opt1	opt2	opt3	opt4	Answer
Colloidal drug carrier systems are	micellar solutions	vacuoles	solid crystal dispersi	Mobile vesicles	micellar solution
A three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of	Hydrogels	Vaccum gels	Non vaccum gels	Polymeric gels	Hydrogels
Controlled release (CR) drugs are	Tinature	Spansules	tamuare	chisuare	Spansules
_____ is the first genetically engineered	Growth hormone	Insulin	HBsAg	HIB	Insulin
Genes for insulin peptides is incorporated into____dur	beta galactosidase gene	Synthetic vectors	pBr322	TMV	beta galactosidase gene
Genetically engineered growth hormone is	Dwarfism	Gigantism	malignancies	Renal failure	Dwarfism
Insulin injection for the treatment of	intramuscularly	intradermally	subcutaneously	intravenously	subcutaneously
Which of the following	intradermal	IM injection	IV injection	Intrathecal injection	intradermal
Which of the following	intradermal	IM injection	IV injection	subcutaneous injection	IV injection
Diagnostic studies such as	ntravenously	intra arterially	intramuscularly	intradermally	intra arterially

For rhematoid arthritis	Intra articularly	Intramedullary	Intraperitoneall	Intrathecally	Intra articularly
Using galvanic current penetration of drugs to	Transmucosal method	Iontophoresis	Trans nasal method	Transrectal method	Iontophoresis
BCG vaccine is	intraderm	intramusc	intraven	subcutaneously	intrader
Sublingually taken drugs are absorbed	pulmonary	hepatic circulation	systemic	renal circulation	systemic
The initial antibody secreted after	IgG	IgM	IgA	IgE	IgM
Toxoids are produced by adding _____to toxins of	Acetic acid	Formic acid	Formalin	Saline	Formalin
BCG vaccine is	Typhoid	Tuberculo	Tetanus	chicken pox	Tuberc
Salk vaccine is a part of	BCG vaccine	Poliomyelorally	MMR vaccine	Hepatitis vaccine	Poliomorally
Sabin vaccine for polimyelitus	subcutaneously		intramuscularly	intravenously	
OPV provides systemic immunity & induces	IgG	IgM	IgA	IgE	IgA
The usual incubation period of	4-6 weeks	1-2 weeks	7-8 weeks	8-10 weeks	4-6 weeks
Which vaccine is given subcutaneou	rubella vaccine	Poliomyelitus vaccine	Anthrax vaccine	rabies vaccine	rabies vaccine

Nerve tissue vaccine is used for	Hepatitis B	Rabies	Mumps	Cholera	Rabies
The first vaccine prepared by rDNA	Hepatitis B vaccine	DPT vaccine	Hib vaccine	MMR vaccine	Hepatitis B vaccine
To prevent neonatal tetanus____is given during	DPT	OPV	MMR	TT	TT
Anti-D (Rho) immunoglob	yellow fever	Encephalitis	Erythro blastosi	Plague	Erythro blastosi
Which of the following is	Rabies vaccine	Plague vaccine	BCG vaccine	Anthrax vaccine	Rabies vaccine
Which of the following is	MMR vaccine	Diptheria vaccine	Varicella	poliomyelitis vaccine	Diptheria
Glycosylated erythropoietin is a	Anemia	Skin disorders	Muscular dystrop	Brain disorders	Anemia
The mean incubation period of	7 years	4.5 years	6.5 years	2 years	4.5 years
Antibodies to HIV develops	2-8 weeks	1-2 weeks	7-8 weeks	8-10 weeks	2-8 weeks
In AIDS patients opportunistic infections	Renal failure	Anti Candidiasis	Pneumonia	NSAID	Pneumonia
Drugs for AIDS is still in infancy	HIV infects T cells	available drugs are toxic	virus develops	antiviruses	available drugs
Which of the following is	Abacavir	Saquinavir	diazepam	Ibubrufen	Abacavir

Azidothymidine is a_____used	NRTI	NNRTI	Protease inhibito	Fusion inhibitor	NRTI
Advantages of	Low selectivity	Depression of bone	Depression of	Depression of immune system	Depression of
Rational combination of anticancer drugs is used to	Provide synergism resulting from the use of anticancer drugs with different	Provide synergism resulting from the use of anticancer drugs with the same	Provide stimulation of immune system	Provide stimulation of cell proliferation	Provide synergism resulting from the use of anticancer
Anticancer alkylating drug, a derivative of	Methotrexate	Cisplatin	Cyclophosphamide	Carmustine	Cyclophosphamide
Tick the anticancer alkylating drug, a derivative of	Mercaptopurine	Thiotepa	Chlorambucil	Procarbazine	Thiotepa
The group of hormonal drugs used for cancer	Mineralocorticoids and glucocorti	Glucocorticoids and gonadal hormones	Gonadal hormones and somatot	Insulin	Glucocorticoids and gonadal
The anticancer drug of	Dactinomycin	Vincristine	Methotrexate	Procarbazine	Vincristine
Action mechanism of alkylating agents is:	Producing carboniu m ions altering	Producing carboniu m ions altering	Structural antagonism	Inhibition of DNA-dependent RNA synthesis	Producing carbonium ions
Methotrexate is	A purine antagonist	A folic acid	An antibioti	An alkylating agent	A folic acid
The antibiotic for cancer	Cytarabine	Doxorubicin	Gentamycin	Etoposide	Doxorubicin
Fluorouracil belongs to	Antibiotics	Antimetabolites	Plant alkaloid	Bone marrow growth factor	Antimetabolite

The action mechanism of anticancer drugs	Inhibition of DNA-dependent RNA synthesis	Cross-linking of DNA	Mitotic arrest at a metaphase	Nonselective inhibition of aromatases	Mitotic arrest at a metaphase
Action mechanism of methotrexat	Inhibition of dihydrofolate	Activation of cell differentiation	Catabolic depletion of	Activation of cell differentiation	Inhibition of dihydrofolate
The anticancer drug belonging to	Dacarbazine	Cisplatin	Methotrexate	Vincristine	Cisplatin
The indication for estrogens in	Leukemia	Cancer of prostate	Endometrial cancer	Brain tumors	Cancer of prostate
Enzyme drug used for acute leukemia	Dihydrofolate reductase	Asparaginase	Aromatase	DNA gyrase	Dihydrofolate reductase
Which one of the following drug is not	Carmustine	Vincristine	Lomustine	Semustine	Vincristine
Estrogen	Leuprolid	Tamoxife	Flutami	Anastrozole	Tamoxi
The antiandroge	Flutamide	Aminoglutethimide	Tamoxifen	Testosterone	Flutamide
The drug belonging to aromatase inhibitors	Octreotide	Anastrozole	Flutamide	Tamoxifen	Anastrozole
The drug belonging to gonadotropin-releasing hormone	Leuprolide	Tamoxifen	Flutamide	Anastrozole	Leuprolide

Which of the following chemotherapy drug is likely to be	Adriamycin	Vinblastine	Paclitaxel	Procarbazine	Procarbazine
High dose chemotherapy given prior to stem cell transplant may be associated with	Busulfan + cyclophosphamide	Cyclophosphamide + TBI	Ifosfamide +carboplatin+ Etoposide	Fludarabine + ATG	Fludarabine + ATG
Incidence of Gallbladder cancer is	Chile	India	United Kingdom	South Africa	Chile
Which of the following is least to occur as	Adenocarcinoma	Squamous cell carcinoma	Lymphoma	Carcinoid tumour	Lymphoma
Which of the following is less likely to be associated	Obesity	Use of tobacco and alcohol	Aflotoxins	Past history of enteric fever	Aflotoxins

UNIT-IV

SYLLABUS

Mechanism of action of drugs used in therapy of Respiratory system – cough, bronchial asthma, pulmonary tuberculosis. Antimicrobial drugs – sulphonamides, trimethoprim, penicillins, aminoglycosides and bacterial resistance, Cancer chemotherapy. Thyroid and antithyroid drugs, insulin and oral antidiabetic drugs, antifertility and ovulation inducing drugs. Pharmacotherapy of gout and rheumatoid arthritis, Immuno therapy – Immunosuppressants and immunostimulants, Enzymes in therapy.

