PHARMACY INDIA

B.PHARMA
IVTH SEMESTER

PHYSICAL PHARMACEUTICS-II

(BP-403T)
MODEL PAPER

PHYSICAL PHARMACEUTICS-II (BP-403T) MODEL PAPER

SECTION A

VERY SHORT ANSWERS TYPE QUESTIONS (10 × 2 = 20)

1. **Classify dispersed systems with examples.**

Answer

Molecular dispersion	Colloidal dispersion	Coarse dispersion
Less than 1nm particle size	From 1nm to 1 μm size	10-1000 μm size
E.g., Oxygen molecule, ordinary ions, glucose	E.g., Colloidal silver solution, natural and synthetic polymers, Cheese Butter, Cream etc.	E.g., Grains of sand, pharmaceutical emulsion, suspension of red blood cells etc.

2. **Define peptization with examples.**

Answer

- It is the process of converting a precipitate into colloidal dispersion by shaking it with dispersion medium in the presence of small amount of electrolyte/ peptizing agent (glycerin, sugar, lactose etc.).
- E.g.,

3. **State the law of flow.**

Answer

- Newton's law of flow states that the shear stress between adjacent fluid layers is proportional to the velocity gradient between two layers. Liquids that obey Newton's law of flow are called as Newtonian fluids.
- E.g., Water, glycerin, chloroform etc.

4. **State the Heckel equation and explain each term involved.**

Answer

- It is the most useful method for estimating the volume reduction under compression pressure in pharmacy.
- It follows the 1st order kinetics, where the pores in the powder are the reactant and the densification of the powder bed as the product.

$$\ln\frac{1}{(1-D)} = kP + A$$

Where,

D = relative density of a powder
P = pressure
k = Constant (Compressed material)
A = Constant

Porosity -

- It is defined as the void volume to the bulk volume.

$$\varepsilon = \frac{Vp - V}{Vp}$$

5. **Explain the nature of flocculated and deflocculated suspensions.**

Answer

Deflocculated Suspension	Flocculated Suspension
Pleasant appearance, because of uniform dispersion of particles.	Slightly sediment and clear supernatant layer.
Supernatant remains cloudy	Supernatant is clear
The sediment is closely packed and form a hard cake.	Sediment is loosely packed network and hard cake cannot form.
Can not be redispersed	Easy to redisperse

6. **Mention the advantages of microemulsion over emulsions.**

Answer

Microemulsion	Emulsion
Transparent	Cloudy
Isotropic	Anisotropic
Ultra low interfacial tension	High interfacial tension
Droplet size is 20-200 nm	Droplet size is > 500 nm
Thermodynamically stable	Thermodynamically unstable

7. **Define ferets diameter.**

Answer

- It is defined as the distance between two tangents on opposite sides of the particle parallel to some fixed direction.

8. **Name the parameter involved in the evaluation of flow properties of pharmaceutical blend.**

Answer

1. Angle of repose
2. Carr's index
3. Hausner ratio

9. **What do you mean by pseudo-zero order kinetics?**

Answer

- A compound decomposing in solution exhibits a 1st order reaction but if more of it is present as insoluble excess, then an equilibrium is maintained between the compound in solution and that in the solid form.
- The concentration of the compound in solution, thus remains essentially constant till any of the insoluble drug material remains. Such a reaction is apparent zero order or pseudo-zero order kinetics.
- E.g.,

Aspirin ⇌ Aspirin
(Solid) (Solution)

10. **Mention the role of dielectric constant on the chemical degradation of**

pharmaceutical products.

Answer

- The dielectric constant of the solvent has significant effect on the rate of reaction.
- For a reaction involving a charged reactant molecule and another ionic species (such as H^+ or OH^-), the effect of the dielectric constant on the reaction rate is given by the equation:

$$\ln k = \ln k_{\varepsilon=\infty} - \frac{NZ_AZ_Be2}{RTr^*}\frac{1}{\varepsilon}$$

where,

k = observed reaction rate in a solvent of dielectric constant
$k_{\varepsilon=\infty}$ = the reaction rate constant in a solvent of infinite dielectric constant
N = Avogadro's number
ZA and ZB = the charges on the two ionic species
e = the unit of electric charge
r* = the distance between the ionic species in the activated complex
ε = the dielectric constant of the solution

SECTION B
LONG ANSWER TYPE QUESTIONS (2×10 = 20)

1. **Explain the effect of electrolytes, coacervation, and peptization on pharmaceutical colloidal dispersion.**

Answer

Effect of electrolytes

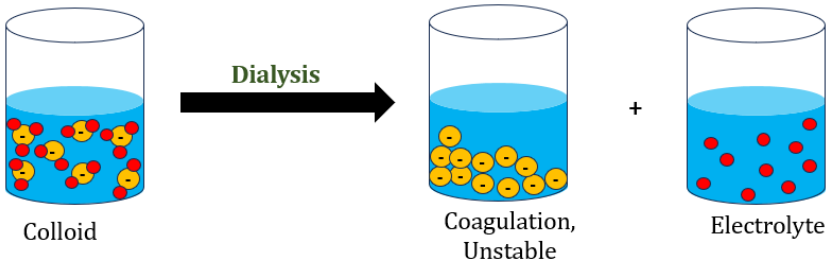
- When the addition or removal of electrolytes in colloidal dispersion may affect the stability of colloids.

i. Removal of electrolytes

- When electrolytes are present in traces, interparticle repulsion decreases. The electrical double-layer potential decreases below a critical value.
- The repulsion between the approaching particles are reduced to such extent that those colliding with certain velocity can join together.

