Topics: bio-pharmaceutics , pharmacology, clinical pharmacology, case study, calculations, pregnancy, geriatrics, paediatrics, toxicology, pharmacoeconomics, Pharmacogenomics, behavioural science, medication safety and epidemiology : Topics are designed to appear for the examination purpose only.

Chapter 1: Basics of general chemistry:

Atom, atomic number, (is number of proton or electrons in atom presented by letter "Z", . atomic mass or mass number is number of nucleons (protons and neutrons), Orbitals are energy levels where the electron revolves around an atom, and valene electrons, electro negativity is the power of atoms to atract electrons.

Octet rule states that an atom tends to have eight electrons in its outermost valence shell by forming covalent bonds through gaining or losing electrons f rom its outermost shell. (2 electron in hydrogen)
Isobar: same number of nucleons (neutron and proton) ie. Same number of total of proton and neutron or same mass number but different atomic number example: Calcium , potassium, argone.etc.
I**sotope**: same atomic number but different mass number or different number of neutrons.

Isomerism: is the phenomenon in which more than one compounds have the same chemical formula but different chemical structures. Chemical compounds that have identical chemical formulae but differ in properties and the arrangement of atoms in the molecule are called isomers.

Types of isomerism: structural or **Constitutiona**l isomerism: with different s**keleton** of molecules and **stereoisomerism:** different orientation of atom or spatial arrangement of atoms.

Structural isomerism: different chain, change position of groups , different functional groups , metamerism (different number of carbon around the functional group, **tautomerism** (due to different position of hydrogen atom), **Tautomers** are structural isomers which readily interconvert to each other**.**

Stereoisomerism: are conformational, geometrical, optical isomerism. Number of stereoisomers from a compound is $= 2^n$, n is the number of **asymmetric** carbon atom. There are two kinds of stereoisomers: **enantiomers** and **diastereomers**. Enantiomers are mirror images of each other, like human hands, and are non super imposable (cannot be placed one over the other) and others are diastereomers.

Optical activity: is the ability of drugs to change the plane of light. it Is due to asymmetric carbon atom or **chiral** molecules (have non superimposable mirror images known as **enantiomers,** these change the path of plane polarized light (optical activitity).
Dextrorotatory is presented by symbol (+) or (d) and levo rotatory (-) (l). D - glucose is dextrorotatory. Equimolar mixture of d & l form known **as racemic mixture** and it has no optical activity, But it has therapeutic activity.

Polarity means bearing charge on molecule and is said to polar and water soluble and less lipid soluble.
I**onic bond** is formed by gaining or losing electron, it is the **strong** bond, **Covalent bond**: is formed between atoms by sharing electrons, and hydrogen bonding (is weak bond present in water).

Valence electrons in the outer most shell or orbitals in the atom and it decides valency of the atom
Carbon has four valency: carbon has single bond in alkanes like **CH4 (methane)**, double bond in alkenes **C2H4 (ethene)** and triple bond in alkynes, like **C2H2:**

Bio-isosterism is a method medicinal chemists use for modification of a lead compound (drugs) into safer, more clinically effective , economical and therapeutically attractive drugs.
Isosters are atoms or groups of atoms which have same valency, similar physical and chemical properties. Example of isosters are SH, NH2, CH3 are isosters of OH, and S, NH, and CH2 are isosters of Oxyegen.

Isosters can be used to check whether a particular group is important for binding with receptor, so by replacing one group with others can change the property of drugs such as **polarity, electronic distribution**, and bonding. If OH group is replaced with CH3 no hydrogen bonding will be present.

Carbohydrate: Carbohydrates: 1g carbohydrate provide 4 kcal of energy. Exhibit stereo isomerism: same structural formula but different spatial arrangement of groups around asymmetric carbon atom.
Penultimate carbon atom is the second last carbon atom chosen to name.
In glucose 5^{th} carbon atom is the penultimate carbon , if OH group is on the right side it is **D- form** and left side is **L- form**. Body can use only D form of glucose.

Epimerism: when sugars differ from one another in a single carbon atom other than reference carbon atom are called **epimers**. Example; mannose and galactose are epimers of glucose, **mannose and galactose** are **diastereomers** because they differ at two carbon atoms.
Anomers are cyclic monosaccharides or glycosides that are epimers, differing from each other in the configuration wearing functional group such as of C-1 (first carbon atom), if they are aldoses or in the configuration at C-2 , they are ketoses. The epimeric carbon in anomers are known as anomeric carbon **or anomeric center.**
Anomerism in gluocose: glucose has two anomers **alpha- D** glucose with a optical rotation of **+119^0** and **beta -D** glucose with optical rotation of **+ 19^0** : by cycling of first carbon of glucose with 5^{th} carbon of same molecule. If the OH group of first carbon is on left side **it is beta -D** glucose and if it in right side it is called **alpha- D glucose**.

Mutarotation is the change in optical rotation by glucose solution on standing or after 24 h.. the two form interconvert to each other and new optical rotation will result: this change its optical rotation due to inter conversion of Beta and alpha form to each other is called **mutarotation**.

Carbohydrate: general formula $(CH_2O)n$, n is the number of units. Hexoses contains six carbon atom and pentoses contains five carbon. Monosaccharides are linked with glycosidic bond in poly sacharides.
Monosacharides: are glucose and fructose, mannose, galactose. **Pentoses**: ribose, deoxy ribose .
Disaccharides has two units of monosacharides**: maltose** with 2 glucose molecule , **lactose** with **:** glucose and galactose. **Sucrose:** glucose and fructose.

Poly sacharides are of two types: heteroglycan and homoglycans: **homoglycan**s are composed of single type of monosacharides: starch, glycogen and cellulose. Starch has two parts: amylose and amylopectin. Both are of glucose. **Glycogen:** is reserve carbohydrate in animals. **Cellulos**e: is plant origin, humans cannot digest cellulose. Cellulose only some fungi and bacteria can digest. **Inulin:** is composed of fructose, is used to check renal function, **Heteroglycans**: are poly sacharide with different monosacharides; example; **agar**: **Agar i**s polymer of galactose, glucose and other sugar, used to make culture media

Dextran is highly branched polymer of glucose, it is used as plasma expander to treat **hypovolemic s**hock. .
Chitin is polymer of glucosamine (sugar with amino acid).
Peptidoglycan: is polymer of sugar and amino acid seen in cell bacterial cell wall.
Lab test or detection: is by **Benedict reagent** test.

Amino acids: classification: mono amino mono carboxylic acid: simple: glycine and alanine.
Branched chain: valine, leucine, isoleucine. **Hydroxyl amino acids**: serine, threonine.
Sulphur containing : cysteine, methionine, containing amide groups: asparagines and glutamine.
Dibasic monocarboxylic acid: lysine and arginine. **Aromatic**: phenylalanine and tyrosine.
Heterocyclic: tryptophan, histidine. Imino acid: proline.

Essential amino acids:
histidine, Arginine, lysine, leucine, phenyl alanine, valine, threonine, tryptophan, isoleucine , methionine, (Pnemonics of essential amino acids **: HALL PVT TIM)**

Isoelectric point or isoelectric pH : is the pH at which the molecule is neutral or carries no net charge. is known as **Ampholytes or zwitter ions** . In acidic solution they become cation and in alkaline solution they become anion. Solubility and buffering capacity will be minimum

Proteins: amino acids linked through peptide bond such as dipeptides, tripeptides, tetrapeptide, oligopeptide, polypeptide (10 -50) and above 50 amino acid is protein. The stability of proteins depends on charge and hydration. The polar groups such as NH2, COOH, OH group will attract water and make a shell of hydration so anything that neutralise the charge will lead to precipitation of proteins.

when saturated salt solution such as ammonium sulphate or sodium sulphate is added to protein solution the shell of hydration is removed and protein is precipitated this is called **Salting out**:

At isoelectric PH the protein will be least water soluble, carry no charge, proteins **precipitates.**
Denaturation: occurs with proteins by heat, salt etc and protein loses its structure.

Classification of proteins: catalytic proteins: are enzymes, structural proteins are collagen ,elastin, **contractile** proteins: myosin and actin, **transport** proteins: haemoglobin, myoglobin, albumin, transferrin, **Regulatory proteins** are**: Hormones:** insulin, growth etc**. Genetic protein**: histones, protective protein : immunoglobulin, interferon, clotting factors

Lipids:
Triglycerides: esters of fatty acid and glycerol.
Phospholipids contains : fatty acid, glycerol + phosphate. **Wax** is formed between long chain alcohol and saturated fatty acid. Eg. Paraffin.
Essential fatty acids: Linoleic acid (omega 6) and linolenic acid (omega 3) are essential fatty acids, body cannot synthesise it. **source**: **evening prime** rose oil : Use for premenstrual syndrome

Cell organells: parts of cell and their function:
Nucleus: all cells have nucleus except RBC, DNA is complexed with proteins to form chromatin and further organised to chromosomes.
Nucleolus is part of nucleus: role is RNA processing and ribosome synthesis.
Endoplasmic reticulum (ER): it is a net work of interconnecting membrane enclosing channel or cisternae that are continuous from nuclear envelope to outer plasma membrane. It is very prominent in cell producing proteins such as immunoglobulins by plasma cells and also protein, glycoprotein, lipoprotein are produced in ER and detoxification of some drugs such as phenobarbitone
Two types of ER, rough and smooth. Rough ER is due to presence of ribosome on the membrane where proteins synthesis take place.