Therapy of respiratory system

Cough

A cough medicine (or linctus, when in syrup form) is a medicinal drug used in an attempt to treat coughing and related conditions. For dry coughs, treatment with cough suppressants (antitussives) may be attempted to suppress the body's urge to cough, while in productive coughs (coughs that produce phlegm), treatment is attempted with expectorants (typically guaifenesin, in most commercial medications) in an attempt to loosen mucus from the respiratory tract. There however is no good evidence for or against the use of these medications in those with a cough. Even though they are used by 10% of American children weekly, they are not recommended in children 6 years of age or younger due to lack of evidence showing effect, and concerns of harm.

Asthma

Asthma is the common chronic inflammatory disease of the airways characterized by variable and recurring symptoms, reversible airflow obstruction, and bronchospasm Symptoms include wheezing, coughing, chest tightness, and shortness of breath. Asthma is clinically classified according to the frequency of symptoms, forced expiratory volume in 1 second (FEV1), and peak expiratory flow rate. Asthma may also be classified as atopic (extrinsic) or non-atopic (intrinsic). It is thought to be caused by a combination of genetic and environmental factors.[12] Treatment of acute symptoms is usually with an inhaled short-acting beta-2 agonist (such as salbutamol). Symptoms can be prevented by avoiding triggers, such as allergens and irritants, and by inhaling corticosteroids. Leukotriene antagonists are less effective than corticosteroids and thus less preferred. Its diagnosis is usually made based on the pattern of symptoms and/or response to therapy over time. The prevalence of asthma has increased significantly since the 1970s. As of

2010, 300 million people were affected worldwide. In 2009 asthma caused 250,000 deaths globally. Despite this, with proper control of asthma with step down therapy, prognosis is generally good.

Pulmonary tuberculosis

Isoniazid (Laniazid, Nydrazid), also known as isonicotinylhydrazine (INH), is an organic compound that is the first-line antituberculosis medication in prevention and treatment. It was first discovered in 1912, and later in 1951 it was found to be effective against tuberculosis. Isoniazid is never used on its own to treat active tuberculosis because resistance quickly develops. Isoniazid also has an antidepressant effect, and it was one of the first antidepressants discovered. Isoniazid can also be used in the treatment of a BCG-oma. The compound was first synthesised in the early 20th century but its activity against tuberculosis was first reported in the early 1950s and three pharmaceutical companies attempted unsuccessfully to simultaneously patent the drug (the most prominent one being Roche, who launched their version, Rimifon, in 1952). With the introduction of isoniazid, a cure for tuberculosis was first considered reasonable. Isoniazid is available in tablet, syrup, and injectable forms (given intramuscularly or intravenously). Isoniazid is available worldwide, is inexpensive and is generally well tolerated. It is manufactured from isonicotinic acid, which is produced from 4-methylpyridine.

Antimicrobial

An anti-microbial is a substance that kills or inhibits the growth of microorganisms such as bacteria, fungi, or protozoans. Antimicrobial drugs either kill microbes (microbiocidal) or prevent the growth of microbes (microbiostatic). Disinfectants are antimicrobial substances used on non-living objects or outside the body.

The history of antimicrobials begins with the observations of Pasteur and Joubert, who discovered that one type of bacteria could prevent the growth of another. They did not know at that time that the reason one bacterium failed to grow was that the other bacterium was producing an antibiotic. Technically, antibiotics are only those substances that are produced by one microorganism that kill, or prevent the growth, of another microorganism. Of course, in today's common usage, the term antibiotic is used to refer to almost any drug that attempts to rid your body of a bacterial

infection. Antimicrobials include not just antibiotics, but synthetically formed compounds as well. The discovery of antimicrobials like penicillin and tetracycline paved the way for better health for millions around the world. Before penicillin became a viable medical treatment in the early 1940s, no true cure for gonorrhea, strep throat, or pneumonia existed. Patients with infected wounds often had to have a wounded limb removed, or face death from infection. Now, most of these infections can be cured easily with a short course of antimicrobials. However, with the development of antimicrobials, microorganisms have adapted and become resistant to previous antimicrobial agents. The old antimicrobial technology was based either on poisons or heavy metals, which may not have killed the microbe completely, allowing the microbe to survive, change, and become resistant to the poisons and/or heavy metals.

Antithyroid agent

An antithyroid agent is a hormone antagonist acting upon thyroid hormones.

The main antithyroid drugs are carbimazole (in the UK), methimazole (in the US), and propylthiouracil/PTU. A less common antithyrioid agent is potassium perchlorate.

Mechanism of action

Carbimazole, methimazole and propylthiouracil inhibit the enzyme thyroperoxidase, and thereby block the binding of iodine and coupling of iodotyrosines, in turn causing reduced synthesiis of thyroid hormones.

Adverse effects

The most dangerous side-effect is agranulocytosis (1/250, more in PTU); this is an idiosyncratic reaction which generally resolves on cessation of drug. It occurs in about 0.2 to 0.3% of cases treated with antithyroid drugs. Others include granulocytopenia (dose dependent, which improves on cessation of the drug) and aplastic anemia, and for propylthiouracil severe, fulminant liver failure. Patients on these medications should see a doctor if they develop sore throat or fever. The most common side effects are rash and peripheral neuritis. These drugs also Methimazole

Indications

Methimazole is a drug used to treat hyperthyroidism, a condition that usually occurs when the thyroid gland is producing too much thyroid hormone. It may also be taken before thyroid surgery to lower thyroid hormone levels and minimize the effects of thyroid manipulation.

Mechanism of action

Methimazole inhibits the addition of iodine to thyroglobulin by the enzyme thyroperoxidase, a necessary step in the synthesis of triiodothyronine (T3) and thyroxine (T4).

It does not inhibit the action of the sodium-dependent iodide transporter located on follicular cells' basolateral membranes. Inhibition of this step requires competitive inhibitors such as perchlorate and thiocyanate. It acts at CXCL10.

Adverse effects

The chance of side effects from methimazole is about 5%. It is important to monitor any symptoms of fever or sore throat while taking methimazole; this could indicate the development of agranulocytosis, an uncommon but severe side effect resulting from a drop in the white blood cell count (to be specific, neutropenia, a deficiency of neutrophils). A complete blood count (CBC) with differential is performed to confirm the suspicion, in which case the drug is discontinued. Administration of recombinant human granulocyte colony-stimulating factor (rhG-CSF) may increase recovery.

Other side effects include

- Skin rash
- Itching
- Abnormal hair loss
- Upset stomach
- Vomiting
- Loss of taste
- Abnormal sensations (tingling, prickling, burning, tightness, and pulling)
- Swelling
- Joint and muscle pain
- Drowsiness
- Dizziness
- Decreased white blood cells
- Decreased platelet
- Aplasia cutis congenita (prenatal exposure)

Methimazole 3

Drug interactions

Adverse effects may occur for individuals who:

• Take anticoagulants ('blood thinners') such as warfarin (Coumadin), beta blockers such as propranolol (Inderal), diabetes medications, digoxin (Lanoxin), theophylline (Theobid, Theo-Dur), and vitamins

• Have ever had any blood disease, such as decreased white blood cells (leukopenia), decreased platelets (thrombocytopenia), or aplastic anemia, or liver disease (hepatitis, jaundice)

• Are pregnant, or going to become pregnant, or are breast-feeding. An alternative anti-thyroid drug, propylthiouracil, is often substituted during pregnancy or breast-feeding. If pregnancy occurs while taking methimazole, switching to propylthiouracil may be an alternative. Early studies suggested that methimazole may harm the fetus; however, more recent studies suggest this may not be the case.

• Are going to have surgery, including dental surgery.

Anti-diabetic medication

Anti-diabetic medications treat diabetes mellitus by lowering glucose levels in the blood. With the exceptions of insulin, exenatide, and pramlintide, all are administered orally and are thus also called oral hypoglycemic agents or oral antihyperglycemic agents. There are different classes of anti-diabetic drugs, and their selection depends on the nature of the diabetes, age and situation of the person, as well as other factors. Diabetes mellitus type 1 is a disease caused by the lack of insulin. Insulin must be used in Type I, which must be injected.

Diabetes mellitus type 2 is a disease of insulin resistance by cells. Treatments include (1) agents which increase the amount of insulin secreted by the pancreas, agents which increase the sensitivity of target organs to insulin, and agents which decrease the rate at which glucose is absorbed from the gastrointestinal tract. Several groups of drugs, mostly given by mouth, are effective in Type II, often in combination. The therapeutic combination in Type II may include insulin, not necessarily because oral agents have failed completely, but in search of a desired combination of effects. The great advantage of injected insulin in Type II is that a well-educated patient can adjust the dose, or even take additional doses, when blood glucose levels measured by the patient, usually with a

simple meter, as needed by the measured amount of sugar in the blood.