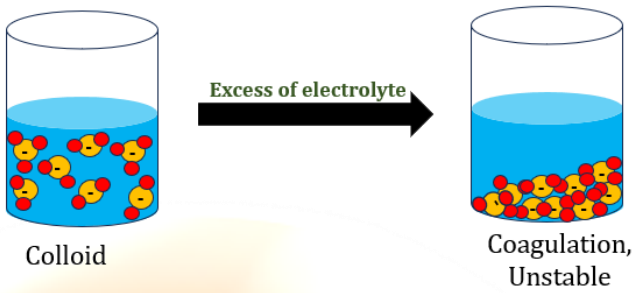
↓

Coagulation occurs



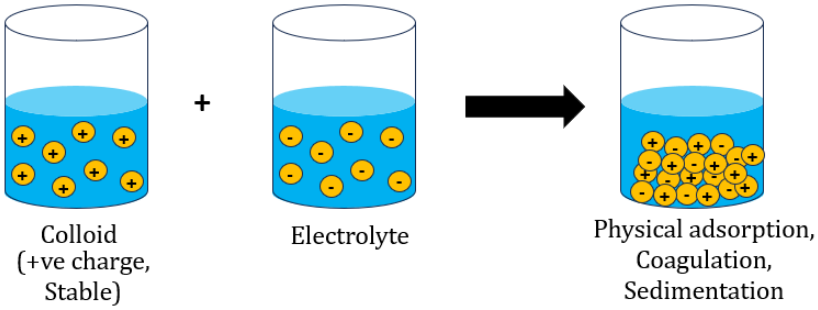
ii. Addition of excess electrolytes

- When excess of electrolytes are added, the particles of dispersion coagulate due to the accumulation of oppositely charged particles.



iii. Electrolytes of opposite charge

- Addition of electrolytes of opposite charge induces the dispersed particles to coagulate.

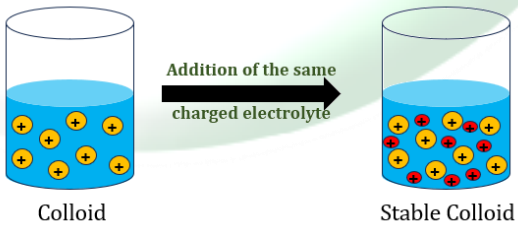


- **Schulze Hardy Rule –** The precipitating power of an ion on a dispersed phase of opposite charge increases with the increase in the valency or charge on the ion.
- Higher the valency of effective ion, greater the precipitating power.

Cation – $Al^{3+} > Ba^{2+} > Na^{+}$
Anion – $[Fe(CN)_6]^{3-} > SO_4^{2-} > Cl^{-}$

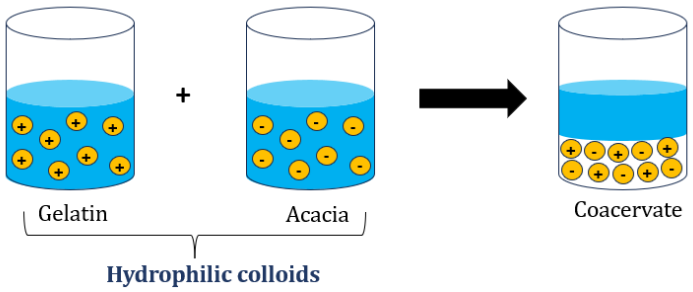
iv. Addition of same charged electrolytes

- If we add same charged particles then particles and electrolytes repel each other & increases the stability of colloids.



Coacervation

- When two opposite charged hydrophilic colloids are mixed, then there will be separation of the colloid rich layer. This layer is known as coacervate and the process is called coacervation.
- Example,



Peptization

- It is the process of converting a precipitate into colloidal dispersion by shaking it with dispersion medium in the presence of small amount of electrolyte/ peptizing agent (glycerin, sugar, lactose etc.).
- E.g.,

2. Describe in brief the various methods used for the determination of particle size.

Answer

- The following methods are generally used for the determination of particle size and particle size distribution:
  1. Microscopic technique
  2. Sieving technique
  3. Sedimentation technique

1. Microscopic Technique

- Optical microscopy is generally used for particle size measurement in the range of 0.2 µm to about 100 µm. At least 300 to 500 particles must be counted in order to obtain a good size distribution analysis of data.
- **Method:**
  - ✓ A dilute suspension of the powder particles whose sizes are to be determined is prepared in a liquid vehicle in which it is insoluble.
  - ✓ If it is slightly soluble, a saturated solution of the powder can be used for the preparation of the suspension.
  - ✓ A drop of the suspension is mounted on a slide or ruled cell and observed under the microscope.
  - ✓ The eyepiece of the microscope is fitted with a micrometer by which an estimate of the particle size can be obtained.
  - ✓ All the particles observed in a field are counted through the eye-piece.
  - ✓ The data may be scientifically represented as size-frequency distribution curve.
  - ✓ From the data, the average particle size as well as the size distribution is determined.
  - ✓ For ease in counting the particles, the field viewed through the

microscope can be projected on a screen or photographed for latter measurement.

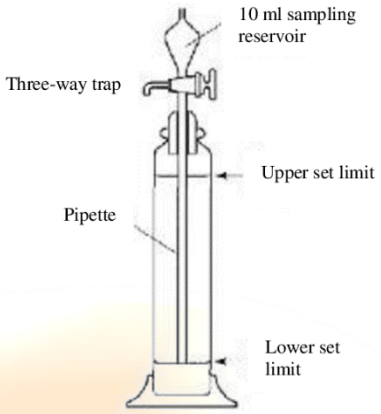
- **Disadvantages:**
  a. The measured diameter of the particles represents two dimensions only. i.e., length and breadth and an estimate of the depth is not obtained.
  b. The method tends to be slow and tedious since at least 300 to 500 particles should be counted to get a reliable data.
- **Advantages:**
  a. Agglomerates as well as particles of more than one component can be detected by this method.