Golgi apparatus: is a net work of flattened smooth membrane and vesicles, it may be considered as the converging area of endoplasmic reticulum. Its function is: sorting, packaging and secretion of protein and lipid. **Lysosomes**: is suicidal organ contains enzyme for removal of cell waste. It contains proteolytic, polysacharide hydrolysing enzymes etc. If cell membrane is damaged it will release these enzyme and damage cell, **Peroxisomes**: contains catalase and peroxidise: it destroys unwanted peroxides and free radicals .
Mitochondria: is the power of the cell, produce ATP for energy need of the body.

Primary lymphoid organs: are bone marrow and the thymus. They create special immune cells called lymphocytes. **Secondary lymphoid** organs: These organs include the lymph nodes, the spleen, **the tonsils.**
G**lycogenesis:** is the formation of glycogen from glucose**,** and break down of glycogen is known as **glycogenolysis,** the break down of glucose to pyruvate or lactate is known as **glycolysis.**

Citric acid cycle (krebs cycle or tricarboxylic acid cycle, TCA cylcle): is common pathway for oxidation of carbohydrate, protein and fat to CO2 (carbon dioxide) and H2O, ATP. Acetyl Co-A is metabolised to CO2 and H20 in the cycle. **Krebs cycle** needs oxygen, so it does not take place in anaerobic condition or in the absence of oxygen. Total ATP produced from one glucose in aerobic respiration is **38 ATPs:**

Metabolism of aminoacids:

Transamination reaction: amino group is removed from amino acids to form a **keto acid** and the amino group is converted to urea in liver and excreted. **Urea cycle**: takes place in liver, in urea cycle ammonia is converted to urea.

Phases or stages of metabolism:

Primary metabolism is the digestion in the Git: where macromolecules like fats and protein and carbohydrates are converted to fatty acid, amino acid and monosacharides like glucose.

Second phase: they are converted to carbon dioxide and water and yielding energy molecules. The final pathway is **TCA cycle.** **Xenobiotics**: are substances foreign to body or not present in the body.

Solubility is defined as : ml or quantity or parts of solvent required to dissolve **1 gm or 1 part** of solute**, it** is important for dissolution and absorption **of drugs form GI tract.**

Solubility types:	Solvent required to dissolve one part of solute or 1 g of solute.
Very soluble	Less than one part
Freely soluble	From 1 – 10 parts
Soluble	10 – 30 parts
Sparingly soluble	30- 100 parts
Slightly soluble	100 -1000 parts
Very slightly soluble	1000 -10000 parts
Practically insoluble soluble	Above 10000

(Solubity related question and important poinst? How to increase solubility or which is more soluble ?)
States of matter. **Polymorphism is** existing of solids in different crystalline structure, they differ in melting point, density, dissolution (solubility), different crystal lattice, no change in m**etabolic** rates.

Solids: are of two types: amorphous and crystalline. **Crystalline solids** have fixed molecular order, distinct melting point and **anisotropy** (properties are not same in all direction).
Amorphous solids: randomly arranged, no sharp melting point, **Isotropy**: (isotropicity is same property in all direction) less stable than crystalline and better dissolution and more solubility.
Anhydrous form drug is more soluble than hydrous form

Alkaloids: are naturally occurring compounds: contains nitrogen, basic in nature, PKa more than 7, alcohol soluble, water insoluble, but salt from is more water soluble (atropine hydrochloride more soluble than atropine base); Alkaloids are used to treat cancer, smooth muscle relaxants, etc
Alkaloids are detected by **Dragendroff' test**. It produce an orange red precipitation.

Dragendroff reagent: is is a solution of potassium bismuth iodide composing of basic bismuth nitrate ($Bi(NO_3)_3$), tartaric acid, and potassium iodide (KI), and when contact with alkaloids, it produces an orange or orange red precipitate.
Glycosides : are compounds contains sugar and aglycone joined through glycosidic linkages. Eg. digoxin,

Particle size recommended are: inhalation: 5- micron, **Eye drop**: < 10 micron, suspension < 5 µ.
c**olloids**: **0.1 - 0.2** micron. **Particle** size can be decreased by: **milling** (communition technics) such as **trituration (dry grinding** in mortar), **pulverization** by intervention for gummy substances such as **camphor** done with solvent like alcohol which then removed, **levigation** (size reduction with a levigating agent (like the process of making cream**,** with solvent in which solute is insoluble) . **micronisation (** using jet mill). Decreasing **Particle size,** ↑ surface area **and** ↑ solubility.
Study of particle size is known as **Micromeritics.**
Example for colloids: albumin soln, starch soln, dextran, colloids are characterised by Turbidity.

Micellar solubilisation: surface active agents has both nonpolar and polar characteristic and they hold together both nonpolar and polar compounds. **CMC:** critical micellar concentration: minimum concentra-

tion of Surface active agents above which the micelles starts. Co –s**olvenc**y: by using two miscible liquids (alcohol and water)

Solid solutions (molecular dispersion): binary mixture of solid solute in a solid vehicle made by fusion method (melting and rapid solidification.) if the solution is transparent, homogenous , brittle , is called **glass solution**. **Solid dispersion**: solute and solid vehicle is dissolved in common solvent like alcohol, and alcohol is removed by freeze drying and drug precipitates as amorphous powder.
Hydrotrophy: is method done by adding another solute **.**

Formation of salt weak acid or weak base .eg. Atropine (base), and **salt is** : Atropine Hydrochloride. Salt is more soluble. **Complexation** increase solubility: **iodine** in KI, forms KI_3, it is more water soluble than I_2

Partition coefficient **P** or also known as **Kow**: Also known as **octanol – water partition coefficient** is the ratio of conc: of substance between two immiscible liquids.
P = concentration of drug in octanol / concentration of drug in water.
if value of Kow is less than 1, drug is water soluble and more than 1 it is lipid soluble. is a measure of lipid solubility or **hydrophobicity**: lipid soluble drugs will have high P – value and water soluble will have low.

Colligative property of a solution depends only on **number of solute** molecules in the solution. Example of colligative properties: Boling Point elevation, lowering of vapour pressure, depression of freezing point or Melting point and **osmosis.**
Roult's law states that vapour pressure of a volatile component in a solution is equal to the product of mole fraction of the component in the solution and vapour pressure of the pure component.

Vapour pressure: is the pressure at which equilibrium is established between molecules of in liquid state and gaseous state or vapour state in closed evacuated container. Vapour pressure is temperature dependant but independent of amount of liquid or gas.
Boiling Point is temperature at which vapour pressure of liquid equals to atmosphere pressure:
Melting point: latent heat of fusion is the heat required to melt 1.g of solid.

Osmosis: (is the passage of solvent molecules from low concentration to higher concentration through semipermeable membrane. Osmotic pressure is given by **Vont Hoff equation**; $\pi V = nRT$ **(**π is the osmotic pressure, V- volume of solution, n- number of moles, R- universal gas constant, T – absolute temperature).
Isotonicity (same osmotic pressure as that of plasma):. Isotonicity based on RBC (check what happens with administration of hyper tonic, and hypotonic, (refer picture in the video).

PH : is negative log of (H^+) or (H_3O^+, hydronium ion) concentration. Or pH is the logarithm of the reciprocal H+ ion concentration.
PH scale is ranging from 0 to 7 (acidic) and 7 to 14 (basic) , ↑ with temperature?, ↑ with ionisation?, neutral PH or pH of water is 7**.** **PH of body parts**: blood: 7.4, stomach: 1.5 - 3.5, small intestine: 6-8, eye pH : 6-8, vagina: 3.5-4.2, skin: 5.5. jejunum has high pH.

Buffer: is mixture of salt and acid or base that resist change in PH when a small qty of acid or base is added. It is made between weak acid and its conjugate base. **PKa** value of the acid selected should be very close to buffer pH value. **Buffer in** present in human plasma is : **sodium bicarbonate** and buffer in (ICF) : intra cellular fluid **: phosphate buffer**
Acid, base theories: Arrhenius theory: acid is H^+ ion donor and base OH^- ion donor in aqueous solution , **Bronsted lowry theory:** states that an **acid is** proton donor and **base a**s proton acceptor.

Solvents: protophylic or basic solvent which can accept a proton. (ether, acetone, ammonia**), protogenic** solvent can donate a proton (formic acid), **amphiprotic:** can donate and accept proton (water and alcohols**).** **Aprotic solvent .** Neither donate nor accept a proton (Eg. hydrocarbons

Electrolytes: are compounds dissociate to ions in the solution**.** strong electrolyte ionise or dissociate completely, **weak electrolyte** dissociate partly. **Most drugs** are weak electrolytes **.**
Non electrolytes does not ionise in solution. Eg. Sucrose, urea, glycerine, glucose**,**

Degree of Ionisation of weak electrolytes is calculated using **Henderson** hassel balch eqn (also known as buffer eqn or acid base partition theory) .
Eqn For acid is: **PH = Pka + log ionised / unionised**, or PH = **Pka + log salt / acid**
For base : PH = **Pka + log** un ionised / ionised**.**

Pka: is dissociation constant. It is the **pH** at which **50% ionisation** occurs**, PKa:** indicates the strength of acid or base. (Lower the PKa value higher the strength of acid).
To make a buffer select acid with PKa value close to the required buffer PH value of the buffer
PKw of water is 14. See calculation video for worked out example.

