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Rai University
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PRACTICAL LAB MANUAL

Physical Pharmaceutics - II

B. Pharm IVth Semester

CONTENTS

1. DETERMINATION OF PARTICLE SIZE DISTRIBUTION BY SIEVING METHOD

AIM: To determine the average particle size and find out their distribution pattern for thr given sample granules by sieve analysis method

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PRINCIPLE: Sieve method gives sieve diameter which is defined as the diameter of the sphere that passess through the sieve aperture. The asymmetric particle sieve method directly give weight distribution. Particles having size range from 50 and 1500µm are estimated by sieving method. In this method, the size is expressed as d_{sieve}. The sieving method finds application in dosage and development of tablets and capsules. Normally 15 percent of fine powder (passed through mesh 100) should be present in granulated material to get a proper flow of material and achieve good compaction in tableting. Therefore, percent of coarse and fine can be quickly estimated. Sieves for pharmaceutical testing are constructed from wire cloth with square meshes, woven from wire of brass, bronze, stainless steel or any other suitable material.

Designations and Dimensions of I.P specification sieves

Sieve Number	Aperture Size Micrometer	Sieve Number	Aperture Size Micrometer
10	1700	44	325
12	1400	60	250
16	1000	85	35
22	710	100	36
25	600	120	34
30	500	150	36
36	425	170	35

Advantages of sieving method

2. It is in expensive, sample and rapid with reproducible results.

3. Sieving method is useful when particles are having size range between 50 and 1500µ

Disadvantage of sieving method

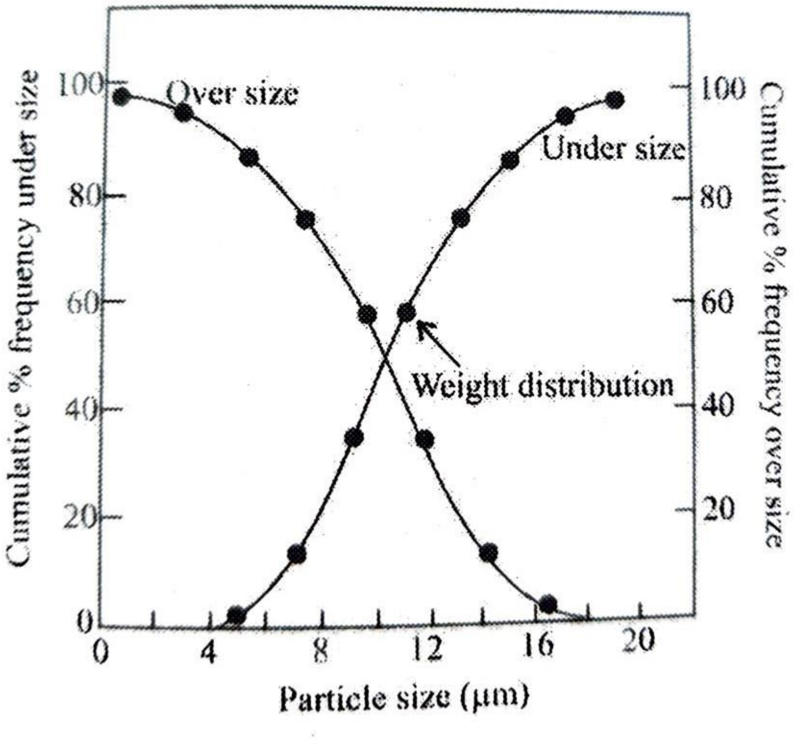
1. Lower limit of the particle size is 50 µm.
2. If the powder is not dry, apertures become clogged with particles leading to impropersieving.
3. During shaking, attrition occurs causing size reduction of particles. This leads to errors in estimation.

Factors influencing the sieving method:

Factors influencing sieving are weight of sample, duration of shaking and type of motion. The types of motion influencing sieving are vibratory motion, (most efficient), side tap motion, bottom pat motion, rotary motion with tap and rotary motion. The type of motion standardized. Care should be taken in order to get reproducible results.

PROCEDURE:

1. Standard sieves set is selected (sieve no: 10, 22, 36, 44, 65, 80, 100,120) and arranged in such manner that the coarsest remains at the top and finest at the bottom.
2. Weigh approximately 50g of sample place the sample on the coarsest sieve no.10.
3. Fix the above sieves set on hand sieve shaker and shaken for 20 minutes.
4. Collect the Sample retained on each sieve into a paper, weigh all the ample.
5. Report the weights retained on each sieve in the table against corresponding sieve number.