Insulin

Insulin is usually given subcutaneously, either by injections or by an insulin pump. Research is underway of other routes of administration. In acute care settings, insulin may also be given intravenously. There are generally above four types of insulin, characterized by the rate which they are metabolized by the body.

Sulfonylurea

- General formula of a sulfonylurea, showing the sulfonylurea backbone itself in red and the side chains that distinguish each compound in blue-Chlorpropamide - Tolazamide -Gliclazide - Glimepiride Sulfonylurea (UK: Sulphonylurea) derivatives are a class of antidiabetic drugs that are used in the management of diabetes mellitus type 2. They act by increasing insulin release from the beta cells in the pancreas.

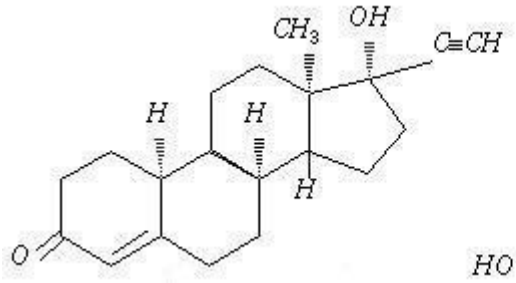
ANTIFERTILITY DRUGS

These are the chemical substances used to control the pregnancy. These are also called *oral contraceptives*. The basic aim of antifertility drugs is to prevent conception or fertilization. Oral contraceptives belong to the class of natural products known as steroids.

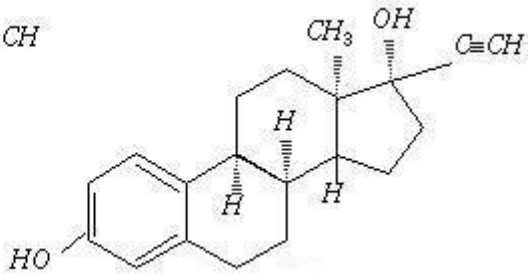
These control the female menstrual cycle and ovulation. The birth control pills are essentially a mixture of esterogen and *progesterone derivatives* which are more potent than the natural hormones.

These common pills are used for a combination of progesterone, norethindrone and estrogen ethynylestradiol.

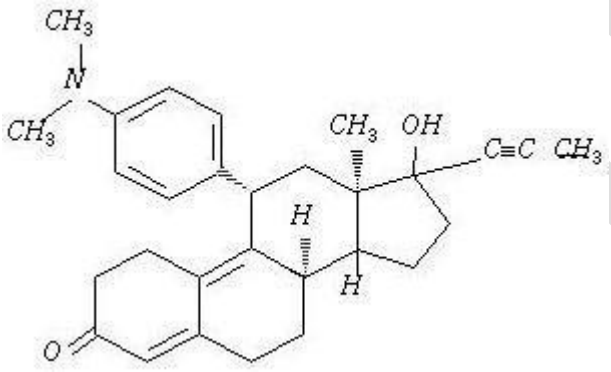
Mifepristone is a synthetic steroid which blocks the effects of progesterone and is used as a "morning after pill" in many countries.



Norethindrone



Ethynylestradiol



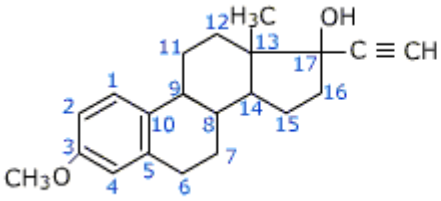
Mifepristone

Ormeloxifene (*Centchroman, Saheli*) has also been developed and tested at the Central Drug Research Institute, Lucknow as an effective antifertility drug to acceptable degree. The oral contraceptives are commonly known as *pills* or *oral pills* and have been used worldwide for birth control.

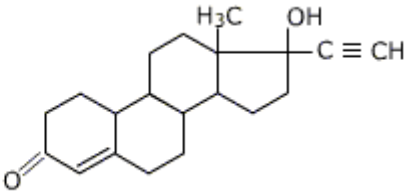
Anti-fertility Drugs

With global population growing by the day, birth control has become essential. There are drugs that control ovulation and if regularly consumed, function as effective contraceptives. Some examples of birth control pills are orthonovum and Enovid. Orthonovum is a mixture of norethindrone (17a - ethynyl - 19 - nortestosterone) and mestranol (17a - ethynyl - 3 - methoxy -

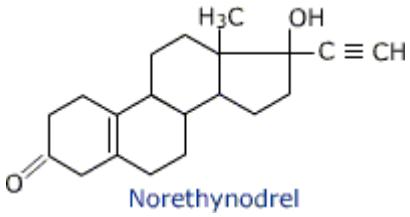
1,3,5(10), estratriene - 17 b - ol). Envoid is a mixture of norethynodrel (17 a - ethynyl - 17 - b - hydroxy - 5 (10)-estern - 3-one) and mestranol.



Mestranol



Norethindrone



Norethynodrel

Ovulation Drugs

Ovulation inducing agents are used in two different ways. First they are used for patients with irregular cycles to normalize ovulation. Secondly, they are used for normally ovulating women as an adjunct to intrauterine insemination. This is because insemination in the natural cycle has poor pregnancy rates. There are two categories of ovulation drugs: oral and injectable. The oral medications are simple to take, inexpensive and have modest results. The injectable drugs are more complex to administer but give far superior results.

CLOMID AND SEROPHENE (ORAL MEDICATIONS)

The first line therapy is oral medication such as Clomid or Serophene. These are identical drugs made by two different companies. They are both oral mild medications with modest results. These drugs work by stimulating the release of FSH and LH, which are the crucial hormones that stimulate egg production. The total pregnancy rate with these agents is 35 - 40% after 4 - 6 cycles of use. It is important to know that the lowest effective dose is best. Also most individuals will get pregnant with lower doses within the first few months of use. A typical dose is one to three 50 mg

tablets daily for 5 days. We typically begin on day 3 of the menstrual cycle. We typically monitor by ultrasound around day 12 to judge the response to the drug dose. Treatment with Clomid for more than 6 cycles is not useful in most cases. While the drug is administered, response can most accurately judged with ultrasound or progesterone levels. The reason some individuals will not get pregnant with this medication is that it thickens the cervical mucus and thins the lining of the uterus. Approximately 90% of all births are single with this medication. One such example is the young lady who appears below: Side effects include hot flushes and mood disturbance. Occasionally ovarian enlargement requiring a rest cycle may be encountered. The multiple pregnancy rate with this medication should be no more than 7-10%. Most multiples seen here will be twins. The incidence of birth defects with Clomid and Serophene is estimated to be 4.7% which is similar to the 3-4% rate expected in the general population.

POSSIBLE QUESTIONS

UNIT-IV

PART-A (20 MARKS)

(Q.NO 1 TO 20 Online Examination)

PART-B (2 MARKS)

1. Discuss used in therapy for bronchial asthma
2. Discuss mechanism of action, adverse reactions and therapeutic uses of antithyroid drugs
3. Explain (i) emitics (ii) Antiemitics drugs

PART-C (8 MARKS)

1. Describe the management of pulmonary tuberulosis
2. Describe the pharmacotherapy of diabetes mellitus
3. How sulfonamides act as antimicrobial drug? Explain the mechanism of action.
4. Discuss pharmacotherapy of peptic ulcer disease.
5. What are all the drugs which can act as digestants?
6. Discuss about anti-fertility drugs.
7. Write pharmacological actions and adverse reactions of ovulation inducing drugs.