2. Sieving Technique

- In this technique the powder whose particle size is to be determined is placed on a nest of standard sieves stacked over one another with the sieve of largest aperture on top followed by sieves of gradually decreasing pore sizes.
- The powder is shaken for a definite period of time using a mechanical shaker and the material that passes through a particular sieve and is retained on the next finer sieve is collected and weighed.
- The data obtained is analysed and the particle size and size distribution is calculated.
- **Advantage:**
  i. Sieving technique is generally useful for coarse particles since the technique is limited by the smallest size of sieve that can be produced and hence measurement of sizes smaller than 50 µm are difficult.
- **Disadvantages:**
  i. Particles may aggregate during sieving due to generation of electrostatic charge.
  ii. Moisture can also lead to aggregation of powders and the actual particle size may not be obtained.
  iii. Attrition of particles during sieving may lead to size reduction.
  iv. Sieve loading and duration of mechanical shaking can influence the results.

3. Sedimentation Technique

- Andreason pipette is generally used for the determination of particle size distribution by the sedimentation technique.
- The apparatus consists of a 550 ml stoppered cylindrical vessel of about 5.5 cm internal diameter with a vertical scale graduated from 0 to 20 cm on it.
- The stopper has an integral 10 ml bulb pipette fitted with a two-way stopcock and a side tube for discharging the sample.
- The stem of the pipette is made up of narrow bore tubing in order to minimize the volume retained in the stem after each sampling.
- When the pipette is fitted into its place in the cylinder, its lower tip is 20 cm below the surface of the suspension.



- **Method:**
  - ✓ For analysis of the particle size distribution, a 1 or 2% suspension of the powder is prepared in a medium containing a suitable deflocculating agent to break any powder aggregates.
  - ✓ The suspension is introduced into the vessel upto the 550 ml mark.
  - ✓ The vessel is stoppered and shaken to distribute the particles uniformly within the medium.
  - ✓ The pipette is then secured in its place and the whole assembly is kept undisturbed in a constant temperature bath.
  - ✓ At various time intervals, 10 ml samples of the suspension are withdrawn through the two-way stopcock into previously weighed china dishes.
  - ✓ The samples are evaporated and weighed and necessary correction is made for the deflocculating agent added.
  - ✓ The particle diameter corresponding to the various time periods is calculated by using the Stoke's equation:

$$V = \frac{h}{t} = \frac{dst2\ (Ps - P0)g}{18\eta 0}$$

Where,

v is the rate of settling.
H is the distance of fall in time t
d_{st} is the mean diameter of the particles based on the velocity of sedimentation,
P_S, is the density of the particle,
P_0, is the density of the medium,
g is the acceleration due to gravity and
η_0, is the viscosity of the medium

3. Explain the role of various physical and chemical factors on the chemical degradation of pharmaceutical products.

Answer

- The incapacity or incapability of a particular formulation in a specific container to remain within a particular chemical, microbiological, therapeutical, physical & toxicological specification.

- Pharmaceutical degradation is of following type. It can be divided into three major types:
  - Physical degradation
  - Chemical degradation
  - Microbiological degradation

Physical Degradation

- It is the degradation which results into the change of physical nature of drug.
- The formulation is totally changed by way of appearance, organoleptic properties, hardness, brittleness, particle size.
- Factors effecting physical degradation are as under:
  - ✓ Loss of volatile components
  - ✓ Loss of H_2O
  - ✓ Absorption of H_2O
  - ✓ Crystal growth
  - ✓ Polymorphic changes
  - ✓ Colour changes

1. **Loss of Volatile components**
   - ➢ Many drugs and excipients may be lost from pharmaceutical products at ambient temperature through vaporization.
   - ➢ These volatile components such as alcohol, ether, Iodine, volatile oils, camphor menthol etc. escape from the formulations rendering them degraded.
   - ➢ **Example:**
     i. Aromatic waters, Elixirs
     ii. Some types of tablets which contain aromatic water (Nitroglycerine tablets)
2. **Loss of H_2O**
   - ➢ Evaporation of water from liquid preparations will cause the concentration of the drug to change with the possibility of crystallization occurring if the solubility of the drug in the solvent is exceeded.
   - ➢ Water loss from oil-in-water creams may result in a decrease in volume and a surface rubbery feel. Further evaporation of the water will cause the emulsion to crack.
   - ➢ **Examples:**
     i. **Saturated solution:** by loss of water, they become supersaturated and precipitate as crystals are formed.
     ii. **Emulsions:** Loss of water lead to separation of the two phases and change to other type.
     iii. **Creams:** especially oil/water, they become dry by loss of water.
3. **Absorption of H_2O**
   - ➢ Hygroscopic drugs absorb the water from external atmosphere causing the physical degradation.
   - ➢ For example, some drugs are delisquent (calcium chloride and potassium citrate), whereas others are hygroscopic (glycerol and dry

plant extracts).

- Effervescent powders and tablets will deteriorate if stored in a moist atmosphere.
- **Examples:**
  i. Powders: liquification and degradation may occur as a result of absorption of water.
  ii. Suppositories in which base is made from hydrophilic substances as Glycerin, Gelatin, and polyethylene glycol. The consistency of these forms becomes a jelly-like appearance.

4. Crystal growth

- Drugs when loose water, become saturated and crystal growth occurs. Molecules in the crystal are not static, they can grow in size and move when there is a medium to travel.
- Crystallization is enhanced in porous tablets.
- **Examples:** Carbamazepine tablets containing stearic acid form column-shaped crystals on tablet surface during storage at high temperature.

5. Polymorphic changes

- Polymorphs are different crystal forms of the same compound.
- Polymorphs differs from one another in the crystal energies, the more energetic ones converting to the least energetic or most stable one.
- Different polymorphs of the same drug may exhibit different solubility and melting points.
- In polymorphic changes crystal forms are changed. A stable crystal form loosens. This may cause alteration in solubility and possibly crystalline growth in aqueous suspensions.
- **Examples:** Chloramphenicol Palmitate, Cocoa Butter.