Observation Table:

Sieve No	**Aperture Size as Per I.P (µm)**	**Arithmetic Mean Size of opening (d) (µm)**	**Weight of Granules Retained on Sieve over Size (gm)**	**% Wt of Retained (Under Size) "n"**	**Cumulative % Granules retained (Under Size)**	**Weight Size (n×d)**	**% Under Size**	**% Over Size (100-% Under Size**
20*/40								
40/60								
			Σn=			**Σ(n×d)=**		

RESULT:

The average diameter of the given granules was found to be............. µm.

2. DETERMINATION OF PARTICLE SIZE AND PARTICLE SIZE DISTRIBUTION USING MICROSCOPIC METHOD

AIM: To determine the average particle size of the given powder sample and study their size distributionusing compound microscope.

Principle: Micromeritics involve the study of small particles and of the order of a few micron sizes. This study involves the characterization of individual particles, particle size distribution shape angle of repose, porosity, true volume, bulk volume, true density and bulk density of powder. Theunit of particle size is micrometer or simply micron, which is equal to 10^{-6} meter or 10^{-3}millimeter.The millimicron is referred as nanometer (nm). Calibration of the eye piece microemeter is the first step for determining the particle size distribution of powder.

Requirements: Microscopic, stage micrometer, MgO powder (water insoluble powder).

CALIBRATION OF EYE PIECE MICROMETR:

STANDARD STAGE MICROMETER:

- ✓ Standard stage micrometer is used to calibrate of eye piece micrometer. Eye piece micrometer is a glass slide (7.5cm into 2.5cm) which has the scales engraved in the scale usefully 0.1mm is length. 1mm divided into 100 divisions. Thus smallest division least count of the stage micrometer represents 0.01mm or 10µm length.
- ✓ In this experiment in the optical combination of 10x eye piece and 45x objective is used
- ✓ The stage micrometer is least on the stage of the microscope. The objective is position to the center of objective
- ✓ Initially disc focus low power the scale of stage micrometer observed (100 divisions)
- ✓ Now the objective is focus to high power (45x)
- ✓ Two points were selected one point on the left side where divisions both scales coincide and another point on the right side
- ✓ The number of small division that is eye piece were counted and big division stage micrometer were counted and recorded.

Number of divisions of eyepiece micrometer (X)= Number of division of stage micrometer (Y)

One division of eyepiece micrometer= Y/X number of division of stage micrometer.
As 1 division of stage micrometer is equal to 10µm, the one division of eyepiece micrometer = **10 x Y/X.**

Procedure:

1. Note down the least count "L" of the stage micrometer. Determine the number of divisions n_1 of stage micrometer that coincide with the eyepiece micrometer divisions n_2. Then 1 division of the eyepiece micrometer = **$[n_1 * l]/n_2$**

2. Prepare a dilute suspension of the given sample powder is distilled water. Place a drop of the suspension on a glass slide and observe the particles under the microscope with calibrated eyepiece micrometer. Determine the average size of the particle by taking mean of the length and breadth of the particle (since most the particles are not spherical).
3. Measure size of 100 particles as in (2) above.

Note: Usually 1 division of stage micrometer = 0.01 mm i.e. L = 0.01 mm

Each division of eyepiece micrometer=________________µm.

Observation and calculation:

Number of divisions of eye piece micrometer (A)=Number of divisions of stage micrometer (B).

One division of eye piece micrometer=B/A number of divisions of stage micrometer.

As one division of stage micrometer is equal to 10 µm, one division of eye piece µm= 10XB/A µm.