Chromatography: adsorption chromatography: has two phase: stationery phase and mobile phase contain the solute to separated. The mobile phase passes over stationery phase solutes are separated
Drug source are : plants, animals, synthetic, E- coli (Escherichia coli) bacteria used in biotechnology.

Biotechnology: recombinant DNA technology involves 1. Identification and isolation of required DNA (eg. gene for insulin), 2. insertion of DNA to a vector gene such as plasmid 3. introduction of this vector to a host called **transformation,** 4. selection of transformed host cells 5. multiplication or expression of introduced gene in host cell.
Properties of biotech product: store at 2 -8^0 C, No freezing, administer parenterally, avoid vigorous shaking ? produce less anaphylaxis (allergic reaction) than other biological products.

Procedure for getting approval for new drug. New drug registration in US (America) is as follows. Submit investigational new drug application (IND) along with pre clinical animal studies and get approval for clinical trials. Submit application **to SFDA (** Saudi food and drug administration) in Saudi Arabia.

Clinical trials: is drug trial in human, it has 4 phases, first three phases are designed to study safety and efficacy and forth new indication, risks and optimal dose of the new drugs .
Phase1: done on healthy volunteers of 10 – 100, study includes **toxicity** and kinetics, safety or pharmacology of drugs for 1 month to 1 year. (Drugs for AIDS and cancer done on patients itself).

Phase 2: (therapeutic investigation): done on 50 – 500 patients at one centre, study include efficacy, potency, toxicity for 1 -2 years.
Phase 3 clinical trial or pivotal trials : (for Therapeutic confirmation of the drugs): a lot of patients of the order of 1000s at multiple centres for 3- 5 years. Study include both single blind and double blind study , after phase 3, the approval for marketing the new drug is granded, and start **Phase** 4 or Post marketing surveillance for any new side effects or indication of the drugs. **Positive control**: a known standard therapy in addition of a placebo to evaluate inferiority or superiority of new drug.

Determination of safety, potency and efficacy of the new drugs : to determine potency and efficacy of a new drug, a plot of effect or efficacy of drug on Y axis and dose on X axis is made. it is known as **graded dose response** curve. Refer video class for graph and see which drug has high potency, high efficacy? Shape of graph, hyperbola ? sigmoid? Agonistic relation ship and antagonist relationship.
EC: 50: means the dose for 50% response of the drug, it decides the potency, E –max. Dose for max. effect

Quantal dose response curve: log dose on X axis and response in population on Y- axis:
values from the graph is : ED:50: (effective dose in 50% of the population and TD50 : toxic dose or LD 50: lethal dose in 50% of the population. Calculate therapeutic index and safety of the drug:

Therapeutic index (TI): is the ratio of lethal / toxic dose to effective dose. It indicates the safety of drugs.

TI = LD50 / ED 50 or TD 50/ ED50. LD50 is the dose to kill 50% of given population and TD 50: toxic dose in 50% of the population, ED 50 is effective dose in 50% of the given population**.**

Therapeutic window refers the dose range between effective dose and toxic dose. (minimum therapeutic concentration and minimum toxic concentration)
Drugs with narrow therapeutic index : digoxin, lithium, warfarin, aminoglycosides, phenytoin, barbiturate, Theophylline. Etc . monitor plasma concentration and precaution in liver or renal failure other factors?

Lipinski's rule of five: is used to predict oral bioavailability of new drug. **Lipinski's rule** states that, in general, an orally absorbed drug should have no more than one violation of the following criteria:
1. No more than 5 hydrogen bond **donors** (total number of nitrogen – hydrogen and oxygen– hydrogen bond **2. No more** than 10 hydrogen bond **acceptors** (all nitrogen or oxygen atoms), 3. molecular weight less **than 500 daltons** 4, An octanol-water partition coefficient (log *P*) that does not exceed 5

Prodrugs: are drugs without action and need in vivo bioactivation in the body by phase 1 metabolism to active form. Example enalapril conveted to enalaprilat.

Beyond use date: is found as per USP guide line 795: it is the time or days a compounded product that can be stored after compounding: The time or days for solid and non aqueous formulation is 6 months or 25% of the remaining shelf life (time to expiry date) takes which comes first. Beyond use date for aqeous product of **oral formulation** , if stored in refrigerator is **14 days** or 7 days in room temperature, And topical aqeous product can be used upto **one month**. **Find beyond** use date of the tablet made on 1st jan 2023. The expiry date of sorce material used to make the tablet is of 31 dec 2023: (answer: 31st march 2023).

Shelf life: is the time the drug can be stored before it becomes unfit to use by physical or chemical change. Temperature affects shelf life. At the end of shelf life the concentration of drug should not be less than 10% of nominal concentration (original concentration).and the decomposed product should be non toxic.
Expiry date: is used to show end date for manufactured product, Expiry date reflects the period after which a drug or any other product is known to lose its strength, quality and purity and the time-period ranging from the manufacturing date to the expiry date is referred to as the Shelf-life

If a medicine has a use by or use before date instead of an expiry date, this usually means that you should not take the medicine after the end of the previous month. For example, if the use by date is July 2023, you should not take the medicine after 30 June 2023

Pyrogens are the metabolic product of micro organism detected by **limulus** test. **Water for injection**: purified by distillation and so contains no pyrogen but **Sterilised water** contains pyrogen.

Compounding: is the process of preparation of drugs by pharmacist as per prescription . **Reference** for compounding guide lines is based on **USP** (united states pharmacopeoia):
The guide lines are: chapter is **797:** for S**terile preparation** and guide line for **Non sterile** products is 7**95:** Hazardous Drugs - USP 800, Radiopharmaceuticals Preparation, Compounding, Dispensing, and Repackaging: USP 825: handled

Labels on the compounded products. Should contain beyond use date details.. **Dispensing labels:** details of drug, pharmacy, qty, precaution, direction for use, indication, patient name, etc.**Label on dispensed medicine**: name of patient, name of medicine, pharmacist, date of dispensing, direction for use,

Auxiliary labels (advisory or cautionery labels): is additional label that the pharmacist attach to dispensed drug: **should contain**: information on how to use, route of adminitration, storage information like refrigerate, , shake well, donot crush or chew, swallow whole, external use only, strength, generic name, expiry date, pharmacy lot number, made in pharmacy sticker, beyond use date,
warning information like; keep away from children, may cause drowsiness and don't drive or operate machinery, dietary instruction: like with food or without food, avoid milk etc. Refill instruction,

Unit dose dispensing: unit of dose a drug for a patient to be administered once is prepared by pharmacist and sent to nurse station and delivered to patient directly reduces the **error and wastage** of drug, and the patient is charged only for drug received **. Orphan drug**: drug used for rare disease are known as orphan drugs. **Essential medicines**: are those that satisfy the priority health care needs of the population.

Simple Syrup NF: (NF: national formulary): is solution of sucrose, its properties are: **nearly saturated**, **self preserving** due to high osmosis, very low solvent capacity due to strong hydrogen bonding between water and sucrose. It doses not need any preservative due to osmosis ?

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Chapter: 2 pharmaceutics:

Linctus: are viscous, liquid oral preparation used for cough relief.
Elixirs: clear aromatic sweetened , aromatic, hydroalcoholic liquid for internal use.
Liniments: liquid or semi liquid preparation to be applied on the skin with **rubbing** or friction.
Lotions: are liquid preparation to be applied on skin without rubbing or friction.

Oral Formulations are tablets, capsule, suspension, liquid. Formulation differ in **dissolution time** and disintegration time. (Which product has high speed of dissolution: answer: solution)
Order **speed** of dissolution of different oral formulation is as follows : solution > emulsion > suspension > powder > capsule > tabs. Solution is faster. Capsule and tablet should undergo **disintegration** then dissolution and so `**rate limiting step** is disintegration.
Extemporaneous product prepared by the pharmacist without an official formula for particular patient.

Excipients
Diluents: are used to increase size**: Includes:** lactose, sucrose, sorbitol, mannitol, starch, microcrystalline cellulose, dibasic calcium phosphate, calcium sulphate and sodium chloride, dextrose, **Diluents** used in external preparations: are talc and kaolin.
Binders used a**re**: starch, acacia, tragacanth, gelatin, glucosee, sorbitol, Sodium alginates, polyvinyl pyrrolidone (PVP).
Disintegrating agent: **starch,** clays: veegum and bentonite**,** microcrystalline cellulose**..**
Rheology is study of flow characters of granules: **lubricants:** reduce friction between tablet and **dye (** punching machine**), S**uch as talc, boric acid, magnesium **stearate,** sodium stearate, colloidal silica.
Glidants: reduce the friction between granules: corn starch, colloidal silicas**,** talc.