Chemical Degradation

- It is the separation of chemical compound into elements or simpler compounds. Change in the chemical nature of the drug is called as chemical degradation.
- Types of chemical degradation are
  - Hydrolysis
  - Oxidation
  - Decarboxylation
  - Isomerization
  - Polymerization

1. Hydrolysis

- The principles that generally govern hydrolysis reactions may be listed as follows:
  - Drugs with ester and amide groups react with one molecule of wate and undergo hydrolysis. Ester groups break faster than amide groups.
  - Drugs are either weak acids or bases. Therefore, these may be available as ionic forms or neutral molecules. Hydrolysis reaction between ionic species proceeds faster than with

neutral molecules (to a large extent it is solubility related phenomenon).

- Hydrolysis reactions are catalyzed by H^+ and (OH^-) ions. Hydroxyl ions catalyze hydrolysis by about 100 to 1000 times more actively than hydrogen ions.
- **Examples:** Drugs decomposed by hydrolytic pathway

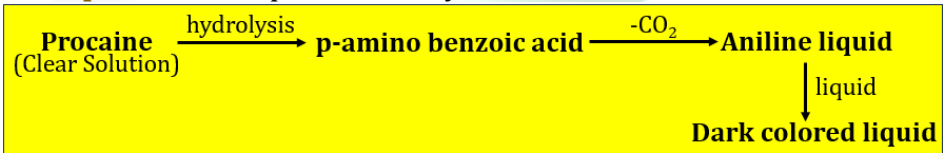
Ester	Amides
Aspirin	Chloramphenicol
Procaine	Ampicillin
Atropine	Cephalosporins

2. Oxidation

- Oxidation involves the removal of electrons from a molecule.
- The reaction between the compounds and molecular oxygen is called autooxidation.
- In fats and oils, autooxidation of unsaturated fatty acids proceeds in the presence of atmospheric oxygen, light and traces of heavy metals or organic peroxides.
- For example, the rate of oxidation of ascorbic acid is increased by a factor 105, when copper ions are present in the concentration of 0.002M.
- The general principles that govern an oxidation reaction-
  - Presence of atmospheric O_2.
  - Presence of light
  - Presence of trace metals
  - Organic peroxides
  - Hydroxyl ions
- **Examples:** Drugs that decomposed by oxidation pathway-
  - Arachis oil
  - Vitamin A
  - Riboflavin

3. Decarboxylation

- This type of reaction is normally observed when a parenteral solution contains sodium carbonate.
- During autoclaving the carboxylic acid groups will be knocked off.
- **Examples:** Sodium p-aminosalicylic acid, Procaine HCl



4. Isomerization

- It is the process by which one molecule is transformed into another molecule which has exactly the same atoms, but the atoms are rearranged e.g. A-B-C → B-A-C
- Conversion of an active drug into a less active or inactive isomer having same structural formula but different stereochemical configuration.

- Types of Isomerization:
  - Optical Isomerization
  - Geometrical Isomerization
- **Optical isomerization:**
  - A change in the optical activity of a drug may result as a change in its biological activity.
  - **Example:**

(-)Adrenaline (greater biological activity)	⟶	**(±)Adrenaline** (+ and – is 50:50 less potent)

  - It is further divided into:
    1. Racemization
    2. Epimerization
- **Racemization**
  - It involves the change of optically active form of a drug into its enantiomorph.
  - **Example:** By the action of heat (-) hyoscyamine is readily converted to atropine which is the racemic mixture of (+) & (-) hyoscyamine.
- **Epimerization**
  - It occurs with the compound having more than one asymetric carbon atom in the molecule.
  - **Examples:** Under prolonged storage solution containing ergometrine is decomposed by hydrolysis and isomerized to ergometrinine.

5. Polymerization

- These types of reactions are not often the initial cause of drug degradation.
- Primary degradation products may react further and polymerize.
- **Examples:**

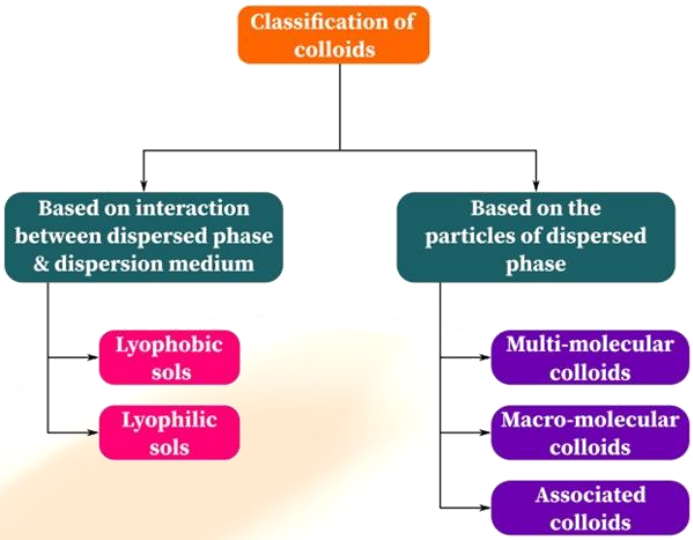
Adrenaline (acid solution)	oxidation ⟶	**Adrenochrome**	Polymerize oxidation ⟶	**Black brown pigment**
Dextrose injection	autoclaving Acidic pH ⟶	**5-hydroxymethyl**	Polymerize ⟶	**Straw coloured solution**

SECTION C

SHORT ANSWER TYPE QUESTIONS (7×5=35)

1. **Classify colloids and compare the general properties of colloidal dispersion.**