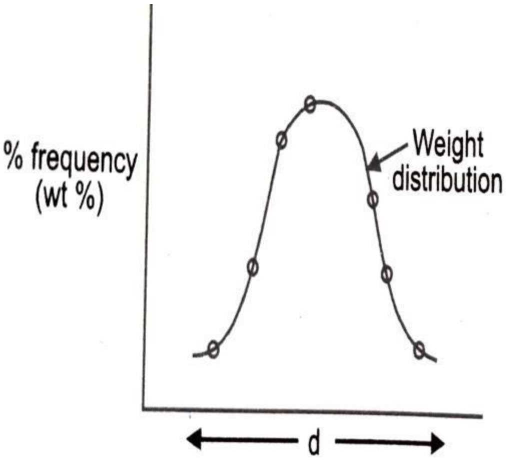
$\sum n$= Total number of particles

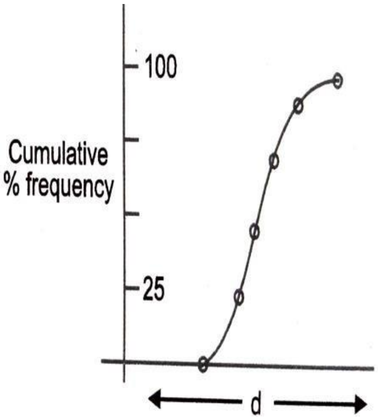
1 micron $=10^{-4}$cm = 10^{-6} m

Average particle size : $\sum NX / \sum N =$

1. Plot the graph of % frequency (i.e. wt. %) vs diameter

2. Plot the graph of cumulative % frequency vs d.





CALCULATION:

$$\text{Length-number mean diameter} = \frac{\sum nd}{\sum n} = \text{microns}$$

$$\text{Surface-number mean } d_s = \sqrt{\frac{\sum(nd^2)}{\sum n}} = \text{microns}$$

$$\text{Volume-number mean } d_v = \sqrt[3]{\frac{\sum(nd^3)}{\sum n}} = \text{microns}$$

Number of division(length))	**Size(length in micrometer)**	**Numberof division (Breadth)**	**Size ((Breadth) inμm**	**Averagesize in μm**	**Size Range**	**Mean size range (μm) (X)**	**No of particles in each class interval (N)**	**NX**
							∑N=	∑NX =

Report: One division of eye piece micrometer________.

3. DETERMINATION OF BULK DENSITY, TRUE DENSITY AND PERCENTAGE POROSITY

Aim: To determine bulk density, true density and percentage porosity of the given granules

PRINCIPLE

Solid bodies retain their volume and shape under atmospheric pressure. An important factor in choosing a suitable sample for density determination is the question of whether the density is required as a characteristic of a material or whether density determination is performed to check for defects in a material. The choice of procedure for density determination will depend on this factor as well. The density of particles, powders, and compacts is an important property affecting the performance and function of many pharmaceutical materials. By definition, all density measurements involve the measurement of mass and volume. Mass is determined with an analytical balance and the key to obtaining reliable density values is in the accuracy and precision of measuring volume.

Bulk density is a characteristic of a volume of divided material such as powders, grains, and granules. It includes the volume of the solid material, open and closed pores, and the interparticle voids. The total volume of interparticle voids can change with packing, thus leading to the concept of tap density, which measures the volume of a mass of sample after inducing a closer packing of particles by tapping the container. Taking this method to the extreme leads to the determination of void volume and compressed density after compressing the sample under extreme forces and measuring the volume change as a function of applied pressure.

True density is the density of the solid material excluding the volume of any open and closed pores. Depending on the molecular arrangement of the material, the true density can equal the theoretical density of the material. True density measurements can be performed on APIs, excipients, blends, and monolithic samples such as tablets. In micrometrics studies high-precision gas pycnometer which gives accurate to 0.02% of the sample volume are used to determine true density.

Porosity consists of volume of the pores relative to the envelope volume used to calculate envelope density. The porosity of pharmaceutical materials and medical devices can impact production,material movement, and pharmacokinetic behaviour. Tablet porosity determines the tensile strength (hardness) of tablets for a given composition. Tablet porosity may be regarded as a measure of the tableting process. Variations in tablet porosity reflect various aspects of tablet press performance. Tablet porosity may relate to tablet disintegration and dissolution. In the case of coated tablets, coating quality may be affected by tablets porosity.

The angle of repose is given by

$(\theta) = \tan^{-1} h/r$
Where, h = height of pile
r = radius of the base of the pile

Bulk density is defined as the ratio of weight of powder to the bulk volume is the volume occupied by certain weight of powder when gently poured into the measuring cylinder.

Bulk density = weight *I* bulk volume

Tapped density is the ratio of weight of powder to the tapped volume. Tapped volume is the volume occupied by certain weight of powder after standard no. of tapping.