Preservatives: are b**enzalkonium** (used in eye and parenteral preparation): benzoic acid and sodium benzoate, **Benzyl alcohol** is contraindicated in **neonates** and infanst because it causes fatal **gasping syndrome: (** respiratory and other system failure in babies).
Colouring agents: mineral colouring agents**: ferric oxide** (yellow and red). **Carbon black**, **titanium dioxide** (also used in **sun block** cream), ultramarine,

Dosage forms: solutions, suspension and emulsion: solutions: are bulkier, less stable,
Suspensions: particles are visible, particle size: 0.5**- 5 micron,** it follows **zero o**rder degradation. it needs dissolution before absorption, dissolution is slower than solution. Particles of the solute do not **dissolve** in the solvent rather they remain suspended in bulk of the solvent . The size of particles of suspension is **(0.5 to 5 microns)** and are large enough to be visible with naked eyes. Suspension can be separated by **physical** methods such as filtration, but solution cannot be separated by filtration.

Two types of suspension **flocculated** and deflocculated; suspension contains hydrophibic drugs and wetting agents help to form suspension, it follows **zero order** degredation

Comparison between flocculated and deflocculated suspension.

Type of supension	floculated suspension	defloculated suspension

Particles forms	loose aggregates and form net work	exists as separate particles
Rate of sedimentation	rapid or high	slow sedimentation
Sediment formation	rapid	slow sedimentation
Type of sediments	loosely packed and no hard cakes	closely packed and form and hard cake
Redispersion	easy	difficulty
floculates stick to the bottle	yes	no

Additives in suspension are flocculating agents, suspending agents, wetting agents, dispersing agents, preservatives, organoleptic agents**:**
Suspending: agents are added to suspensions to increase viscosity: **Natural** polysascharides: are **Gums**: from plants: like **acacia** (gum Arabic) and **Tragacanth**:
Semi synthetic: methylcellulose: (insoluble in hot water, soluble in cold water, it is **non ionic)**.
Carboxy methyl cellulose **(CMC) :** is **anionic**,

Inorganic Clays: **veegum**: **anionic,** exhibit **thixotropy, (Thixotropy**: means **:** forms a gel on standing and becomes fluid on agitation, (**rheopex**y is negative thixotropy or anti thixotropy).
From animals; gelatin and casein**,**
Gelatine: (Type A) which is obtained from an acid-treated precursor (collagen), has an iso-electric point is **pH : 9 and is cationic** and Type B: from an alkali-treated precursor has an iso-electric point is = PH4.7, is anionic, **from sea weeds**: agar, alginate **.** gelatinised starch**,**

Synthetic thickening agents: **carbomers** (carboxy vinyl polymer). Xanthan gum
Wetting agents: reduce interfacial tension between solid particles and liquids: example, sodium carboxy methyl cellulose, alumium, magnesium silicates, glycerine, glycols, bentonite.

Emulsions:
Type of emulsions: solid in gas: example: smoke, dust**,** **Liquid** in solid: cheese, butter jellies, **liquid in liquid**: milk, hair cream. **Liquid in gas:** fog, mist, cloud, insecticide spray.
Emulsion: consists of two phases of heterogeneous system of two immiscible liquids such **as oil and water**: an internal, dispersed phase, or **droplet phase:** (drop size or globule size is: **0.5 – 25 micron**).

C**oncentration o**f internal phase is usually 40 - 60% of the total emulsion, maximum amount of internal phase can be upto 74 %, **second phase** is continuous phase and an emulsifier acts as surfactant or detergent and reduce the surface tension between oil and water..

Types of emulsions: w/o, o/w, w/o/w, o/w/o. most popular emulsion **is O/W**
Emulsion with large globules are called coarse emulsion, emulsion with globule size 5 micron are known as fine emulsion, emulsion with globule size10 nm (nanometer) are called microemulsion.

Example for **natural emulsion is milk. Lotion**, creams, ointment and pastes are emulsion of water and oil. **Ointment** has high potency than cream. **Lotions** are mostly oil in water, small amount of oil and high amount of water. **Advantage of emulsion**: more stable than aqueous solution, better taste, increased solubility, prolonged drug action.

Emulsifying agents used in oil /water emulsion are acacia, tragacanth, methyl cellulose, saponins.
Emulsifying agensts used in water in oil type emulsion is wool fat, resins and bees wax
How to identify emulsion type: dilution test with water or oil ? when water is added to emulsion if emulsion is O/W emulsion remain intact, emulsion cracks if it is W/O.
C**onductivit**y test: O/W emulsion conducts electricity, **dye test**: with amaranth or scarlet red dye: shows **red colour** globules of oil in case of **o/w**, **fluorescence test:** on exposure to ultra violet radiation **w/o** shows continuous fluorescence and spoty fluorescence in o/w. **Cobalt chloride test**: filter paper soaked with cobalt chloride and dipped in o/w emulsion and dried turns blue to pink.

Microemulsion: is clear (transparent), thermodynamically stable, isotropic (same in all direction) mixture of oil, water, surfactant and cosurfactant. With particle size 1- 100 nm.

Emulsifying agents: classification: **natural emulsifiers:** acacia (forms low viscosity emulsion, creams easily) , tragacanth, agar, gelatin, methylcellulose, carboxymethylcellulose: pectin **Methyl** cellulose: non-**ionic** used with cod liver oil, mineral oil, forms **o/w, used in 2% strength . Carboxy**methylcellulose **(**CMC) **is anionic**. ↑viscosity, it tolerates alcohol up to 40% and form basic Solution,

Surfactants: are molecules or ions adsorbed at the interface: they are amphilic means like both polar and non polar drugs. Examples are straight chain alcohol, amines and acids, the hydrophilicity decrease as size or number of carbon increase**.** The scientists **Griffin** devised an arbitrary scale of lipophililty or hydrophylicity. Know as **HLB** (hydrophilic lipophylic balance**)**: it indicates the balance of lipophilic and hydrophilic parts in emulsifier:
Higher the value of HLB, the more water soluble is the emulsifier and forms **O/W type** of emulsion).
Lower HLB values is lipophilic and forms **W/O type of emulsion**:
The value above 9 is hydrophilic and below 9 is lipophylic.

Synthetic surfactant: are anionic, cationic, non-ionic: they are **amphiphilic**: (having both lipophilic and hydrophilic parts; some tend to be hydrophilic and some lipophilic: It is decided by **HLB scale** (hydrophilic, lipophilic balance):
Synthetic: Anionic emulsifying agents : sulphuric acid esters: **sodium lauryl sulphate** (is an example of only externally used emulsifier). **Sulphonic acid** derivative: **dioctyl sodium sulfosuccinate (** docusate).
Cationic synthetic agents**:** benzalkoniun chloride, benzethonium chloride, cetrimide.

Non ionic synthetic agents**: Sorbitan esters**: **spans:** are hydrophobic, forms **w/o type of emulsion, & polysorbates** (**tweens**:) are hydrophilic and forms **O/w type of emulsion,**
Tyndal effect: the light scattering by particle and emulsion appears white. Droplet scatters light only if its size more than the wave of incident light. Emulsion **appears white** due to reflection and refraction.

Method of **Preparation of emulsion**:
Wet gum method (English method): is as follows. Mix water and acacia with triturartion and then add oil little by little mix with trituration:
Dry gum method or continental method: mix acacia with oil and then add water little by little**.**
Bottle method: is used for volatile oils:

Types of oils: **fixed oil** are **castor** oil, almond oil, **arachis** oil and cod liver oil, **volatile oils** are: turpentine oil, peppermint oil and cinnamon oils, **Mineral** oil is: liquid paraffin

Ratio of ingredients: with fixed **Oil: water: acacia are : 4: 2 :1.** With volatile oil: oil :water: acacia is **: 2:2:1and for mineral oil: liquid paraffin: 3:2:1**
Phase inversion: is the change of continous phase and internal phase; like O/W becomes W/O

Semi solid dosage forms:
Ointment: are semi solid preparation used to make skin pliable (soft), to protect skin, as vehicle with drug**.**
Ointment bases include: oleaginous, absorption, emulsion base, water soluble base.
Oleaginous bases: are anhydrous, **water insoluble** hydrocarbons, vegetable oils, animal fats and waxes; greasy, not washable with water: i**ncludes**: petrolatum, lanolin and **synthetic esters**:

Petrolatum (soft paraffin): is semi solid hydrocarbons obtained from petroleum. Is good base for oil insolu ble ingredients, it forms occlusive film over the skin, absorbs less than 5% water.
Synthetic esters: used in oleaginous bases are glyceryl monostearate, isopropyl myristate, isopropyl palmitate, butyl stearate, butyl pamitate, long chain alcohols like cetyl alcohol, sterayl alcohol, PEG,

Two types of paraffins: yellow soft paraffin and white soft paraffin made by bleaching yellow paraffin, so **white paraffin** can not be used for ophthalmic preparation,
Hard paraffin: obtained from petroleum is used to harden ointment.

Absorption base : anhydrous and water insoluble but not washable with water **can absorb water**, water soluble drugs can be included by making solution of drug and then mixing. Examples: are 1.**wool fat:** (anhydrous lanolin), contains high % of cholesterol, and esters of alcohol, melts at $36 - 42^0$C.
2. **Hydrophilic petrolatum.**

Emulsion base includes o/w or w/o types. **w/o** are water insoluble and not washable but can absorb water.
1. **Hydrous** wool fat (lanolin). Contains 25% water, emollient, forms an occlusive film, prevent water loss
2. Cold cream: w/o prepared by melting white wax , spermaceti and almond oil**,**
3. Hydrophilic ointment: is **o/w** emulsion**,** uses sodium lauryl sulphate as emulsifier easily removed
4. Vanishing cream: o/w, contains large amt of water and humectants and prevent **moisture loss.**
Large amt of stearic acid helps form a thin film when water evaporates.