Answer



General properties colloidal dispersions

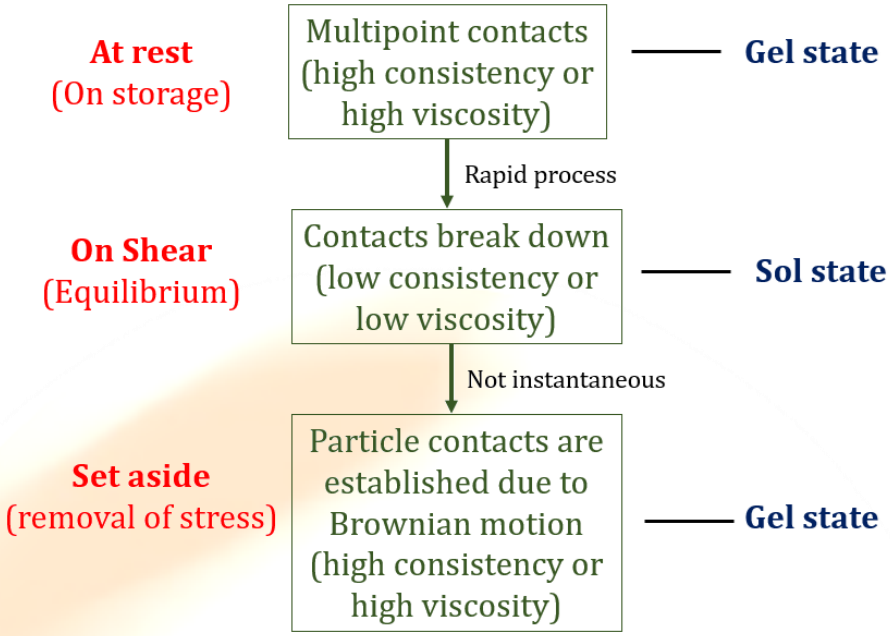
Lyophilic Colloids	Lyophobic Colloids	Association Colloids
Mostly organic molecules	Largely inorganic particles	Aggregation of surface active agents
Lyo means solvent; phillic means loving i.e. Solvent loving colloids	Lyo means solvent; phobic = hating i.e. Solvent hating colloids	Known as amphiphilic colloids
Interaction are stronger in both phase, solvent sheath around particle	Little interaction	Aggregates are solvated
Less charged but solvated	Highly charged	Charged micelles but solvated
Prepared readily from sol	Special methods are required	Readily from when concentration is equal to CMC
Thermodynamically stable. So easy to operate	Thermodynamically unstable. So difficult to prepare	Thermodynamically stable
Viscosity of dispersion medium increase with addition of dispersed phase	Viscosity of medium doesn't increase with addition of dispersed phase	Viscosity increases with increase in concentration of amphiphilics
Stable in presence of electrolyte	Unstable in presence of electrolyte	CMC is reduced by addition of electrolyte
Reversible in nature	Irreversible	Reversible
Rubber, Polystyrene	Gold, Silver, Sulphur in water	Surfactant

2. Describe the effects of thixotropy in pharmaceutical formulations with suitable examples.

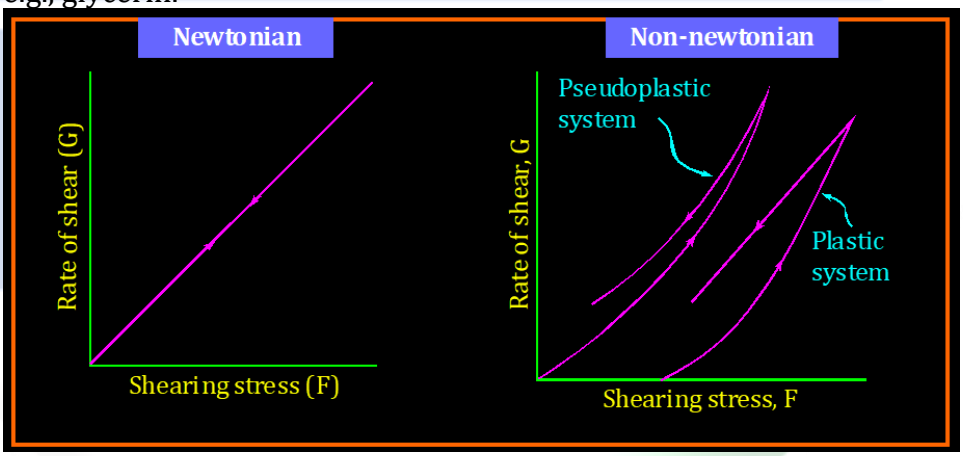
Answer

- Thixotropy is defined as an isothermal and comparatively slow recovery, on

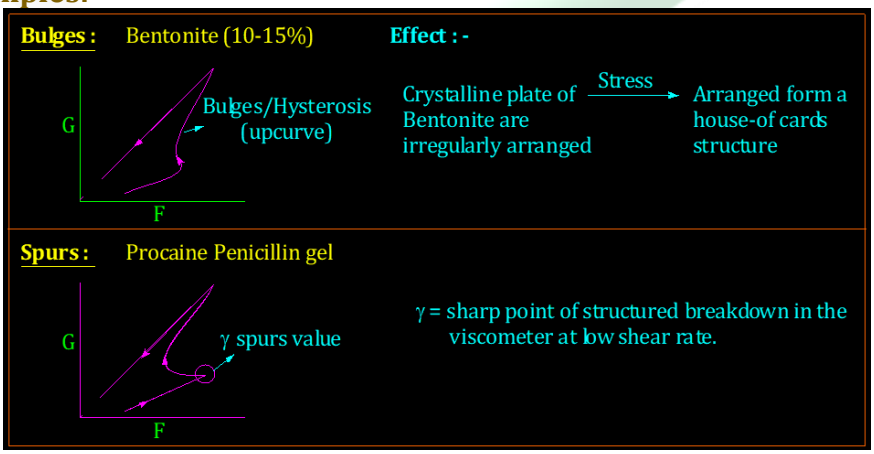
standing of material of a consistency lost through shearing.