Questions	opt1	opt2	opt3	opt4	Answer
The main mechanism of most drugs absorption	Active transport (carrier-mediated diffusion)	Filtration (aqueous diffusion)	Endocytosis and exocytosis	Passive diffusion (lipid diffusion)	Passive diffusion (lipid diffusion)
The mechanism of Cytiton action is	Direct activation of the respiratory	The reflex mechanism	The mixed mechanism	Active transport	The reflex mechanism
What kind of substances can't permeate	Lipid-soluble	Non-ionized substances	Hydrophobic substances	Hydrophilic substances	Hydrophilic substances
Choose the unwanted effects of	Parkinson's syndrome	Sedative and hypnotic	Agranulocytosis and aplastic	Dry cough and respiratory depression	Sedative and hypnoti
The tissues most sensitive to	The salivary, bronchial	The gastric parietal	Smooth muscle and	The heart	The salivary, bronchi
Compared with atropine, scopolamine has all of the	More marked central effect	Less potent in decreasing bronchial, salivary and sweat	More potent in producing mydriasis and cycloplegi	Lower effects on the heart, bronchial muscle and intestines	Less potent in decreasing bronchi
Contraindications to the use of antimuscarinic drugs are all of	Glaucoma	Myasthenia	Bronchial asthma	Paralytic ileus and atony of the urinary bladder	Bronchial asthma
A bronchial smooth	$Alfa_1$ receptor	$Alfa_2$ receptor	Beta $_1$ receptor	Beta $_2$ receptor	Beta $_2$ receptor
Which of the following sympathomimetics is used in the	Formoterol	Norepinephrine	Methoxamine	Dobutamine	Formoterol

Pick out the bronchodilator drug	Atropine	Orciprenaline	Adrenaline	Theophylline.	Theophylline
Pick out the bronchodilator drug	Isoprenaline	Ephedrine	Atropine	Salbutamol	Ephedrine
Propranolol is used in the treatment all of the following	Cardiovascular diseases	Hyperthyroidism	Migraine headache	Bronchial asthma	Bronchial asthma
This drug is contraindicated in	Propranolol	Clonidine	Enalapril	Nifedipine	Propranolol
Which of the following vitamins is given along with	Nicotinic acid	Riboflavin	Pyridoxine	Ascorbic acid	Pyridoxine
Combined chemotherapy of tuberculosi	Decrease mycobacterium drug-resistance	Increase mycobacterium drug-	Decrease the antimicrobal activity	Decrease the onset of antimycobacterial drugs	Decrease mycobacterium
Which of the following enzymes improves GIT	Pepsin	Urokinase	L-asparaginase	Lydaze	Pepsin
All of the following drugs stimulate	Vitamins	Bitters	Fepranone	Insulin	Feprapone

Serious side effects of glucocorticoids include the following, EXCEPT:	Acute peptic ulcers	Iatrogenic Cushing's syndrome (rounding, puffiness, fat deposition and plethora alter the	Salicylism (vomiting, tinnitus, decreased hearing, and vertigo)	Hypomania or acute psychosis	Salicylism (vomiting, tinnitus, decreased hearing, and vertigo)
Gastric acid secretion is under the control of	Histamine	Acetylcholine	Serotonin	Gastrin	Serotonin
Indicate the drug belonging to proton	Pirenzepine	Ranitidine	Omeprazole	Trimethaphan	Omeprazole
All of the following agents intensify the secretion	Pepsin	Gastrin	Histamine	Carbonate mineral waters	Pepsin
Which of the following drugs is an agent of	Gastrin	Hydrochloric acid	Hystamine	Carbonate mineral waters	Hydrochloric acid
An adverse effect of oral iron	Anemia	Thrombocytopenia	Headache	Constipation	Constipation

Mental confusion and hallucinations, peripheral atropine-like toxicity (e.g. Cycloplegi	Sinemet	Benztropine	Tolkapone	Bromocriptine	Benztropine
Adverse peripheral effects, such as loss of accommodation, dry mouth, tachycardia	Alpha adrenoreceptor blockade	Muscarinic cholinoreceptor blockade	Supersesitivity of the dopamine receptor	Dopamine receptor blockade	Muscarinic cholinoreceptor blockade
Sedation, peripheral atropine-like toxicity (e.g. Cycloplegia, tachycardia, urinary retention, and constipation), orthostatic hypotensio	Sertaline	Amitriptyline	Phenelsine	Bupropion	Amitriptyline
Choose the drug that causes	Sodium bicarbonate	Aluminium hydroxide	Calcium carbonate	Magnesium oxide	Aluminium hydroxi

Which of histamine H1 antagonists is noted for the	Diazoline	Loratadine	Suprastine	Dimedrol	Diazoline
Combination of sulfonamides with	Decreases the unwanted effects of	Increases the antimicrobial	Decreases the antimicrobial activity	Increases the elimination of sulfonamides	Increases the antimicrobial
Indicate a beta-blocker, which is particularly	Pindolol	Sotalol	Phentolamine	Propranolol	Propranolol
Which of the following hormones is	Thyroxine	Thyroid-stimulating hormone	Thyrotropin-releasing hormone	Thyroglobulin.	Thyroxine
Thyroid hormones produce various pharmacological effects.	Decline of the basal metabolic rate in the body	Increase in the rate and force of contraction of the heart	Increase in the blood cholestrol level	Increase in the heat production	Decline of the basal metabolic rate in the body
Currently used antithyroid drugs include the	Propylthiouracil (PTU)	Diatrizoate sodium (Hypaque)	Methimazole (Tapazole)	Potassium perchlorate	Potassium perchlorate
Secretory products of pancreatic β-cells are	Glucagon, proglucagon	Insulin, C-peptide, proinsulin, islet amyloid polypeptid	Somatostatin	Pancreatic polypeptide (PP)	Insulin, C-peptide, proinsulin, islet amyloid
Insulin cannot be	Oral route	Intravenous route	Subcutaneous route	Intramuscular route	Oral route

Diabetic coma is treated by	Lente insulin	Glucose	Crystalline insulin	Oral anti-diabetic drugs	Crystalline insulin
Which of the following oral hypoglycaemic drugs stimulates both	Glibenclamide	Phenformin	Buformine	Metformin	Glibenclamide
The action of insulin is	Sulphonylureas	Glucagon	Biguanides	Glibenclamide	Biguanides
Insulin causes reduction in blood sugar level by the	Increased glucose uptake in the peripheral tissue	Reduction of breakdown of glycogen	Diminished gluconeogenesis	Decreased glucose absorption from the gut	Decreased glucose absorption from the gut
Sulphonyl ureas act by	Reducing the absorption of carbohydrat	Increasing the uptake of glucose in peripheral	Reducing the hepatic gluconeogenesis	Stimulating the beta islet cells of pancreas to produce insulin	Stimulating the beta islet cells of
The primary reason for a physician to	It has a faster onset of action than other insulins	It has a shorter duration of action than other	It can be given to patients who have an allergy	It is more effective in preventing the complications of diabetes than	It can be given to patients who
Mechanism of sulfonamides’	Inhibition of dihydropteroate reductase	Inhibition of dihydropteroate	Inhibition of cyclooxygenase	Activation of DNA gyrase	Inhibition of dihydropteroate
Mechanism of Rifampin action is	Inhibition of mycolic acids synthesis	Inhibition of DNA dependent RNA polymeras	Inhibition of topoisomerase II	Inhibition of cAMP synthesis	Inhibition of DNA dependent RNA

Choose the drug which is a H2-receptor	Omeprazole	Pirenzepine	Carbenoxolone	Ranitidine	Ranitidine
All of the following drugs are proton pump	Pantoprozole	Omeprazole	Famotidine	Rabeprazole	Famotidine
Indicate the drug belonging	Cimetidine	Ranitidine	Pirenzepin	Omeprazole	Pirenzepin
Which of the following drugs may cause	Omeprazole	Pirenzepine	Cimetidine	Sucralfate	Cimetidine
Select an endocrine drug which is an amino	Insulin	Hydrocortisone	Calcitonin	Thyroxine	Thyroxine
Thiazolidinediones act by	Diminishing insulin resistance by increasing glucose uptake and metabolism	Reducing the absorption of carbohydrate from the gut	Stimulating the beta islet cells of pancreas to produce insulin	Stimulating the alpha islet cells of pancreas to produce glucagon	Diminishing insulin resistance by increasing glucose
Tamoxifen	Antiprogesti	Antiandro	Antiestrog	Androgen	Antiestr
The major natural	Estradiol	Estron	Progestero ne	Estriol	Progesterone
Progestero ne is	Ovarian follicles	Corpus luteum	Granulosa cells	Theca cells	Corpus luteum
Mifepristo ne (RU-	Antiprogesti n	Antiandro gen	Antiestrog en	Androgen	Antiprogestin
An endogenous vasoconstrictor that can	Angiotensinogen	Angiotensin I	Angiotensin II	Angiotensin-converting enzyme	Angiotensin II