Water soluble base: anhydrous or may contain water, washable, and absorb water to the point of solubility. PEG (poly ethylene glycol 40%, PEG 3350 and 60% PEG 400 prepared by fusion method).
Incorporation drug to base is done by is by **levigation** (with spatula and ointment Slab) or fusion (melting) method.

Suppository: are **solid / semisolid** preparation, drug absorption has two steps, first drug release from vehicle and diffuse through mucosa to vein then to circulation.
Vaginal suppository (pessaries) : weighs: 5g. base used is **polyethylene glycol,** diluents used is : lactose.
Rectal suppository weighs 2gm. Selection of base depends on the solubility of drugs, use oily base for water soluble drugs and aqueous base for oil soluble drugs for better drug absorption.

Suppository Bases : **theobroma oil** (**cocoa butter**, it contains triglycerides, poor water solubility, exhibit polymorphism, melts at 34^0C, good for **rectal supp**),
Witepsol: (major component is lauric acid**) . wecobee:** derived from coconut**, PEG**. (poly ethylene glycol)
Water soluble base: PEG 400 – 600 is liquid at room temp. PEG 1000 is semisolid, PEG 1500 – 1600 is solids, PEG 3350 -6000 are wax like solids

Criteria for base for suppository : should be firm at room temperature, inert, narrow melting point, non irritating, with wetting property, solubility of drug in it (for lipid soluble drugs use water soluble base so drug will pass to blood).
Decoction: is a method of extraction of drugs by boiling of dissolved chemicals, or herbal or plant material.
Demulscent: are substance that relieve irritation of the mucous membrane in the mouth and throat by forming a protective film.

Aerosol: is doage form of metered dose inhaler, actuation of netered dose inhaler means how to use inhaler
Advantage of inhaler: Convenience of dispensing, stability due to closed container, less contamination, **disadvantage**: disposal and Gas leak to atmosphere and is **expensive:** **propellants** used in aerosol are **Compressed gases**: carbon dioxide, nitrogen, Nitrogen oxide. Aerosol which contain compressed gas tend lose pressure when it is used, this is reflected by **expansion of neck space,** so it is initially filled with high pressure.

Incompatibility: Chemical incompatibility is due to hydrolysis, oxidation, decomposition reaction.
Physical incompatibility occurs between drug and container or diluents such as dextrose or saline.
Container incompatibility: due to **DEHP** (diethyl hexyl pthalate) added as plasticizer to **pvc** containers.
Drug may be absorbed or adsorbed to PVC containers, so use **polyolefin,** polypropylene **or** glass containers.
Calcium and ceftriaxone is **incompatible** so never mix the together.

Drugs that need normal **saline** as diluents are phenytoin, ampicillin, infliximab, daptomyicn and

those needs **dextrose** solution as diluenst : bactrim, amphotericin.

Use 0.22 micron **filters to filter IV solutions** . **Furosemide a**nd phenytoin c**rystalise** if stored in cold temperature so store in **room temperature**. **Precipitation:** may occur due to: change in PH, concentration, salting out, complexation. This is specially a problem with drug **causing thrombophlebitis** (diazepam) and drugs causing extravasation (leakage from vein. eg. Sod.bicarbonate).

Mixing of semisynthetic pencillins such as cephalosporin and pencillin may form allergenic product when added to protein, material. **Ampicillin** when added to glucose or lactate **lose its potency**.

Blood product: drug may damage RBC. Hypertonic mannitol: **crenation of RBC**, dextran rouleaux formation and interfere with cross matching. Glucose cause clumping of RBC. Fat emulsions crack when drugs are added. More incompatibility is seen with amino acid, mannitol, sod. Bicarbonate soln.

Tablet dosage form:
Has high dosing accuracy, high stability,economical but long dissolution time than capsule, Liquids, and suspension. **Tablet coating: purpose**? Coating Material ? release delayed from which coating ? what happens if EC or SR coated tablet are Broken or chewed. ?
Sugar coating: is thick and increase in size of tablet by 50% and **film coating** is thin : both are for masking the bitter taste : not much problem if tablets are broken.

IR: immediate release tablet; release drug immediately after dissolution and produce peak action. Used for immediate effects.

CR: controlled release, **SR**: sustained release, PR: prolonged action, **ER**: extended release: are designed to **prolong duration** of action and to reduce dosing frequency. **Drugs selected** for controlled release should have : half life: ≥ 4 h., small dose, wide therapeutic index. Drug **release f**rom these controlled release depends on partly on **dissolution**. If taken with alcohol leads to dose dumping or drug release. If tablets are broken it leads **to over dose.**

Enteric coating (EC) : is to done to by pass the stomach and to release drug in small intestine, the material used to coat the tablet is **cellulose acetate phthalate**, which is insoluble in acidic media and so does not disintegrate in stomach. The **purpose** is to protect the drug from acid also to protect the stomach from acid .
Drug release is delayed in this because the drug has to reach the small intestine to release drugs.
Advise patient no to crush chewing or do not take with milk, antacid: these will destroy the coating.

Effervescent tab: are prepared by compressing granular effervescent salts with or **citric acids, tartaric** acid, sodium bicarbonate, magnesium bicarbonate :etc: that release carbon dioxide when in contact with water.

Tablets testing: Quality analysis: of tablets include: size, thickness, shape, **organoleptic** properties like **colour and odour**, weight and content uniformity, dissolution, hardness, friability.

Friability: is test used to measure ability of tablet to with stand abrasion during handling.
Mottling is colour variation of tab. **Capping** breaking and forming layers, **lamination**: layering,
Leaching: leaking of packing material to the drug; **picking**: attachment to dye or punching mechine.
Content uniformity test: to confirm that each tablet contains desired amount of drug in each of the tablet or to see **potency of drugs.**

Powders: more stable than liquids, faster onset of action than capsule or tablet, **disadvantage**: time consuming, inaccuracy in dosing , **mixing o**f powders: with spatulation movement with spatula, trituration, **geometric** dilution, **sifting:** by passing through sifters, **tumbling**: is mixing of powders in large container rotated by motor.
Classification of powders: bulk powders for internal use: like laxative,
bulk powders for external use: dusting powders, **insufflation**s, **snuffs** and **dentrifices.**
Dusting powders: are of two types: medical (for skin) and surgical: for body cavity and wounds.

Deliquescent powders: (absorb moisture and become solution): examples are: ammonium chloride, iron, ammonium citrate, phenobarbitone, sodium iodide, potassium citrate, zinc chloride.

Hygroscopic powders: Ammonium citrate, pepsin, phenobarbitone, sodium bromide, sodium iodide, potassium citrate, zinc chloride etc. Such substances are usually supplied in granular form to expose less surface area to the atmosphere. These powders should not be finely powdered. **Dessicants** are substances used to protect **hygroscopic substances**, examples are **silica gel, calcium oxide**, calcium chloride, calcium sulphate

Desiccators are sealable enclosures containing desiccants used for preserving moisture sensitive items such as cobalt chloride paper for another use. **A common** use for desiccators is to protect chemicals which are hygroscopic or which react with water from humidity.

Effloresсent Powder: liberate water on exposure to humid atmosphere or on trituration and become wet, **they** are composed of crystallized powders such as atropine, citric acid, codeine, alums and caffeine, ferrous sulphate. This Powder would become sticky if exposed to a low-humidity environment, as the water gets liberated from the Powder. Use anhydrous form or use an inert substance to solve this issue.

Insufflations: are the extremely small fine solid particles of the pharmaceutical powder used to inject into the body. The Powder can be easily injected into the patient's body body cavity like nose, throat, ears, and vagina with the help of the **insufflators.**
Snuff is **a type** of smokeless tobacco product made from finely ground or pulverized tobacco leaves. It is snorted or "sniffed"
Eutectic mixture: is mixture of two or more substances with lowest freezing point or melting point.

Capsules: are solid dosage forms, two types of csapsules: soft and hard gelatine capsule: hard gelatine capsule is made from gelatin**, sulphur** is added to prevent degredation during manufacturing**,** and **hypromellose**(hydroxypropyl methylcellulose **HPMC) or** from the plants. And coloured with **titanium dioxide.**

Storage: store capsule in tightly cosed containers, protect from humidity and temperature, capsule contains 12 % to 16% water, in low humidity capsule becomes **brittle** and in high humidity capsule becomes **flaccid**

Capsules sizes: is presented by numbers such as "000" (largest capsule), 00, 0, 1, 2, 3, 4, 5):
Capsule: numbered **000** is the largest and number 5 is the smallest capsule**.**
Filling the capsule: first remove cap and fill the body of capsule first.
Soft gelatin caps. glycerine or sorbitol is added to make capsule soft or plastic. **Shapes** of soft capsule: elliptical or spherical or oblong. **Preservative** used are methyl or propyl parabens, to prevent growth of fungi. It is mainly used for liquid preparations. Example: vitamim E capsule
A **desiccan**t is added to protect capsule from **moisture**.
A desiccant: is a hygroscopic substance (substance that absorb water) that is used to induce or sustain a **state of dryness** (desiccation) in its vicinity; it is the opposite of a humectant.