Tapped density = weight *I*tapped

volumeCarr's index may be

defined as
Carr's index = (Tapped density -bulk density *I*tapped density) x 100

Hausner's ratio is the no. i.e. co-related to flowability of the

powder.Hausner's ratio=Tapped density *I*bulk density

REQUIREMENTS:

Chemical Requirements: Lactose, calcium carbonate, talc, zinc oxide
Apparatus: Measuring cylinder, weighing balance, funnel, burette stand

PROCEDURE:

1. *Determination of bulk density and tap density*

2. 10gm of powder sample was weight accurately. Then it was transferred in to a 100ml measuring cylinder. The volume was noted as bulk volume V_1. Then the measuring cylinder was tapped 100 times. The volume noted as tapped volume.
Bulk Density=Weight/Bulk Volume

Tapped Density=Weight/Tapped Volume

1.Determination of carr 's index and hausner's ratio: -

Carr's Index= {(Tapped Density -Bulk Density) /Tapped Density}

x 100Hausner's Ratio=Tapped Density/Bulk Density.

2. Determination of angle of repose: -

A clean and dry funnel was taken and attached to a burette stand. A white paper site was placed 5cm below the tip of the funnel in a dry plat form. Gently this sample was pore into the funnel. Using a pencil circle was drawn around the tip of powder. The height of the hip also measured.The same procedure was followed 3 times to obtain average reading.

Angle of repose (Ө)=tan-^{1}h/r , Where h = Average height of heap

r = Average radius of heap

3. Determination of flow rate

Flow Rate=Weight of Powder/Time Required to Flow

CARR'S INDEX	**TYPE OF FLOW**
5-15	EXCELLENT
12-16	GOOD
18-21	POOR
>23	VERY POOR

ANGLE OF REPOSE	FLOWABILITY
<25	EXCELLENT
25-30	GOOD
30-40	PASSABLE
>40	VERY POOR

1. Calculation of bulk density:

Bulk density (pB) = Mass/Bulk Volume

2. Calculation of true density

True density (pi) =

3. Calculation of Porosity:

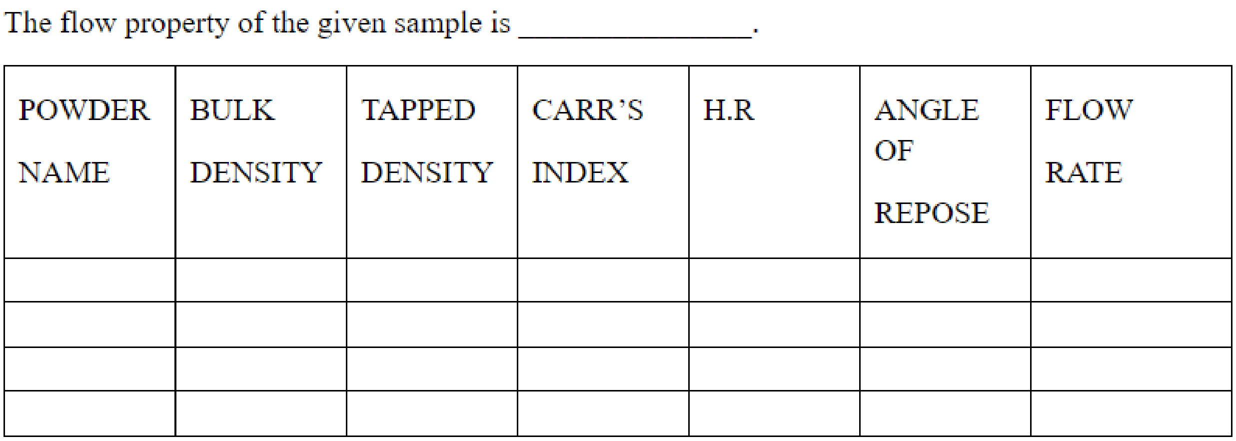
Porosity

Total porosity =

Observations:

1. Weight of powder (w1) =25.grams
2. Volume of measuring cylinder occupied by powder (V1) =….mL
3. Volume of measuring cylinder occupied by powder after tapping (V2) =......... mL
4. Volume of density bottle (V3) =........ mL
5. Weight of powder in density bottle = 10 grams
6. Volume of solvent added to density bottle (V4)=..........mL.
7. True volume of powder (VT) = V3 — V4 mL

Calculations:



The flow property of the given sample is _______________.