Choose the vasodilator which	Nifedipine	Hydralazine	Minoxidil	Sodium nitroprusside	Sodium nitroprusside
Tick the drug belonging to non-	Salbutamol	Isoprenaline	Salmeterol	Terbutaline	Isoprenaline
The mechanism of methylxant	Inhibition of the enzyme phosphodiesterase	Beta2 - adrenoreceptor stimulatio	Inhibition of the production of	Inhibition of M cholinoreceptors	Inhibition of the enzyme
Choose an emetic drug of	Ipecacuanha derivatives	Promethazine	Tropisetron	Apomorphine hydrochloride	Apomorphine hydroch
Indicate an antiemetic agent which is	Metoclopramide	Nabilone	Tropisetron	Prochlorperazine	Prochlorperazine
The mechanism of stimulant	Increasing the volume of non-absorbable	Increasing motility and secretion	Altering the consistency of the	Increasing the water content	Increasing motility and

UNIT-V

SYLLABUS

Brain – Neurotransmitters, encephalins and endorphins; general function of autonomic and somatic nervous system; cholinergic transmission and receptors; adrenergic transmission and receptors; muscarinic receptors. Non-steroidal and anti-inflammatory drugs; adrenergic blocking drugs; cholinergic blocking drugs; muscatrinic blocking drugs; parkinson's disease; Alzhiemier's disease. Neurodegenerative disorders – Amylotropic, lateral sclerosis, senile dementia, schizophrenia, Huntington's disease.

Non-steroidal anti-inflammatory drug

Non-steroidal anti-inflammatory drug Coated 200 mg Ibuprofen tablets, a common NSAID Nonsteroidal anti-inflammatory drugs, usually abbreviated to NSAIDs or NAIDs, but also referred to as nonsteroidal anti-inflammatory agents/analgesics (NSAIAs) or nonsteroidal Anti-inflammatory medicines (NSAIMs), are drugs with analgesic and antipyretic (fever-reducing) effects and which have, in higher doses, anti-inflammatory effects.

The term "nonsteroidal" is used to distinguish these drugs from steroids, which, among a broad range of other effects, have a similar eicosanoid-depressing, anti-inflammatory action. As analgesics, NSAIDs are unusual in that they are non-narcotic.

The most prominent members of this group of drugs are aspirin, ibuprofen, and naproxen, all of which are available over the counter in many areas.

Medical uses

NSAIDs are usually indicated for the treatment of acute or chronic conditions where pain and inflammation are present. Research continues into their potential for prevention of colorectal cancer, and treatment of other conditions, such as cancer and cardiovascular disease. NSAIDs are generally indicated for the symptomatic relief of the following conditions

- Rheumatoid arthritis
- Osteoarthritis
- Inflammatory arthropathies (e.g. ankylosing spondylitis, psoriatic arthritis, Reiter's syndrome)
- Acute gout
- Dysmenorrhoea (menstrual pain)
- Metastatic bone pain

- Headache and migraine
- Postoperative pain
- Mild-to-moderate pain due to inflammation and tissue injury
- Pyrexia (fever)
- Ileus
- Renal colic

Adverse effects

The widespread use of NSAIDs has meant that the adverse effects of these drugs have become increasingly prevalent. The two main adverse drug reactions (ADRs) associated with NSAIDs relate to gastrointestinal (GI) effects and renal effects of the agents.

NON-STEROIDAL DRUGS

Prostaglandins are a family of chemicals that are produced by the cells of the body and have several important functions. They promote inflammation, pain, and fever; support the blood clotting function of platelets; and protect the lining of the stomach from the damaging effects of acid.

Prostaglandins are produced within the body's cells by the enzyme cyclooxygenase (COX). There are two COX enzymes, COX-1 and COX-2. Both enzymes produce prostaglandins that promote inflammation, pain, and fever. However, only COX-1 produces prostaglandins that support platelets and protect the stomach. Nonsteroidal antiinflammatory drugs (NSAIDs) block the COX enzymes and reduce prostaglandins throughout the body. As a consequence, ongoing inflammation, pain, and fever are reduced. Since the prostaglandins that protect the stomach and support platelets and blood clotting also are reduced, NSAIDs can cause ulcers in the stomach and promote bleeding.

Adrenergic blocking drugs

Beta blockers (sometimes written as β-blockers) or beta-adrenergic blocking agents, beta-adrenergic antagonists, or beta antagonists, are a class of drugs used for various indications, but particularly for the management of cardiac arrhythmias, cardioprotection after myocardial infarction (heart attack), and hypertension. As beta adrenergic receptor antagonists, they diminish

the effects of epinephrine (adrenaline) and other stress hormones. In 1958 the first beta blocker, dichloroisoproterenol, was synthesised by Eli Lilly Laboratories, but it was Sir James W. Black in 1962, who found the first clinically significant use of beta blockers with propranolol and pronethalol; it revolutionized the medical management of angina pectoris and is considered by many to be one of the most important contributions to clinical medicine and pharmacology of the 20th century. Beta blockers block the action of endogenous catecholamines (epinephrine (adrenaline) and norepinephrine (noradrenaline) in particular), on β-adrenergic receptors, part of the sympathetic nervous system which mediates the "fight or flight" response. There are three known types of beta receptor, designated β1, β2 and β3 receptors. β1-adrenergic receptors are located mainly in the heart and in the kidneys. β2-adrenergic receptors are located mainly in the lungs, gastrointestinal tract, liver, uterus, vascular smooth muscle, and skeletal muscle.

Anticholinergic (Cholinergic Blocking) Agents

Typical anticholinergic (cholinergic blocking) agents include (but are not limited to) the following:

- Atropine sulfate
- Benztropine mesylate
- Biperiden hydrochloride
- Dicyclomine hydrochloride
- Ipratropium bromide
- Propantheline bromide
- Scopolamine hydrobromide
- Scopolamine transdermal therapeutic system
- Trihexyphenidyl hydrochloride

Anticholinergic (cholinergic blocking) agents prevent the neurotransmitter acetylcholine from combining with receptors on the postganglionic parasympathetic nerve terminal (muscarinic site). Effects include reduction of smooth muscle spasms, blockade of vagal impulses to the heart,

decreased secretions (e.g., gastric, salivation, bronchial mucus, sweat glands), production of mydriasis and cycloplegia, and various CNS effects. In therapeutic doses, these drugs have little effect on transmission of nerve impulses across ganglia (nicotinic sites) or at the neuromuscular junction. Several anticholinergic drugs abolish or reduce the symptoms of Parkinson's disease, such as tremors and rigidity, and result in sonic improvement in mobility, muscular coordination, and motor performance. These effects may be due to blockade of the effects of acetylcholine in the CNS.

Cardiac failure

Heart failure (HF), often called congestive heart failure (CHF) or congestive cardiac failure (CCF), is the inability of the heart to provide sufficient pump action to distribute blood flow to meet the needs of the body. Heart failure can cause a number of symptoms including shortness of breath, leg swelling, and exercise intolerance. The condition is diagnosed with echocardiography and blood tests. Treatment commonly consists of lifestyle measures (such as smoking cessation, light exercise including breathing protocols, decreased salt intake and other dietary changes) and medications. Sometimes it is treated with implanted devices (pacemakers or ventricular assist devices) and occasionally a heart transplant.

Common causes of heart failure include myocardial infarction and other forms of ischemic heart disease, hypertension, valvular heart disease, and cardiomyopathy. The term "heart failure" is sometimes incorrectly used to describe other cardiac-related illnesses, such as myocardial infarction (heart attack) or cardiac arrest, which can cause heart failure but are not equivalent to heart failure.

Antihypertensive drug

Antihypertensive therapy seeks to prevent the complications of high blood pressure, such as stroke and myocardial infarction. The antihypertensives are a class of drugs that are used to treat hypertension (high blood pressure). Evidence suggests that reduction of the blood pressure by 5 mmHg can decrease the risk of stroke by 34%, of ischaemic heart disease by 21%, and reduce the

likelihood of dementia, heart failure, and mortality from cardiovascular disease. There are many classes of antihypertensives, which lower blood pressure by different means; among the most important and most widely used are the thiazide diuretics, the ACE inhibitors, the calcium channel blockers, the beta blockers, and the angiotensin II receptor antagonists or ARBs. Which type of medication to use initially for hypertension has been the subject of several large studies and resulting national guidelines? The fundamental goal of treatment should be the prevention of the important endpoints of hypertension, such as heart attack, stroke and heart failure. Patient age, associated clinical conditions and end-organ damage also play a part in determining dosage and type of medication administered. The several classes of antihypertensives differ in side effect profiles, ability to prevent endpoints, and cost. The choice of more expensive agents, where cheaper ones would be equally effective, may have negative impacts on national healthcare budgets. As of 2009, the best available evidence favors the thiazide diuretics as the first-line treatment of choice for high blood pressure when drugs are necessary.