Sterilisation method:
physical methods: dry heat sterilisation in **hot air oven** at **160^0 C for** two hours. and 170^0 C for 1 hour, this method is used to sterilise glass ware, powders like sulphacetamide, fixed oil innection and surgical instruments. Dry heat will destroy cellulose material like paper, cloth, some chemical, rubber, plastic. So it is used for glass ware, anhydrous oils, metallic ware, oil containers must be large to allow oil to expand on heating. It provide state of dryness, and prevent dilution.
Thermal method: depends on temperature, time and moisture,

Moist heat sterilisation by using an **autoclave,** Killing microbes by protein **coagulation**. Temperature is **121 C for 20 -60 min**.(most commonly used method), used for surgical dressing, containers and closures.
Moist heat sterilisation;
More effective than dry heat, but no pyrogen is destroyed, since steam less denser than air it displaces air in the autoclave

Tyndallisation: technic is used to sterilse culture media, done by heating at 100 for 1 hour for three consecutive days, pasteurisation is used to sterilise milk.
using radiation: UV and ionising radiation such as gamma rays or X – rays.

Chemical with ethylene oxide gas: for plastics, which cannot withstand high temperatures , Owing to its nature as a gas, ethylene oxide penetrates well into the cell, reaching the DNA of the microorganism and killing it by **alkylation.**

Mechanical sterilisation: (known as **cold sterilisation).** by using different type of filters: such as cermic , seitz filters, sinetered glass metal and **memebrane** filte**rs:** made from cellulose, **nitrate, nylon, poly vinyl chloride, poly carbonate, poly sulofone and Teflon,**

The filter with **pore size of 0.22** micron is used to filter and remove bacteria. Virus will pass through it.
Opthalmic preparations are sterilised by **filtration method** through bacterilal fiter pore 0**.22 micron**.
D-value (decimal reduction time) is the number of minutes needed reduce viable bacteria by 90%.
Dry heat sterilisation temp

Sublimation: is process of changing solid directly into gas and vice versa. Deposition is the correct word for changing gas to solid
Freeze drying or **lyophilisation (gelsication) :** drying in vaccum by **sublimation** for drug destroyed by heat & moisture.(drying only, improves stability and solubility).
Clarification for obtaining liquid and filtration for matter, ultra filtration is separation of intermicellar liquids from solids by applying pressure through a semi permeable membrane**.**

HEPA filter: (***high efficiency particulate air filter***): is used to purify air in **laminar air flow hood.** They are designed to protect samples and parts from particulate contamination.
Air flows in a uniform direction with a constant speed within the enclosed bench with little or no cross over air stream, the air borne contamination is filtered through HEPA: (filter 99.99% @ 0.3micron) or ULPA (99.99% @ 0.12 µ filters).
There are two type **horizontal and vertical laminar flow hood**. **choice d**epends on direction of air flow, operator safety, clearance requirements, work space required.
How handle hygroscopic substance is with **wax** paper.
Class A (class III) balance: is weighing machine. **Specification** of class A balance are: 1. **sensitivity requirement** (SR= 6 mg), least weighable quantity is 120mg, allowed error in weighing is 5%.
Percentage error in weighing is found by the formula: **error = sensitivity requirement / wt of drug X 100**

Calculate error involved in weighing 100 mg on a class A balance with SR of 6 mg. (6 /100 then multiply with 100.) **Geome**tric dilution is method of mixing of large quantity of substance with 1:1 dilution..

Aliquot method is used weigh for small quantity on class A balance, below the least weighable qty. Suppose 5 mg is the dose, then weigh 120 mg (24 doses) and find out weight of diluents to be mixed with it , it is 24 X 120 – drug amount = 24 x120 -120 = 2880-120 = 2760 mg. Mix 2760 mg of diluents with 120 mg of drug geometrically and then weigh 120 mg from mixture which contains 5 mg of drug.

Drug storage criteria: where to or how to store drugs:
some should be kept inside refrigerator, some in the **freezer,** at room temparture, protected from light,
Problems with plastic containers are: 1. permeation of gas, moistures, vapours and liquids to the contents from out side, 2**. Leaching**: is the process of moving container ingredients to drug 3. **Sorption**: is the movement of drugs to the container, 4.chemical reactivity between container and drugs.

Physical incompatibility occurs between drug and container, **due to DEHP** (diethyl hexyl pthalate in container) added as plasticizer to **PVC** containers. Drug may be absorbed or adsorbed to PVC, containers so use **polyolefin, polypropylene** or glass containers.

Types of glasses used to make containers to store drugs.
Various types of glass used for pharmaceutical packaging as per USP are as follows: **Type I** -borosilicate glass, **Type II -** treated soda-lime glass, **Type III** – regular soda-lime glass, **Type IV** (NP) – general purpose soda-lime glass:

Type I: has a high melting point, so it can withstand high temperatures, has high hydrolytic resistance, and resistant to chemical substances, provides reduced leaching action, and can withstand sterilization. Type I borosilicate glass is used for **laboratory glass apparatus**, water for injection , for **parenteral** and non-parenteral use.

Type II glass : is treated soda-lime glass, is fairly resistant to attack by water for a period of time. Sulfur treatment neutralizes the alkaline oxides on the surface, thereby rendering the glass more chemically resistant. It has a high hydrolytic resistance.
Type II treated soda-lime glass is used for **alkali-sensitive products**, infusion fluids, blood and plasma, and large-volume containers.

Type III regular soda-lime glass containers high concentrations of alkaline oxides and imparts alkalinity to aqueous substances, flakes easily, and may crack due to sudden change of temperature. It has a moderate hydrolytic resistance. Type III regular soda-lime glass is used for all solid dosage forms **(**tablets, powders, and so on) and oily injections.
Type IV (NP) general purpose soda-lime glass is non-parenteral glass. Type NP general purpose soda-lime glass is only used for oral and topical purposes.
Metals used to make containers are: Tin, iron, aluminium, lead.

Modes of drug degradation: 1. By Hydrolysis; it is most common type of degradation because most drugs are esters, amides, lactams. H^+ and OH^- are the most common catalyst in the solution.
Esters are rapidly degraded in solution so esters are not usually formulated in liquid form.
2. by **oxidation**: drugs react with atmospheric dissolved oxygen or oxygen in the head space of container , so packaged in inert atmosphere (nitrogen) to exclude air. **Antioxidants** in the formulation react with free radicals by providing electron and easily available hydrogen atoms. 3. photolysis: is degradation by light

Drug degradation reactions: oxidation – reduction, hydrolysis and photolysis. Oxidation is losing electron and reduction is gaining of electrons. Oxidation mainly occurs with compound containing hydroxyl group attached to aromatic ring and oxidation increase in the presence of oxygen, temperature, light, change in pH, and metal ions. To prevent oxidation add chelating agents to remove metal ion, anti oxidants, protect from light.
Hydrolysis: is cleavage of bond by water: mainly occurs with esters, amides and lactams, to prevent hydrolysis, keep away from **bath room.** Close tightly and add dessicants to remove moisture.
Example: asprin will hydrolyse to salicylic acid and acetic acid and lose effect.

Radiations: electromagnetic radiation are : radio waves, microwave, infrared, visible light, ultra violet, X-ray, gamma ray**. Particle radiation**: alpha and beta radiation. **Ionising** radiation: gamma ray, X- ray. Ray with high penetration is **Gamma ray.**

Order of increasing speed of radiations are: alpha < beta 5 < gamma. Gamma has high speed.
Units of radiation: Curie (Ci= $3.7 * 10^{10}$ atom/ sec.): SI unit is Becquerel (Bq):

Epidemic in one place always, **endemi**c wide spread . **tolerance:** loss of activity upon continued administration**, tachyphylaxis**: immediate develop of tolerence.
No salt: (salt substitute Kcl instead of Nacl for heart failure patients on salt restriction)

Needle size: expressed by gauge number: is the outside diameter of the needle shaft such as 20 G or 21 G. Large is the number small is the needle size. 25G is smaller than 21G. 13 the largest and 27 is the smallest.
For SC injection: 24-25, IM: 19-22, for compounding parenteral is : 18-20.

Bevel is the slanting edge cut in needle.
Drug storage in body: in proteins, fats and in bone (eg. Tetracyclines gets deposited in bone and teeth).
Mutagenicity: mutation by drugs leading to cancer, it is tested is **by Ames test:** done salmonella bases on

Pregnancy classification of drugs: based on safety of drug during pregnancy in animals and humans:
Class A; drugs safe in both animal and human, can be used safely during pregnancy . **Class B:** safe in animal but no human study is done or not available, **Class C:** teratogenic in animals but no human data available . **Class D:** causes defects in both animal and humans**, so use** only if benefit out weighs risk.
Class x: drugs are contra indicated during pregnancy.