POWDER NAME	BULK DENSITY	TAPPED DENSITY	CARR'S INDEX	H.R	ANGLE OF REPOSE	FLOW RATE

Report

- ✓ The bulk density of the given sample of granules was found to be = g/cm^3
- ✓ The true density of a given powder was found to be = g/cm^3
- ✓ The percentage porosity of the a given powder is =%

4. DETERMINE THE ANGLE OF REPOSE AND INFLUENCE OF LUBRICANT ON ANGLEOF REPOSE

AIM: To determine the effect of glidants on lubricants of angle of repose

REQUIREMENTS

- Lactose powder
- Starch paste
- Talc
- Mortar and pestle
- Funnel, stand

PRINCIPLE

When a powder material passes through an orifice, they are called free flowing, while those do not pass even through the particle are very much smaller than orifice, are called cohesive. Angle of repose is one of the simplest technique used to determine the flowability of powder materials.

The angle of repose (θ) is defined as the angle of elevation to the horizontal at which the powder commences to slide upon itself. The angle of conical heap can be determined from the diameter or radius of the base and height of the cone.

$$\tan \theta = \text{height} / \text{radius}; \text{ thus } \theta = \tan^{-1} (\text{height}/ \text{radius})$$

The high value of θ is the indication of cohesive nature of powder and low value for free flowing. When the angle is at minimum i.e., 25°, the powder will flow easily.

Lubricants are glidants that reduces friction during tablet ejection, happen between the surface of the tablet and the walls of the die cavity. The most widely used lubricants are steric acid and steric acid derivatives such as calcium and magnesium stearate and talc. Glidants are intended to increase flow of powder from hopper to die cavity during tableting. It increases flow of the granulation of powder materials by reducing friction between the particles. The most widely used glidants have been derivation of talc and corn starch.

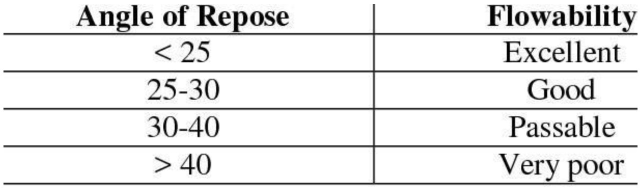
PROCEDURE:

- Select a glass funnel which has a round shape of 15-30mm of diameter with flat edge
- Fix the funnel with a clamp (on the ring)

- Place the glass plate on the ring and arrange it below the glass funnel
- Keep on graph paper on the glass funnel
- Weigh approximately 100gm of granules
- Pour the granules while blocking the orifice of the funnel be thumb
- Remove the thumb the granules load at flow down into the graph paper and form a cone shaped
- Adjust the thumb the funnel clamp so that the gap between the bottom of the funnel peak of the powder pile is about 3mm
- Repeat the 5-7 steps.
- Finally pour the granules back into funnel and allow to flow
- Mark four points which are opposite to each other on the circular base on the graph paper
- Record the readings in table, this value is the diameter calculate the radius in ®
- Measure the height of the pile using two rulers
- Keep one ruler vertically and another horizontally to touch the peak of the pile, then read thevalue for the vertical scale.
- Substitutes the value in equation to obtained the angle of repose, generally the (h/r) measure isthe angle of repose data were plotted semi-long paper and copies of curves made available for the purpose of calculating angle
- Repeat the procedure 2 more time and take on average

Calculation:

Angle of Repose $\theta = \tan^{-1} h/r$



Angle of Repose	Flowability
< 25	Excellent
25-30	Good
30-40	Passable
> 40	Very poor

REPORT

The angle of repose of the given granules (without glidant) =

The concentration is

The effect of glidants of lubricants of angle of repose is =

Inference is that the flow of granules

TRIAL	HEIGHT (cm)	RADIUS (r) (cm)	h/r	Angle of Reposeθ= $\tan^{-1} h/r$
I				
II				
	Average angle of Repose =			

5. DETERMINATION OF VISCOSITY OF LIQUID USINGOSTWALD'S VISCOMETER

Aim: To determine the viscosity of the unknown liquid by using Ostwald's viscometer

REQUIREMENTS:

- Ostwald's viscometer,Stop clock,Specific gravity bottle,Sample,Distilled water

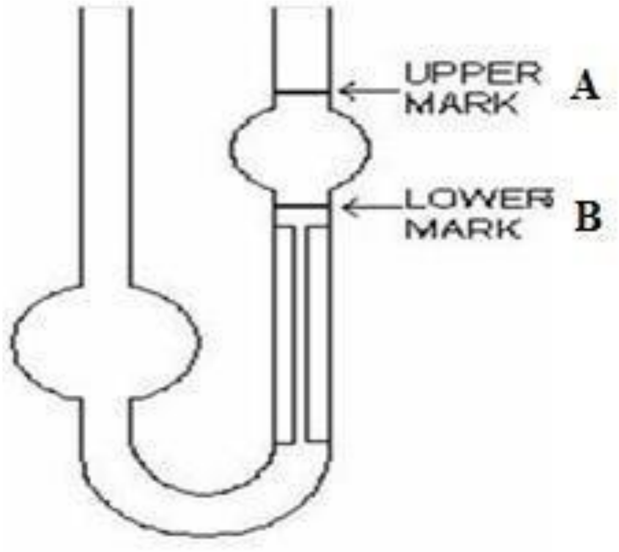
PRINCIPLE:

The viscosity of liquid is a resistance to flow of a liquid. All liquids appear resistance to flow change from liquid to another, the water faster flow than glycerin, subsequently the viscosity of water less than glycerin at same temperature. Viscosity occurs as a result of contact liquid layers with each other. The viscosity is measured by Ostwald viscometer. Relative Viscosity is the ratio of the absolute viscosity of the fluid on the viscosity of water at a certain temperature. The viscosity coefficient is force (dyne) necessary to move the layer of liquid 1 cm^2 in speed 1 cm/sec on another layer of liquid and the distance between them is 1cm. The SI unit of viscosity is the Pascal-second (Pa·s), or equivalently kilogram per meter per second (kg·m−1·s−1). The CGS unit (g·cm−1·s−1 = 0.1 Pa·s) is called the poise (P) named after Jean Léonard Marie Poiseuille. When fluid is forced through a tube, the fluid generally moves faster near the axis and very slowly near the walls therefore some stress (such as a pressure difference between the two ends of the tube) is needed to overcome the friction between layers and keep the fluid moving. For the same velocity pattern, the stress required is proportional to the fluid's viscosity. A liquid's viscosity depends on the size and shape of its particles and the attractions between the particles. A liquid whose viscosity is less than that of water is sometimes known as a mobile liquid, while a substance witha viscosity substantially greater than water is called a viscous liquid. For two different liquids viscosity of unknown liquid can be determined using the following equation:

$$n_2/n_1=t_2\rho_2/t_1\ \rho_1$$

n_2= Viscosity of sample liquid (glycerin)

t_2= time taken by sample liquid
ρ_2= density of sample liquid (1.26 gm/ml)
n_1=Viscosity of reference liquid (water = 0.91**centi poise** at 25 °C)
t1 =time taken by reference liquid
ρ1=density of reference liquid (1.0 gm/ml)



OSTWALD VISCOMETER

PROCEDURE:

- Wash the relative density bottle with distilled water and dried.
- Take the weight of empty bottle and filled given liquid
- Clean and rinse the viscometer properly with distilled water
- Fix the viscometer vertically in the stand and filled the specific amount of given unknown liquid in viscometer
- Time of flow recorded when the liquid starts to flow from the mark c and d above and below the bulb a. the experiment repeated 3-4 times to get viscosity of the given unknown liquid.

OBSERVATION:

Room temperature = 25°C
Time of flow of water (t_1) = ...sec
Time of flow of Sample liquid (t_2) =..................... sec

LIQUID	**FLOW TIME IN (SEC)**			**AVERAGE (SEC)**	**DENSITY (g/ml)**
	1	2	3		
distilled water					
given sample					

REPORT:

The viscosity of the unknown liquid is = …centipoise

6. DETERMINATION OF SEDIMENTATION VOULME WITH EFFECT OF DIFFERENT SUSPENDING AGENT

AIM: To determine the sedimentation volume with effect of different suspending agent.

REQUIREMENTS:

Chemicals: Zinc oxide powder (ZnO), Acacia, Carboxymethylcellulose (CMC), tragacanth, distilled water etc.

Glassware and apparatus: Mortar, pestle, measuring cylinder etc.