- In non-newtonian fluid, the down curve is frequently displaced to the left of the up-curve. The material has low consistency at any one rate of shear on the down curve compared to that it had shown on the up-curve.
- In a Newtonian system, the down curve is superimposed on the up curve e.g., glycerin.



- **Examples:**



3. Describe the theories of emulsification.

Answer

Surfactants

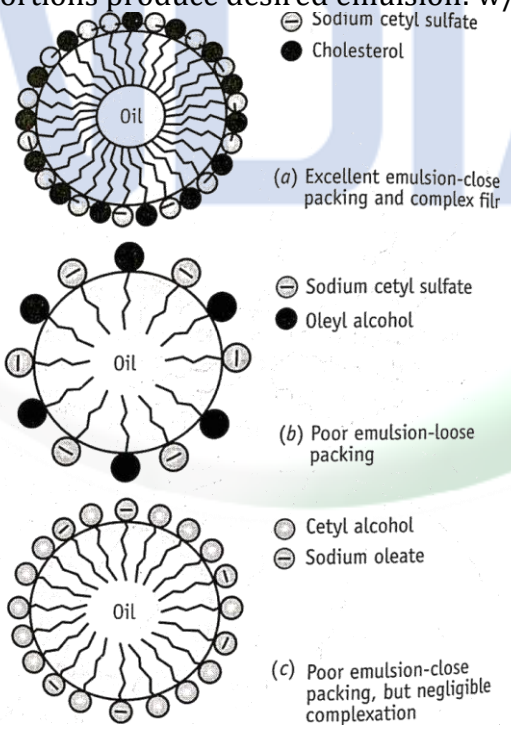
- Surfactants are used as emulsifying agent/emulgents.
- They decrease interfacial tension.
- They prevent coalescence of droplets and stabilize the system by acting as barrier to droplets.
- Classified by presence of water and fat solubilizing group in same molecule.

Theories of emulsification

1. Monomolecular adsorption
2. Multimolecular adsorption
3. Solid particle adsorption

1. Monomolecular adsorption

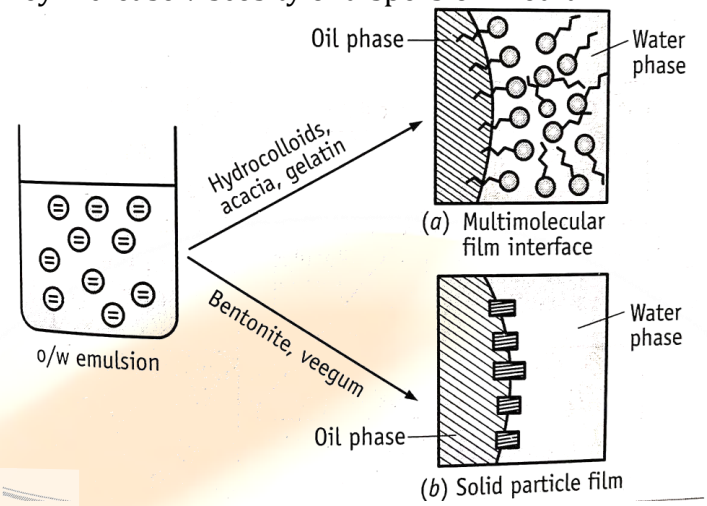
- Amphiphiles (surfactants) reduce interfacial tension(to 1 dyne/cm) because of adsorption at interface o/w.
- Droplets are surrounded by coherent monolayer that help prevent coalescence (merging) between two droplets.
- Surface Charge cause repulsion between globules.
- Combination of surfactants is generally used as it is more effective.
- Combination of Sodium cetyl sulphate and cholesterol leads to complex film that produce excellent emulsion.
- Hydrophilic tween can be combined with lipophilic span, varying proportions produce desired emulsion: w/o or o/w.



2. Multimolecular adsorption

- Hydrophilic colloids (mucilage of gum acacia) are different in action from surfactants.

- They do not cause lowering of interfacial tension.
- They form multimolecular layer at o/w interface.
- They increase viscosity of dispersion medium.



3. Solid particle adsorption

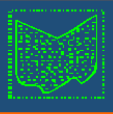
- Solid particles that can be wetted by oil as well as water can act as emulsifying agent.
- Their concentration is higher at interface.
- They form particulate film around dispersed droplets to prevent coalescence.
- **Example of agents:** Bentonite ($Al_2O_3.4SiO_2.H2O$), Veegum (Magnesium Aluminum Silicate).

4. State and explain the evaluation parameters used for characterization of the derived properties of powder.

Answer

- The derived properties of powders are-
  1. Density
  2. Porosity
  3. Packaging arrangement
  4. Flow properties

Density

	TRUE DENSITY	GRANULE DENSITY	BULK DENSITY
Formula	$\frac{\text{Weight of powder}}{\text{True volume of powder}}$	$\frac{\text{Granule weight}}{\text{Granule volume}}$	$\frac{\text{Mass of powder (m)}}{\text{Bulk volume } (V_b)}$
Determined by	(i) Gas displacement method (He, N is used) (ii) Liquid displacement method	Mercury displacement method	Bulk density apparatus
Representation			
Explanation	Density of powder itself	Density of powder + Intra particle space	Density of powder itself + Density of intraparticles + Interparticle space

Porosity

- It is defined as the void volume to the bulk volume
- Void volume = V = bulk volume - true volume

$$V = V_b - V_p$$

$$\text{Porosity } (\varepsilon) = \frac{Vb - Vp}{Vb}$$

Packaging arrangements

- Arrangement of particles in a powder influences volume occupied by it.
- Types of packing arrangement-
  1. Closet or rhombohedral packing - 26% porosity
  2. Open/loosest/cubic packing - 48% porosity

Flow Properties

- Flow properties depends on particle size, shape, porosity, density etc. of the bulk powder.