Diuretics

Hydrochlorothiazide, a popular thiazide diuretic

Diuretics help the kidneys eliminate excess salt and water from the body's tissues and blood.

• Loop diuretics:
• Bumetanide
• Ethacrynic acid
• Furosemide
• Torsemide
• Thiazide diuretics:
• Epitizide
• Hydrochlorothiazide and chlorothiazide
• Bendroflumethiazide
• Thiazide-like diuretics:
• Indapamide
• Chlorthalidone
• Metolazone

• Potassium-sparing diuretics:

• Amiloride

• Triamterene

• Spironolactone

Vasodilation

Vasodilation refers to the widening of blood vessels resulting from relaxation of smooth muscle cells within the vessel walls, particularly in the large arteries, smaller arterioles and large veins. The process is essentially the opposite of vasoconstriction, or the narrowing of blood vessels. When vessels dilate, the flow of blood is increased due to a decrease in vascular resistance. Therefore, dilation of arterial blood vessels (mainly arterioles) leads to a decrease in blood pressure. The response may be intrinsic (due to local processes in the surrounding tissue) or extrinsic (due to hormones or the nervous system). Additionally, the response may either be localized to a specific organ (depending on the metabolic needs of a particular tissue, as during strenuous exercise), or systemic (seen throughout the entire systemic circulation). Factors that result in vasodilation are termed vasodilators.

Diuretic

This illustration shows where some types of diuretics act, and what they do. A diuretic is any drug that elevates the rate of urination and thus provides a means of forced diuresis. There are several categories of diuretics. All diuretics increase the excretion of water from bodies, although each class does so in a distinct way.

Types

High ceiling loop diuretic High ceiling diuretics are diuretics that may cause a substantial diuresis – up to 20% of the filtered load of NaCl and water. This is huge when compared to normal renal sodium reabsorption which leaves only ~0.4% of filtered sodium in the urine.

Loop diuretics have this ability, and are therefore often synonymous with high ceiling diuretics. Loop diuretics, such as furosemide, inhibit the body's ability to reabsorb sodium at the ascending loop in the nephron which leads to a retention of water in the urine as water normally follows sodium back into the extracellular fluid (ECF). Other examples of high ceiling loop diuretics

include ethacrynic acid, torsemide and bumetanide.

Thiazides

Thiazide-type diuretics such as hydrochlorothiazide act on the distal convoluted tubule and inhibit the sodium-chloride symporter leading to a retention of water in the urine, as water normally follows penetrating solutes. Frequent urination is due to the increased loss of water that has not been retained from the body as a result of a concomitant relationship with sodium loss from the convoluted tubule. The short-term anti-hypertensive action is based on the fact that thiazides decrease preload, decreasing blood pressure. On the other hand the long-term effect is due to an unknown vasodilator effect that decreases blood pressure by decreasing resistance.

Anti-diuretic drugs

Chlorpropamide is a drug in the sulphonylurea class used to treat type 2 diabetes mellitus. It is a long-acting sulphonylurea. It has more side effects than other sulphonylureas and its use is no longer recommended.

Chlorpropamide

Mechanism of action

Like other sulfonylureas, chlorpropamide acts to increase the secretion of insulin, so it is only effective in patients who have some pancreatic beta cell function. It can cause relatively long episodes of hypoglycemia; this is one reason why shorter-acting sulfonylureas such as gliclazide or tolbutamide are used instead. The risk of hypoglycemia makes this drug a poor choice for the elderly and patients with mild to moderate hepatic and renal impairment.

Chlorpropamide is also used in Partial Central Diabetes Insipidus.

Gout (also known as podagra when it involves the big toe) is a medical condition usually characterized by recurrent attacks of acute inflammatory arthritis—a red, tender, hot, swollen joint. The metatarsal-phalangeal joint at the base of the big toe is the most commonly affected (approximately 50% of cases). However, it may also present as tophi, kidney stones, or urate

nephropathy. It is caused by elevated levels of uric acid in the blood which crystallizes and the crystals are deposited in joints, tendons, and surrounding tissues.

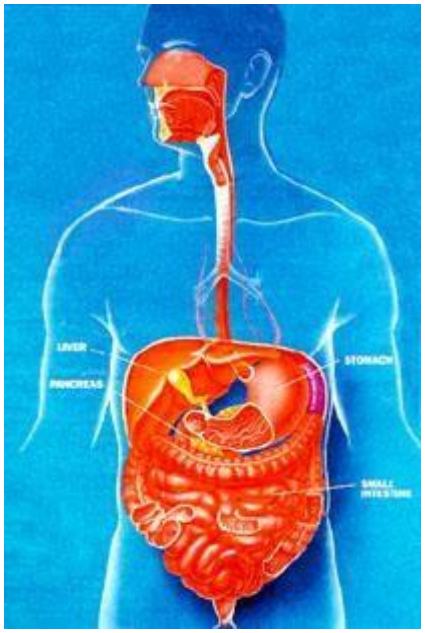
A clinical diagnosis is confirmed by the visualization of the characteristic crystals in joint fluid. Treatment with nonsteroidal anti-inflammatory drugs (NSAIDs), steroids, or colchicine improves symptoms. Once the acute attack has subsided, levels of uric acid are usually lowered via lifestyle changes, and in those with frequent attacks allopurinol or probenecid provide long-term prevention.

Gout has increased in frequency in recent decades affecting approximately one to two percent of the Western population at some point in their lives. The increase is believed to be due to increasing risk factors in the population, such as metabolic syndrome, longer life expectancy and changes in diet. Gout was historically known as "the disease of kings" or "rich man's disease".

Rheumatoid arthritis (RA) is a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks flexible (synovial) joints. The process involves an inflammatory response of the capsule around the joints (synovium) secondary to swelling (hyperplasia) of synovial cells, excess synovial fluid, and the development of fibrous tissue (pannus) in the synovium. The pathology of the disease process often leads to the destruction of articular cartilage and ankylosis (fusion) of the joints. Rheumatoid arthritis can also produce diffuse inflammation in the lungs, membrane around the heart (pericardium), the membranes of the lung (pleura), and white of the eye (sclera), and also nodular lesions, most common in subcutaneous tissue. Although the cause of rheumatoid arthritis is unknown, autoimmunity plays a pivotal role in both its chronicity and progression, and RA is considered a systemic autoimmune disease.

ENZYME THERAPY

To the Right: A picture of the digestive system of the human body.



Below: A chart of the numerous digestive enzymes of the body and their functions.

Amylase	digests starches
Bromelain	a proteolytic, anti-inflammatory food enzyme from pineapple. Aids digestion of fats
Catalase	works with SOD to reduce free radical production
Cellulase	digests cellulose, the fibrous component of most vegtable matter
Chymotrypsin	helps convert chyme
Diastase	a pontent vegtable starch digestant

Lactase	digests lactose, or milk sugar, (almost 65% of humans are deficient).
Lipase	digests fats.
Mycozyme	a single-celled plant enzyme for digestion of starches.
Pancreatin	a broad spectrum, proteolytic digestive aid, derived from secretions of animal pancreas; important in degenerative disease research.
Papin and chymopapain	proteolytic food enzymes from unripe papaya; a veegatable pepsin for digesion of proteins. These enzymes help loosen nercotic and encrusted waste material from the intestinal walls.
Pepsin	a proteolytic enzyme that breaks down proteins into peptides. Can digest 3500 times its weight in proteins.
Protease	digests proteins
Rennin	helps digest cow's milk products.
Trypsin	a proteoytic enzyme

Immunotherapy

Immunotherapy is a medical term defined as the "treatment of disease by inducing, enhancing, or suppressing an immune response". Immunotherapies designed to elicit or amplify an immune response are classified as activation immunotherapies. While immunotherapies that reduce or suppress are classified as suppression immunotherapies.