PRINCIPLE:

SUSPENSION: Pharmaceutical suspension may be defined as a coarse dispersion in which insoluble solids are suspended in liquid medium. It is also known as heterogeneous system (or) more precisely biphasic system. The insoluble solids may have size range from 10- 10000µm and liquid medium is normally water or a water based vehicle.

SUSPENDING AGENT: Suspending agent is defined as physiologically inert substance which increases the viscosity when added to suspensions. It helps in the keeping the dispersed particles. Suspended thus there enhanced the physical stability and re-dispersion of the sediment or shaking.

PHYSICAL STABILITY: Physical stability may be defined as a condition in which particles remain uniformly distributed throughout the dispersion with any signs of sedimentation. In practice Physical stability may be defined as a condition in which particles should be easily re-suspended by a moderate shaking. If they settle suspensions when kept aside. The solids tends to settle at the bottom of the container due to gravitational pull on the particles of higher size. It is not possible to prevent the sedimentation volume and its case of re-dispersion are the common evaluation procedure for assessing the physical stability. The two sedimentation parameters are employed such as

1. Sedimentation volume
2. Degree of flocculation

$$\boxed{\frac{dx}{dt} = \frac{2r^2(\rho_1 - \rho_2)g}{9\eta_2}}$$

SEDIMENTATION VOLUME:

- Sedimentation volume is defined as F
- When a suspension is taken in a measuring cylinder volume and height is proportional and height can be conveniently measured through the term volume isincluded in the terminology

sedimentation volume “F” is a dimension less number. Most pharmaceutical suspension has an “F” value less than one. If f=1 the product has no sediment and no clear supernatant on standing which is an ideal condition. Normally “F” value lies between 0 and 1. Sometimes the network of flow is loose and fluffy and ultimate volume of sediment increase. In this situation. “F” value will be greater than one.

$$\boxed{F = \frac{V_u}{V_o} \times 100}$$

PROCEDURE:

1. Weigh 5gm of calcium carbonate and place in a mortar and add small quantity of water and triturate the sample. After suspending the powder uniformly transfer the suspension into a 100ml measuring cylinder makeup the volume to 100ml with distilled water.
2. Separately prepare 5% w/v of calcium carbonate suspension with 1% of different suspending agent such as bentonite, methyl cellulose, respectively in different vessel add small quantity of water and triturate well. After powder is uniformly suspended transfer the suspension into separate 100ml measuring cylinder.
3. Makeup the volume to 100ml with distilled water
4. Shake the suspension simultaneously and kept aside
5. Note the volume of sediment at time periods 0, 10, 20, 30, 60 minutes. Calculate the sedimentationvolume.
6. Draw the plot by taking “F” values on “Y” axis and the time on “X” axis.

OBSERVATION:

Volume of Sediment and sedimentation volume of suspensions :

Time(min)	**ZnO**		**ZnO + CMC**		**ZnO+Tragacanth**		**ZnO + Acacia**	
	Vu	**F**	**Vu**	**F**	**Vu**	**F**	**Vu**	**F**
10								
20								

30								
40								
50								
60								

Where, Vu is volume of sediment at time (t) minutes and F is sedimentation volume in ml.

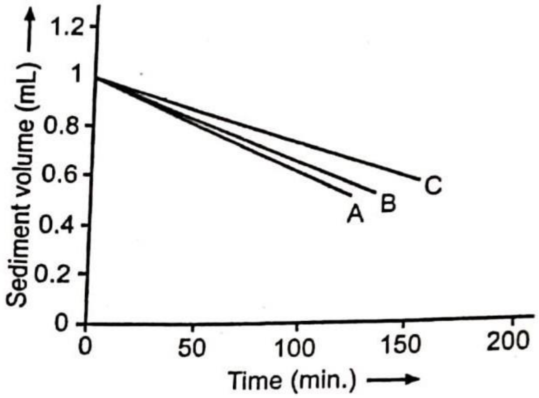
CALCULATIONS:

Sedimentation volume :

Sedimentation volume of all suspensions at different concentrations is calculated using following equation

$$\boxed{F = \frac{V_u}{V_o} \times 100}$$

Plot the graph of sedimentation volume (F) vs. Time (min) for each suspending agent.



A plot of sedimentation Volume vs. Time

Precautions:

1. Note sediment volumes accurately at different time intervals.
2. Allow suspensions to stand undisturbed.
3. Use good quality suspending agents.
4. Use calibrated measuring cylinders to measure volumes.