Latin words:
Ad: upto, adomve: apply**,** Ana: **a.a- each, ante: a.- before. hora** somni**: hs :** bed time, indies: In.d **: daily,** intercibos **: i.c :** during meals**,** mane **: man –** morning, . Oris**: os –** mouth
omni hora: **omn.hor:** every hour, omni mane**: o.m.** every morning, omni nocte: **o.n:** every night**.. primo** mane: prim.m: early morning.. per os**: p.o:** orally by mouth, post cibos : **p.c:** after meals, pro re nata: **p.r.n**. when necessary.

q: every , qh: every hour**, Quaque** quarta hora: **q.q,h :** every fourth hour**, q4h**: every 4 hour, quater in die: **q.i.d :** four times a day, qds: 4 times , **qod**: every other day, **q1d**: every day, qd: every day,
ter in die: **t.i.d** : three time day, bis in die: **b.i.d:** twice a day : **s.i.d**: semel in die: once a day, Od: omni die: once daily, . Gutta : **gtt**: drops,
Rx: recipe: treatment or you take, sine: **s** : without.. ss: semis, semi: one half, **si opus** sit: **s.o.s:** if necessary.. statim; **stat**: immediate; sumendus: **sum:** to be taken,

d.t.d: denture tales doses: give such doses.. **ft: fi**at: make.. **M.**: mice: mix... **sig.** signa: write direction on label.. . Ocular sinister: **left eye**. Ocular dexter: Right eye: **auris de**xter: a.d: to right ear**, auris** laevus: a.l : to left ear... Oculo utro: **O.U:** each eye, pulvis : pulv: powder,

Unguentum: ung: ointment, **B/s**: bite and swallow, PR: rectal, PV: vaginally, ATC: around the clock, **NPO:** nil per os: nothing by mouth or nothing orally, **NBM**: nil by mouth, **MR**: may repeat, **NR**: no refills, ASAP: as soon as possible. **Impalpable:** not perceptible to touch.

Abbrevations: Dx: diagnosis, **EMU**: early morning urine**, FBC**: full blood count, h. Hour, **Hx**; history, **IVP:** intravenous pylogram (x –ray of urinary tract) , **Ix:** investigations, **LMP**: last menstrual period, **NAD**: nothing abnormal discovered, **nocte:** every night, **noc:** in the night, **o/e**: on examination, **p/c:** presenting complaint, **qs**: quantity sufficient, **TCI** : to come in,

TTA: to take away, **TTO:** to take out**, ud**: as directed , **X3**: three times, **X4**: four times, **Wa**: while awake, **VO:** verbal order, **trit**: triturate, **non rep**: don't repeat**, tr, tinct**: tincture**, tal**: such,

o.d (oculus dexter) right eye**,** oculus sinister **'OS' left eye, ou:** (Oculus uterque) both eye.
auris dextra '**ad'** right ear, auris laeva: 'al'or (auris sinistra) '**as':** left ear **, a.u**: (auris utraque) each ear, **M.dict**: as directed, **O, Oct:** a pint, **Ex aq**: in water, **emp**: as directed, **d/c**: discharge, **cont**: continue, **ad lib:** at pleasure:

Drug category description letters: **P**: purchasable: **NP**: non purchasable: **C**: controlled drugs, **N**: narcotics: **PCH**: drug to be dispesed at primary health care: **H**: drug to be dispesed at hospital

The following are abbreviation not approved and correct abbreviations:

Abbreviation not allowed	meaning of abbreviation	correct method of writing the message
U	unit	unit
IU	international units	International units
Q.D	every day	every day

Q.O.D	every other day	every other day
. Xmg	0. X mg	0.Xmg
X.0	X mg	X mg: never write zero after number like 5. 0 mg
MS	morphine sulphate	morphine sulphate,
LA	long acting	long acting
HD	hypodermic	hypodermic
IS	intrasynovial	intrasynovial
P.L	intra pleural	intra pleural
S.C	subcutanous	Sub Q or subcutaneous
HS	at bed time	at bed time
qhs	at every bed time	at every bed time
SS	one half, semis	one half, semis

The word **as directed** is not allowed in prescriptions or labels and similary should specify the time and maxium repeatition in words,

Toxicology: management of poisoning:
Common poisoning agents are: opiods, organophosphates, salicylates, carbon monoxide, paracetamol, beta blockers, cocaine, stimulants drugs antidepressants, benzodiazepines, barbiturates.
Diagnosis: look for the history, empty tablets, time of ingestion

The Glasgow Coma Scale (GCS): was first published in 1974 at the University of Glasgow by neurosurgery professors Graham Teasdale and Bryan Jennett. The Glasgow Coma Scale (GCS) is used to objectively describe the extent of impaired consciousness in all types of acute medical and trauma patients. The scale assesses patients according to three aspects of responsiveness: eye-opening, motor, and verbal responses

Toxidromes: are symptoms and signs, lab report indicating a particular toxin: **symptoms of** some toxins are as follows **1.** coma, dilated pupil, tachycardia, increased muscle one, increased reflexes are seen in TCA and orphenadrine(muscle relaxants) poisoning. 2. **Coma**, hypotension, respiratory depression, ↓ muscle tone, by barbiturates, benzodiazepines with alcohol. **3.** Coma, slow respiration, pin point people by opiods, 4. Tinnitus, deafness, hyperventilation : salicylates. 5. agitation, tremor, dilated pupil, tachycardia: **amphetamine,**

Steps to follow in poisoning or first aid in poisoning:
Call ambulance and hospitalise the patient, in case of doubt about treatment or poison or for details of the poison consult primary clinical toxicological data base **Toxbase**: or call national poison centre.
Poisindex is a data base used by poison centres.

General care in poisoning are the following: support vital functions such as air way, breathing, circulation (ABC). Maintain Respiration (breathing): by opening air way by **chin lift** or jaw thrust or if no breathing give rescue breathing. **Blood pressure**: if SBP is less than 70, it may lead to irreversible brain damage and renal tubular necrosis. So Correct BP by raising foot of bed or giving normal saline or colloid fluid.
Heart: cardiac conduction or arrhythmia may develop with TCA, antipsychotics, or antihistamines. Becomes normal on correction of hypoxia, acidosis.

Body temperature: in case of hypothermia preserve body heat and in hyperthermia remove unwanted clothes and sponge body with tepid water (tape water).
Treat **Convulsions:** if it lasts more than 5 minutes with lorazepam or diazepam.
Methaemoglobinemia. is due high level of methemoglobin due to conversion **of ferrous iron to ferric** and decreased oxygen carrying capacity. Treat with **methylene blue** (methylthioninium chloride).

If the patient is mentally depressed give 50 ml of 50% dextrose in adult and 1ml / kg in children by IV push. Thiamine 100 mg IV push (glucose can precipitate Wernicke korsakoff syndrome in thiamine deficiency, Naloxone 0.4 to 2 mg if opiate ingestion is suspected

Removing toxins: Keep low level of poison by increasing elimination and decreasing absorption, combat toxic effect at site of action by giving antidote or blocking action of the toxins
Decontamination of toxin (removal of toxin): from GIT :
Removal is indicated only when toxin is dangerous and unabsorbed.
Methods: 1. **gastric emptying by vomiting** with apomorphine, copper sulphate, and ipcac syrup but **Emesis with ipecac** is contraindicated in Children less than 6 months, in poisoning with strong acid, alkali, or hydrocarbons, patient with depression, epilepsy, coma,

Gastric lavage: removal from GIT.
2. Administration of charcoal **within 1 hr** but it does not adsorb ethanol, iron, lithium,, cyanide, lead, mercury, methanol, potassium , strong acid and strong alkali.
In case of poisoning with controlled release tablet can be given in **less than six hour**.

3. **Whole bowel irrigation** by enteral administration of large amount of polyethylene glycol electrolyte soln to expel poison through rectum before it is absorbed for over dose of iron, sustained release tablets with **Cathartics u**sed for bowel irrigation are ; magnesium citrate and mag. Sulphate.
Skin decontamination by washing, never neutralise acid with alkali or sodium bicarbonate.

Elimination of toxin by diuresis:
Elimination through urine by ion trapping: by increasing ionisation and water solubility by manipulating the pH as per Henderson theory :
Through dialysis:
Drugs with small Vd, low protein binding, high water solubility, low molecular weight are removed by **Extra corporeal** drug removal by **dialysis or peritoneal dialysis**.

Hemoperfusion : in hemoperfusion blood passes through a column of adsorbent and adsorbs the toxin it does not remove fluid and electrolytes like dialysis.
Plasmaphersis is replacement of plasma to lower antibody levels to treat autoimmune disease)..

List of Antidotes and toxins

poison / drug	antidote
Salicyates	Sodium bicarbonate
paracetamol	acetyl cystein, methionine
cyanide	hydroxy cobalamine, sod. Thiosulpahte, sodium nitrate
methotrexate	leucovorin
Ca antagonist	insulin high dose
methemoglobinemia	methylene blue
opiods	naloxone
sulphonyl urea induced hypoglycemia	octreotide acetate
lead, mercury, copper	pencillamine
lead	EDTA(ethylene diamine tetraacetic acid)
lead, mercury, arsenic	dimercaprol(british antilewisite (BAL)
iron	deferoxamine
INH	pyridoxine
benzodiazepine	flumazenil

Beta blocker, Ca antagonist	glucagone or high dose insulin with glucose
black widow spider venom	antivenin for latrodectus
carbon monoxide	oxygen
ethanol	supportive care and correct hypoglycemia
anticholinergic	physostigmine

Cyanide poisoning: cyanide rapidly complexes **with iron** in cytochrome oxidase and block oxidative metabolism and cell death. Iron in methemoglobin has high affinity for cyanide than iron in cytochrome oxidase.. **Cyanide poising is treated** with following Steps: 1: inhale amyl nitrite (keep crushed pearls in nostrils) 2. Intravenous infusion of **sodium nitrate** 10ml IV push (Nitrite convert iron in haemoglobin to ferric to form known as methemoglobin which binds with cyanide, 3. thiocyanate 50 ml of 25% Iv push . Hydroxycobalamin is also approved now for cyanide treatment.