Immunomodulators

The active agents of immunotherapy are collectively called immunomodulators. They are a diverse array of recombinant, synthetic and natural preparations, often cytokines. Some of these substances, such as granulocyte colony-stimulating factor (G-CSF), interferons, imiquimod and cellular membrane fractions from bacteria are already licensed for use in patients. Others including IL-2, IL-7, IL-12, various chemokines, synthetic cytosine phosphate-guanosine (CpG), oligodeoxynucleotides and glucans are currently being investigated extensively in clinical and preclinical studies. Immunomodulatory regimens offer an attractive approach as they often have fewer side effects than existing drugs, including less potential for creating resistance in microbial diseases.

Cell based Immunotherapies are proven to be effective for some cancers. Immune effector cells such as lymphocytes, macrophages, dendritic cells, natural killer cells (NK Cell), cytotoxic T lymphocytes (CTL), etc., work together to defend the body against cancer by targeting abnormal antigens expressed on the surface of the tumor due to mutation.

Immunosuppressive drug

Immunosuppressive drugs or immunosuppressive agents are drugs that inhibit or prevent activity of the immune system. They are used in immunosuppressive therapy to:

• Prevent the rejection of transplanted organs and tissues (e.g., bone marrow, heart, kidney, liver)

• Treat autoimmune diseases or diseases that are most likely of autoimmune origin (e.g., rheumatoid arthritis, multiple sclerosis, myasthenia gravis, systemic lupus erythematosus, focal segmental glomerulosclerosis, Crohn's disease, Behcet's Disease, pemphigus, and ulcerative colitis).

• Treat some other non-autoimmune inflammatory diseases (e.g., long term allergic asthma control).

These drugs are not without side-effects and risks. Because the majority of them act non-selectively, the immune system is less able to resist infections and the spread of malignant cells. There are also other side-effects, such as hypertension, dyslipidemia, hyperglycemia, peptic ulcers, liver, and kidney injury. The immunosuppressive drugs also interact with other medicines and affect their metabolism and action. Actual or suspected immunosuppressive agents can be evaluated in terms of their effects on lymphocyte subpopulations in tissues using immunohistochemistry.

Immunosuppressive drugs can be classified into five groups:

• Glucocorticoids

• cytostatics

• Antibodies

• Drugs acting on immunophilins

Immunostimulant

Immunostimulants, also known as immunostimulators, are substances (drugs and nutrients) that stimulate the immune system by inducing activation or increasing activity of any of its components. One notable example is the granulocyte macrophage colony-stimulating factor.

Classification

There are two main categories of immunostimulants:

• Specific immunostimulants provide antigenic specificity in immune response, such as vaccines or any antigen.

• Non-specific immunostimulants act irrespective of antigenic specificity to augment immune response of other antigen or stimulate components of the immune system without antigenic specificity, such as adjuvants and non-specific immunostimulators.

Deoxycholic acid, also known as deoxycholate, cholanoic acid, and 3α,12α-dihydroxy-5β-cholanate, is a bile acid. Deoxycholic acid is one of the secondary bile acids, which are metabolic byproducts of intestinal bacteria. The two primary bile acids secreted by the liver are cholic acid and chenodeoxycholic acid. Bacteria metabolize chenodeoxycholic acid into the secondary bile acid lithocholic acid, and they metabolize cholic acid into deoxycholic acid. There are additional

secondary bile acids, such as ursodeoxycholic acid. Deoxycholic acid is soluble in alcohol and acetic acid. When pure, it comes in a white to off-white crystalline powder form.

parkinson's disease

Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system that mainly affects the motor system. The symptoms generally come on slowly over time. Early in the disease, the most obvious are shaking, rigidity, slowness of movement, and difficulty with walking. Thinking and behavioral problems may also occur. Dementia becomes common in the advanced stages of the disease. Depression and anxiety are also common, occurring in more than a third of people with PD. Other symptoms include sensory, sleep, and emotional problems. The main motor symptoms are collectively called "parkinsonism", or a "parkinsonian syndrome".

The cause of Parkinson's disease is generally unknown, but believed to involve both genetic and environmental factors. Those with a family member affected are more likely to get the disease themselves. There is also an increased risk in people exposed to certain pesticides and among those who have had prior head injuries, while there is a reduced risk in tobacco smokers and those who drink coffee or tea. The motor symptoms of the disease result from the death of cells in the substantia nigra, a region of the midbrain. This results in not enough dopamine in these areas. The reason for this cell death is poorly understood, but involves the build-up of proteins into Lewy bodies in the neurons. Diagnosis of typical cases is mainly based on symptoms, with tests such as neuroimaging being used to rule out other diseases.

There is no cure for Parkinson's disease, with treatment directed at improving symptoms. Initial treatment is typically with the antiparkinson medication levodopa (L-DOPA), with dopamine agonists being used once levodopa becomes less effective.As the disease progresses and neurons continue to be lost, these medications become less effective while at the same time they produce a complication marked by involuntary writhing movements. Diet and some forms of rehabilitation have shown some effectiveness at improving symptoms. Surgery to place microelectrodes for deep brain stimulation has been used to reduce motor symptoms in severe cases where drugs are ineffective. Evidence for treatments for the non-movement-related symptoms of PD, such as sleep disturbances and emotional problems, is less strong.

Treatment

Parkinson's disease can't be cured, but medications can help control your symptoms, often dramatically. In some later cases, surgery may be advised.

Your doctor may also recommend lifestyle changes, especially ongoing aerobic exercise. In some cases, physical therapy that focuses on balance and stretching also is important. A speech-language pathologist may help improve your speech problems.

Medications

Carbidopa-levodopa, Carbidopa-levodopa infusion, Dopamine agonists, MAO B inhibitors, Catechol O-methyltransferase (COMT) inhibitors.

Alzhiemier's disease

Alzheimer's disease (AD), also referred to simply as Alzheimer's, is a chronic neurodegenerative disease that usually starts slowly and worsens over time. It is the cause of 60–70% of cases of dementia. The most common early symptom is difficulty in remembering recent events (short-term memory loss). As the disease advances, symptoms can include problems with language, disorientation (including easily getting lost), mood swings, loss of motivation, not managing self-care, and behavioural issues. As a person's condition declines, they often withdraw from family and society. Gradually, bodily functions are lost, ultimately leading to death. Although the speed of progression can vary, the typical life expectancy following diagnosis is three to nine years.

The cause of Alzheimer's disease is poorly understood. About 70% of the risk is believed to be genetic with many genesusually involved. Other risk factors include a history of head injuries, depression, or hypertension. The disease process is associated with plaques and tangles in the brain. A probable diagnosis is based on the history of the illness and cognitive testing with medical imaging and blood tests to rule out other possible causes. Initial symptoms are often mistaken for normal ageing. Examination of brain tissue is needed for a definite diagnosis.[4] Mental and physical exercise, and avoiding obesitymay decrease the risk of AD; however, evidence to support these recommendations is not strong. There are no medications or supplements that have been shown to decrease risk.

No treatments stop or reverse its progression, though some may temporarily improve symptoms. Affected people increasingly rely on others for assistance, often placing a burden on the caregiver; the pressures can include social, psychological, physical, and economic elements. Exercise programmes may be beneficial with respect to activities of daily living and can potentially improve outcomes. Behavioural problems or psychosis due to dementia are often treated with antipsychotics, but this is not usually recommended, as there is little benefit with an increased risk of early death.

Diagnosis

There's no specific test today that confirms you have Alzheimer's disease. Your doctor will make a judgment about whether Alzheimer's is the most likely cause of your symptoms based on the information you provide and results of various tests that can help clarify the diagnosis.

Doctors can nearly always determine whether you have dementia, and they can often identify whether your dementia is due to Alzheimer's disease. Alzheimer's disease can be diagnosed with

complete accuracy only after death, when microscopic examination of the brain reveals the characteristic plaques and tangles.

To help distinguish Alzheimer's disease from other causes of memory loss, doctors now typically rely on the following types of tests.

Physical and neurological exam

Your doctor will perform a physical exam, and is likely to check your overall neurological health by testing your:

- Reflexes
- Muscle tone and strength
- Ability to get up from a chair and walk across the room
- Sense of sight and hearing
- Coordination
- Balance

POSSIBLE QUESTIONS

UNIT-IV

PART-A (20 MARKS)

(Q.NO 1 TO 20 Online Examination)

PART-B (2 MARKS)

1. Explain about anti-inflammatory drugs.
2. How to manage shock?
3. Discuss mechanism of action, adverse reactions and therapeutic uses of catecholamines
4. Explain pharmacotherapy of Gout.