1. **Particle size -** Particle size, flow properties. An appropriate blend of coarse and fine particles improves flow.
2. **Nature of particle -** Smooth surface of particles improves the flow whereas surface roughness leads to poor flow due to friction and cohesiveness.
3. **Moisture content -** Higher the moisture content, the greater the risk of cohesion & adhesion.
4. **Angle of repose**
   - **Fixed cone method**

$$\theta = \tan^{-1}\frac{h}{r}$$

where,

θ – angle of repose
h – height of pile
r – radius of the base of pile

   - **Rotating cylinder method**
   - **Tilted box method**

Angle of repose	Powder flow
<25	Excellent
25-30	Good
30-40	Passable
>40	Very poor

5. **Carr's Consolidation Index -**
   - Also known as compressibility
   - Carr's Index is the indication of the flowability of a powder.
   - In a free-flowing powder, the bulk density and tapped density would be close in value, therefore, the Carr index would be small.

- On the other hand, in a poor-flowing powder where there are greater interparticle interactions, the difference between the bulk and tapped density observed would be greater, therefore, the Carr index would be larger.

$$\text{Carr's index} = \frac{\textit{Tapped density} - \textit{bulk density}}{\textit{Tapped density}} \times 100$$

6. Dispersibility -

$$\text{Dispersibility (\%)} = \frac{\textit{Weight of powder in a watch glass}}{\textit{Initial weight of sample}} \times 100$$

7. Hausner's ratio-

$$\text{Hausner's ratio} = \frac{\textit{Tapped density}}{\textit{Bulk density}}$$

Flow of powder	Carr's index	Hausner's ratio
Excellent	5-15	1-1.11
Good	12-16	1.12-1.18
Fair	18-21	1.19-1.25
Passable	23-28	1.26-1.34
Poor	28-35	1.35-1.45
Very poor	35-38	1.46-1.59
Extremely poor	>40	>1.6

5. Explain the steps for the determination of order of a chemical reaction.

Answer

- Normally, order of reaction can be determined by following methods,
  1. Half Life Method
  2. Graphical Method
  3. Initial Rate Method
  4. Van't Hoff Differential Method

1. Half-life method

- This technique is utilized only when the rate law involved by only single concentration term.

$$t_{(1/2)} = \alpha\, a^{1-n}$$

$$t_{(1/2)} = k\,\frac{1}{a^{n-1}}$$

$$\log t_{(1/2)} = \log k' + (1 - n)\, a$$

- Graph of log $t_{1/2}$ vs log a, displays a straight line with slope (1 - n), where 'n' is the order of the reaction. Defining the slope we can find the order (n). If half-life at different concentrations is given, then

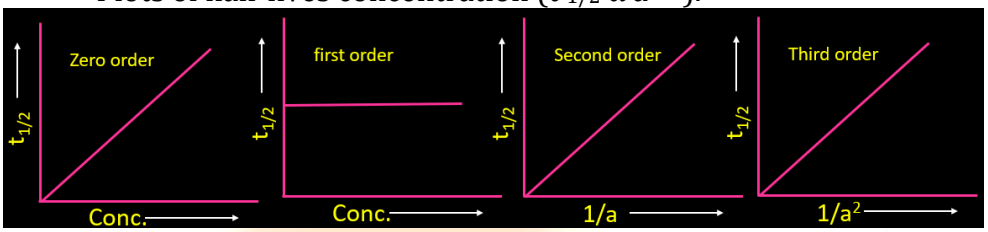
$$t_{(1/2)}\, \alpha\, \frac{1}{a_1^{n-1}}$$

and $$t_{(1/2)} \alpha \frac{1}{a_2^{n-1}}$$

- Taking logarithm and rearranging

$$n = a + \frac{\log(t_{1/2}) - \log(t_{1/2})}{\log a_2 - \log a_2}$$

- Plots of half-lives concentration ($t_{1/2} \alpha a^{1-a}$).



2. Graphical Method

- This technique is utilized in presence single reactant. If the plot of log [A] vs t is a straight line, the reaction follows first-order.
- If the plot of $\frac{1}{[A]}$ VS t is a straight line, the reaction follows second order. If the plot of $\frac{1}{[A]^2}$ is a straight line, the reaction follows third order.
- Normally, for a reaction of n^{th} order, a graph of $\frac{1}{[A]}$ (n-1) vs t must be a straight line. Here [A] is the concentration of reactant at any given time of the reaction (other t = 0) [A] = (a - x) where a is the initial concentration and x is the extent of reaction at time t.

3. Initial rate method

- In this technique, initial reaction rate is governed through changing the concentrations of one reactant though keeping others are constant.

$$R = k[A]^x [B]^Y [C]^Z$$

- If [B] and [C] = Constant then for two different initial concentrations of A we have,

$$R_{0_1} = K[A_0]_1^a$$

And $$R_{0_1} = K[A_0]_1^a$$

$$\frac{R_{0_1}}{R_{0_1}} \left(\frac{[A0]_1}{[A0]_2}\right)_n$$

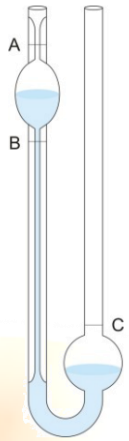
6. Mention the working principle and applications of capillary, falling sphere and rotational viscometers used for the determination of viscosity.

Answer

Capillary viscometer (Ostwald viscometer)

Working Principle

- The viscosity of a Newtonian liquid can be determined by measuring the time required for the liquid to pass between two marks as it flows by gravity through a vertical capillary tube known as an Ostwald viscometer.