Digoxin poisoning: clinical presentation: confusion, anorexia, nausea, and vomiting in mild case and dysrhythmias in severe case. **Check level of** digoxin , electrolytes especially potassium, and monitor ECG. **Treatmen**t: activated charcoal, treat hyper or hypo kalemia and inotropic support. **Admin**: digoxin specific Fab antibodies: (digibind), **dose in mg** = (serum digoxin conc: ng/ml X weight in kg/100 X mg /vial).

Treatment of hyper Magnesium: available in oral, rectal, parenteral preparation.
Clinical presentation: mild case: depression of deep tendon reflex , lethargy, and weakness. In severe case: respiratory paralysis, heart block, prolonged PR, QRS, and QT interval .

Lab data : mild case > 4 meq / L and in severe case >10 meq/L.
Treatment: 10% calcium chloride 10 to 20 ml to temporarily antagonise cardiac effects.
In severe case; dialysis.

Potassium: dosage forms: oral and parenteral: potassium is primarily an intra cellular cation. Changes in acid base produce shift serum K - level. For 0.1unit increase in pH, K decrease in 0.1 to 0.7 meq /L ; **clinical presentation**: cardiac irritability and peripheral weakness . cardiac **dysrhythmias** including bradycardia and asystole. Lab: ECG data include peaked T wave and prolonged QRS complex.

Treatment of hyper kalemia: administer 10 to 20ml of calcium chloride 10% to antagonise cardiac effects of hyperkalemia . 2. sodium bicarbonate 1 to 2 meq / kg, IV to increase serum pH and causes intracellular shift of K 3. IV push of 50 ml of 50% Glucose and 5 to 10 u of regular insulin drives potassium to cells 4. cation exchange resin exchange potassium with another cation such as sodium. **Sodium polysterene sulfonate** (Kayexalate) is given 15g /60ml with 23.% sorbitol or
remove potassium by hemodialysis.

Iron (Fe): toxicity is based on percentage of elemental iron: sulphate 20%, fumarate 33%, gluconate 12%. Iron absorbed from duodenum and jejunum.
Clinical presentation: **Phase 1**: nausea, vomiting, diarheoa, GI bleeding, hypotension**. Phase 2**. Clinical improvement seen in 6 to 24 h. Phase 3. Metabolic acidosis, renal, hepatic failure, sepsis, pulmonary edema and death. **Lab data**; serum iron level, total iron binding capacity. ABGs (arterial blood gas) , haemoglobin, LFTs and hematocrit. **Treatment:** gastric lavage, bowel irrigation. Chelate iron wih desferoxamine.
Isoniazid (INH):
Clinical presentation; nausea, vomiting, slurred speech, ataxia, generalised tonic clonic seizure and coma.
Lab data: severe lactic acidosis, hypoglycaemia and leukocytosis.
Treatment; decontamination with charcoal, avoid emesis or vomiting, may cause seizure. **Pyridoxine** reverses INH induced seizures, pyridoxine given gram doses equivalent to the dose of INH. And Sod. Bicarbonate to correct acidosis.
Lithium:

Clinical presentation in mild case: polyuria, blurred vision, weakness, slurred speech, ataxia, tremor.
In severe case: delirium, coma, seizure, and hyper thermia.
Lab data : therapeutic range: 0.6 to 1.2 meq/L, mild; 1.5 to 2.5 meq /L, moderate: 2.5 to 3 and severe case: above 3 meq / L.
Treatment: supportive care, electrolyte replacement, decontamination. Ipecac is not used now, charcoal ineffective. Bowel irrigation or dialysis or use polysterene sulfonate .

Alcohols: ethylene glycol and methanol is converted to toxic metabolites by alcohol dehydrogenase. Ethylene glycol is converted to oxalic acid, it is toxic, treated with fomepizole (inhibit the conversion of methanol and ethylene glycol to toxic metabolite) or **ethyl alcohol** (engage the enzyme alcohol dehydrogenase and prevent conversion to toxic metabolites).
Methanol is converted to formic acid, it is also treated with ethyl acohol, fomepizole and folic acid is given to increase metabolism of formic acid,

Carbon monoxide poisoning:
it binds to hemoglobin and forms carboxy hemoglobin and **decrease** oxygen carrying capacity, leading to cerebral ischemia. Treatment is natural fresh air breathing and administer oxygen
The information on toxic substance can be found in POISINDEX (**micromedex**)

Model questions with answers:

1. Small Particle size will increase absorption why ? (↑ surface area and dissolution rate)
2. Prepn with fast dissolution is .. **liquids,** suspension, capsule, tablets,
3. Polymorphs have same: Bioavailability , solubility, density, **metabolic rates** and same effect
4. Not true of Tablet : better stability, ease of administration, accurate dosing, **fast dissolution than liq.**
5. As per hassel balch eqn an acid with pKa of 4.5 will remain 50% at pH ? (**pH 4.5**)
6. Which is least water soluble: haloperidol **decanoate,** halo: lacate, Halo: hydrochloride, none of them
7. Not True of alkaloids: contains Nitrogen, basic, acidic, having Pka less than 7, alcohol soluble
8. Not True of lyophylisation: involves sublimation, improves stability, for heat sensitive, sterilisation
9. Black box warning: warning about side effect in **product literature,** storage condition, none of them
10. Not a use of starch: diluents, binding, disintegrating agent, **preservative, lubricant**
11. Process of making of cream is: levigation, lyophylisation, trituration, milling
12. Which will pass through 0.2micron: bacteria, virus, fungus, protozoa, pyrogen
13. Solution characterised by: visibility, invisibility, molecular dispersion, more stable than tablets
14. True regarding suspension are: should posses thixotropy, contains more drug than soln, follows zero order degradation, particle size is 0.5 -5micron, visible, **all of them**
15. Chelating agents used in eye preparation is: **edetate**, tetracylcine, calcium chloride
16. Solubility of weak acid can be increased by .. decreasing PH, increasing PH. By adding surfactants
17. Tick weak electrolyte: sodium chloride, lactose, **ephedrine,** sucrose, glucose, urea.
18. Eqn to check stability at room temperature by study at high temp is ? Arrhenius, fick's, Henderson
19. not action of lubricant: improving flow, Wetting , preventing adhesion to punches, ejection from dye
20. Which is not diluent:, dicalciumphosphate, mag.sterate, lactose, starch
21. Which is weak electrolyte: sod.chloride, urea, glucose, ***ephedrine,*** sucrose
22. mechanism is responsible for most of drug degradation**: hydrolysis**, oxidation, reduction, photolysis
23. vanishing cream is : water soluble base, **emulsion base**, oleaginous base, absorption base, vanishing b.
24. As per buffer eqn aspirin with Pka of 3.49 will have high solubility at PH of : 1, 2 ,3 , 4 **, 6**
25. Which is not true regarding zero order degradation: degradation decreases as **temperature increases**, most drug degrade by first order, degradation result in loss of activity, and toxicity.
26. Advise to patient who come for ipecac syrup for poisoning: **not used now days**, call poison centre.

27. A father ask for ipcac syrup as a home remedy for poisoning what we tell him. 1. Ipecac is not used now a days, 2. Give him toll free number, 3. ask him to give 15 ml **4. (1 and 2)**
28. Role of pharmacy and therapeutic committee is: storage drugs, monitor adverse effect, **make formulary**
29. an unconscious poisoned patient was given 50ml of 50% glucose, 100mg thiamine , and 1mg nalaoxone and then regains consciousness , this shows that the poison is: cocaine, amphetamine, diazepam, **heroin,**
30. contraindication of ipecac is: unconscious patient, pt with tonic clonic seizure, patient ingested caustic substance., **All of the above**
31. what happens if SR tablet is broken? (It will lead to over dose ?)
32. From which formulation drug release is delayed? (from Enteric coated tablet)
33. Compounding Guide line chapter of USP for sterile is **(797)** ? and Non sterile? (**795)**
34. Auothority responsible for: new drug registration in Saudi ? (**SFDA), r**esponsible for Narcotics: (MOH,
35. Radiation with high speed and penetration power is ? (gamma rays)?
36. Most commom form of sterilisation methd is ? (Moist heat sterilisation)
37. How carbon monoxide cause toxicity? (Bind to RBC and block oxygen carrying)
38. After whch phase of clinical trials you get approval for drug marketing ? (after phase 3)
39. Which preservative cause gasping syndrome in infants? (**benzyl alcohol)**
40. Which will have faster dissolution: amorphous or crystalline. (amorphous)

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Chapter 3 :
PHARMACO- KINETICS