PART-C (8 MARKS)

1. Write about the pharmacotherapy of cardiac failure
2. Describe diuretic and antidiuretic drugs?
3. How to manage hypertension?
4. Explain pharmacotherapy of Rhumatoid arthriris
5. How are vasodilators used as drugs for angina pectoris?

Questions	opt1	opt2	opt3	opt4	Answer
The protein fraction with immuno	Albumin	alpha globulin	beta globulin	gamma globulin	gamma globulin
Human normal Ig is also called	Histafine	immunese rum	hyperimmu neserum	human specific Ig	Histafine
_____ ____ is used intreatment of Rhematoid	muromab	infliximab	daclizumab	rituximab	infliximab
Cyclosporin is a cyclic _____	undecapeptide	hexapepti de	octapeptide	nonapepti de	undecapepti de
_____ _is a T cell growth differentiati	IL-4	IL-2	IL-6	IL-8	IL-2
Tacrolimus is obtained	Aspergillus niger	Beauveria nivea	E.coli	Streptomy ces	Beauveria nivea
Cyclosporin is produced	Aspergillus niger	Beauveria nivea	E.coli	Streptomy ces	Aspergillus niger
Thalidomid e is a selective _____	TNF-alpha	TNF-beta	TNF-gamma	TNF-delta	TNF-alpha
Daclizumab is a geneticall engineered human____	IgG	IgA	IgD	IgE	IgG
_____ is an	Interferon	glatiramer acetate	lavamisole	Sirolimus	glatiramer acetate
_____re store cutaneous delayed hypersensiti	amantadine	tilorane	levamisole	BCG	levamisole

____&____ ___ stimulate humoral immune system	Amantidine&levamisole	tilorane&levamisole	BCG&clofazimine	amantidine&tilorane	amantidine&tilorane
Drugs which increase the rate of urine formation together with natriuresis	Anti-diuretics	Vasopressin	osmotic diuretics	diuretics	Anti-diuretics
Which of the following is a osmotic diuretic	furosemide	chlorthalidone	bumetamide	mannitol & sucrose	mannitol & sucrose
Extravasation of mannitol may cause	intracranial tension	pulmonary edema	confusion	thrombophlebitis	thrombophlebitis
_____ present in the cilia which is improtant in the production of aqeuous humour	electrolytes	carbonic anhydrase	xanthine	sucrose	carbonic anhydrase
_____ should be avoided for fear of causing respiratory depression	dexamethason	nifedipine	dexamethason and nifedipine	sedative hypnotics	sedative hypnotics

Excessive renal loss of Na and chloride with potassium loss can cause	hyponatremia	hyponatremic hypochloremia	hypokalemic hypoclore mic alkalosis	weak diuretics	hypokalemic hypocloremic alkalosis
_____ is an anti-bacterial drug possessing mild diuretic activity	osmotic diuretic	potassium sparing diuretic	benzothiadiazine diuretic	high ceiling diuretic	benzothiadiazine diuretic
Diabetes insipidus treated with _____ decrease the urine volume	mannitol	furosemide	aminophylline	benzothiadiazine	benzothiadiazine
_____ acts as a competitive aldosterone antagonist	thiazides	mannitol	spironolactone	weak diuretics	spironolactone
Absense of _____ may cause diabetes insipidus	Desmopressin	arginine vasopressin	high ceiling diuretics	osmotic diuretics	arginine vasopressin
In gout plasma level of uric acid is----------	2 to 7 mg/dl	10 to 15 mg/dl	below 7mg/dl	above 7mg/dl	above 7mg/dl

colichicine is used for the treatment of ----------	chronic gout	acute gout	RA	Anaemia	acute gout
Lesch-Nyhan syndrome leads to---------- gout	chronic gout	acute gout	chronic and acute gout	RA	chronic gout
uricosuric drugs are employed in the treatment of ----------	chronic gout	acute gout	RA	Epilepsy	chronic gout
The colichicine is rapidly absorbed from ----------	GI tract	duodenum	intestine	stomach	GI tract
Myopathy is caused by the chronic administration of ----------	colichicine	allopurinol	probenecid	stomach	colichicine
The derivative of phenylbutazone which is used as uricosuric agent is	probenecid	sulfinpyrazone	Azapropazone	benzbromarone	sulfinpyrazone
The drug used in the treatment of RA	muromab	infliximab	daclizumab	rituximab	infliximab

cyclophosphamide used in the treatment of RA is a ----------	analgesic	NSAID	daclizumab	DMARD	daclizumab
Which of the following is used for the treatment of patients with severe RA who have'nt responded to NSAID&slow acting	methotrexate	cyclophosphamide	daclizumab	Ibuprofen	methotrexate
Enzyme used in the treatment of gastrointestinal distribution is _____	urokinase	bibrinolysin	pepsin	hyaluronidase	pepsin
Cretain snake and bee venum contains	hyaluroonidase	disastase	trypsin	streptokinase	hyaluroonidase
_____ in highly purified form is used in opthalmic surgical procedures	potassium hyaluronidase	sodium hyaluronidase	chymotrypsin	collagenase	sodium hyaluronidase

Streptokinase is produced by certain strains of_____ __	stephylococci	bacilli	pneumococci	beta hemolytic streptococci	beta hemolytic streptococci
Trypsin is obtained from	bovine pancreas	ox pancreas	horse pancreas	bacterial strains	ox pancreas
The activity of collagenase is optimal at_____ __	pH 6-8	pH 5-8	pH 3-5	pH 7	pH 6-8
The concentrated protease enzyme bromelains obtained from	carcia papaya	pineapple	ox pancreas	bacterial strains	pineapple
Collagenase enzyme is derived from fermentation of _____ used to liquefy excessive bronchial secretions	cl.bromelains	cl.histolyticum	cl.papase	cl.botulinum	cl.histolyticum
	aerosal trypsin	bovine pancreas	chymoral	collagenase	aerosal trypsin
Streptokinase has its maximum activity between	pH 6.0-7.0	pH 7.3-7.6	pH 2.5-6.2	pH 5-7	pH 7.3-7.6

Aspirin is chemically ----------	sodium salicylate	salicylamide	acetyl salicylic acid	salicylate	acetyl salicylic acid
Aspirin is an example for ----------	NSAID	Adrenergic drug	Cholinergic drug	Emitic drug	NSAID
Aspirin inhibit ---------- activity	Cyclooxygenase	Esterase	Xanthine oxidase	Oxidase	Cyclooxygenase
NSAID repress the sensatoin of pain by decreasing ---------- synthesis	PGE2	PGI2	PGF2 alpha	PGF2 beta	PGE2
Aspirin ---------- thromboxane production.	reversibly inhibit	irreversibly inhibit	reversibly activate	irreversibly activate	irreversibly inhibit
Hyperkalemia is the increase of ----------	sodium	Magnesium	Calcium	Potassium	Potassium
Therapeutic action of aspirin is ----------	Anti inflammation	anti tumour	diuretic	antiemitic	Anti inflammation
A cyclooxigenase inhibitor used in the long term treatment of RA, osteo arthritis and .angkylosing spondilitis	Diclofenac	Ketorolac	Tolmetin	Ibuprofen	Diclofenac

The inactive prodrug closely related to indomethacin which is used as NSAID is ----------	Diclofenac	Sulindac	Etodolac	Fenamates	Sulindac
Orally administered aspirin is usually absorbed from --------	GI tract	Intestine	Stomach	Liver	Stomach
---------- is the competitive block of alpha 1 and alpha 2 receptor	Prazosin	Perazosin	Phentolamine	Propranolol	Phentolamine
All beta blockers are competitive ----------	Agonist	Antagonist	Agonst and Antagonist	beta blocker	Agonist
Labetalol is a ---------	alpha blocker	beta blocker	alpha and beta blocker	gamma blocker	alpha and beta blocker
All of them are competitive blockers of alpha 1 receptor except ---------- drug related to nitrogen mustard	Prazosin Phenoxybenzamine	Terazosin Propramolol	Daxazosin Labetalol	Propranolol Esmolol	Propranolol Phenoxybenzamine

Drug used in the treatment of pheochromocytoma is	Phenoxybenzamine	Propramolol	Labetalol	Acebutolol	Phenoxybenzamine
The other name of anticholinergic drug is	anti adregenic	anti muscuranic	anti inflammatory	anti emitic	anti muscuranic
Which one is not anticholinergic drugs?	Atrophin	scopalamine	dicyclomine	labetalol	labetalol