- The time of flow of the liquid under test is compared with the time required for a liquid of known viscosity (usually water) to pass between the two marks. If η1 and η2 are the viscosities of the unknown and the standard liquids, respectively, ρ1 and ρ2 are the respective densities of the liquids, and t1 and t2 are the respective flow times in seconds, the absolute viscosity of the unknown liquid, η1 is determined by substituting the experimental values in the equation:

$$\frac{\eta 1}{\eta 2} = \frac{\rho 1\, t1}{\rho 2\, t2}$$

Applications

- Used for the quality control purposes in the formulation and evaluation of pharmaceutical dispersion systems such as colloids, dil. Suspensions, emulsions etc.
- To the study the flow of liquid through capillary tube.

Falling Sphere viscometer

Working Principle

- It is a falling ball instrument which uses a short , nearly vertical glass tube of large diameter and closely fitting ball of either steel or glass.
- The sample and the ball are loaded into the inner cylinder and brought to the temperature of measurement by means of a constant temperature outer jacket.
- The loading pin is released and the apparatus is inverted to place the ball in the initial stating position .
- The time for the ball to transverse the distance between two marks is measured.
- A minimum 30 sec time is used for best result.

Applications

- Used to determine the viscosity of non-Newtonian systems.

Rotational viscometer

Working Principle

- Based on the principle that the fluid whose viscosity is being measured is sheared between two surfaces.
- In these viscometer one of the surface is stationary and other is rotated by an external drive and fluid fills the space in between.
- The measurements are conducted by Appling either a constant torque and

measuring the changes in the speed of rotation or applying a constant speed and measuring the changes in the torque.

Applications

- Used to determine the viscosity of non-Newtonian systems.

7. Write a brief note on photolytic degradation of pharmaceutical preparations and its prevention.

Answer

Photolytic degradation

- The drug molecule is degraded by exposure of light it affects substantial degradation of drug molecule.
- When molecules are exposed to electromagnetic radiation, they absorb light (photons) at characteristic wavelength which cause increase in energy which triggers decomposition, retained or transferred and result in light emission at a new wavelength (fluorescence, phosphorescence).
- Natural sun light lies in wavelength range (290-780 nm) of which only higher energy (UV) range (290-320) cause photo degradation of drugs.
- Examples of phototoxic drugs include furosemide, acetazolamide and cyanocobalamin.

Example

- Sodium nitroprusside in aqueous solution (which is administered by IV infusion for management of acute hypertension).
- If protected from light it is stable to at least 1 year. If exposed to normal room light it has a shelf life of 4 hrs.

Protection

- Use of amber coloured bottles.
- Storing the product in dark, packaging in cartons also act as physical barrier to light.
- Coating of tablets with polymer films.

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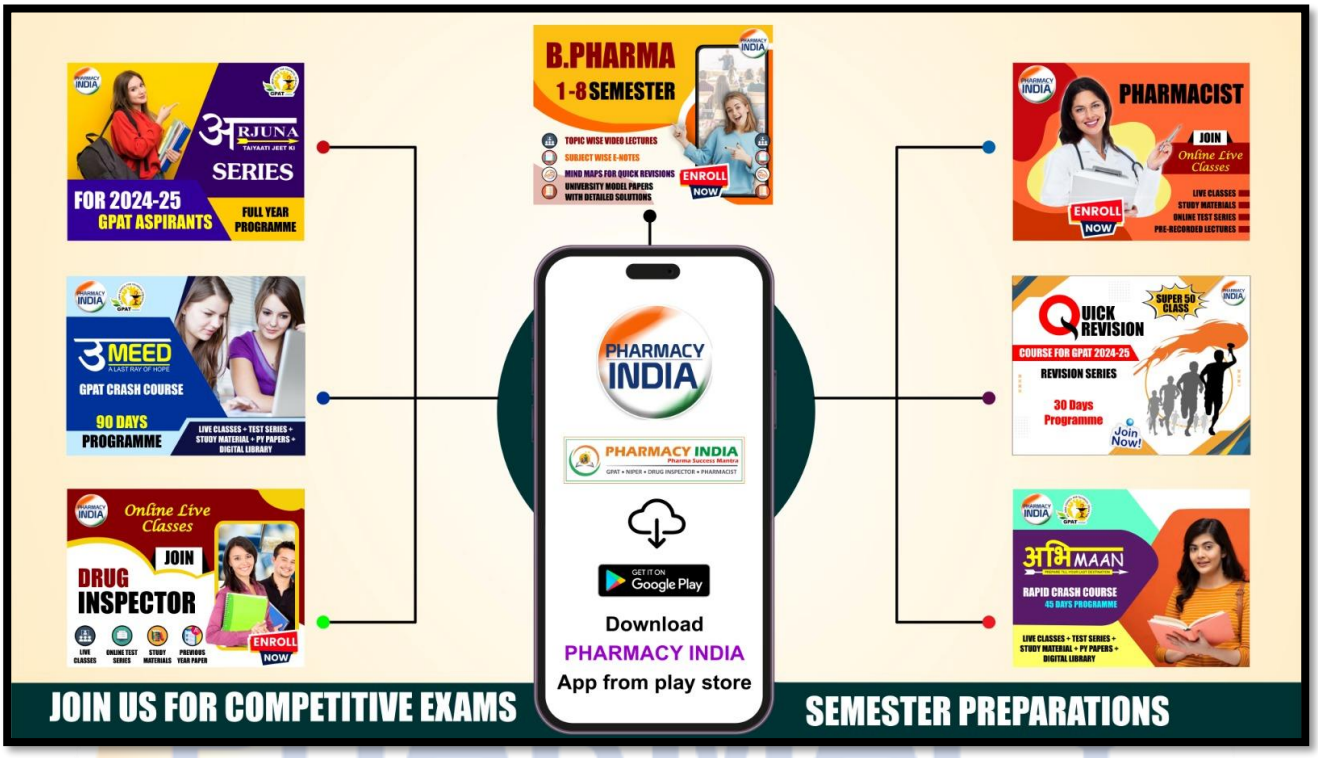

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