REPORT:

5% calcium carbonate suspension 1% carboxy methyl cellulose as suspending was found to be morephysically stable compared with other suspending agent

7. DETERMINATION OF SEDIMENTATION VOLUME WITH EFFECT OF DIFFERENT CONCENTRATION OF SINGLE SUSPENDING AGENT

AIM: Determination of Sedimentation volume With Effect of Different Concentration of Single Suspending Agent

REQUIREMENTS:

Chemicals: Zinc oxide powder (ZnO), Carboxymethylcellulose (CMC), distilled water etc.
Glassware and apparatus: Mortar, pestle, measuring cylinder etc.

PRINCIPLE:

Pharmaceutical suspension may be defined as a coarse dispersion in which insoluble solids are suspended in liquid medium. It is also known as heterogeneous system (or) more precisely biphasic system. The insoluble solids may have size range from 10-10000µm and liquid medium is normally water or a water based vehicle.The concentration of suspending agent decreases the sedimentation volume of dispersion. This increase in the concentration of the suspending agents may be explained by the increase in the viscosities of the dispersion. Higher dispersion viscosity tends to slow down the rate of particle sedimentation in accordance to Stokes Law but may not prevent the incidence of caking when the particles eventually sediment. Sedimentation volume is potentiated by increase in concentration of the suspending agents. The effect of concentration of the suspending agents on sedimentation volume may be attributed to linear relationship between their concentration and viscosity of their aqueous dispersions in conjunction with Stokes law, which reveals an inverse relationship between sedimentation rate and the viscosity of the dispersion medium.

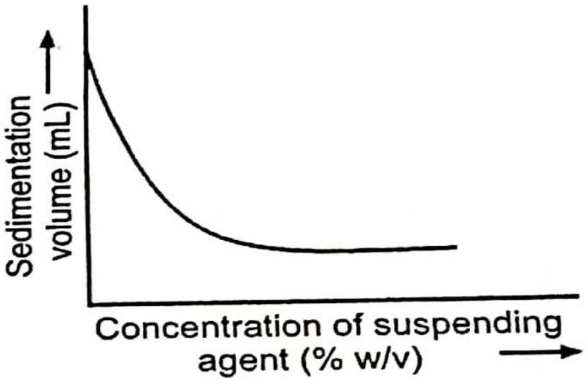


Fig : Effect of concentration of suspending agent on sedimentation volume of dispersion

PROCEDURE:

1. Prepare 500 ml each of 5% w/v Zinc oxide suspension in distilled water . Accurately weigh 25 g of Zinc oxide and transfer to mortar and triturate with small volume of distilled water (approximately 50-100 ml) to make a paste. Make up total volume to 500 ml with remaining water.

2. Transfer 100 ml each to different measuring cylinders and add 2,4,6 and 8 % w/v CMC assuspending agent.
3. Use fifth suspension as a control that contains no suspending agent.
4. Shake well all suspensions and leave them for sedimentation . Note down the volume ofsediment in each of measuring cylinder at definite time period.
5. Determine the sedimentation volume (F).
6. Plot the graph of sedimentation volume Vs time in minute.

OBSERVATION:

1. Original volume of sediment (Vo) =100 ml
2. Final volume of sediment (Vt) = _________ ml
3. Time of Sedimentation = ___________min.

Conc. of suspending agent(%)	**V_t (ml)**	**Time(in minutes)**	**F= Vu/Vo**	**%F= Vu/Vo×100**
0		0		
2		10		
4		20		
6		30		
8		40		
10		50		

Observation Table:

Volume of Sediment and sedimentation volume of suspensions :

Where, Vu is volume of sediment at time (t) mins and F is sedimentation volume in ml.

Calculations:

1. **Sedimentation volume :** Sedimentation volume of all suspensions at differentconcentrations is calculated using following equation:

F=Vu/Vo and F% = (Vu/Vo)*100

Plot the graph of sedimentation volume (F’) vs. Concentration of suspending agent (%w/v).

Precaution:

1. Carefully make-up final volume of suspension to 100 ml.
2. Note sediment volumes accurately.
3. Allow suspensions to stand undisturbed.
4. Use calibrated measuring cylinders to measure volumes.

Result:

REPORT:

- Increase the concentration of suspending agent and also increase the viscosity so lower the sedimentation volume
- The concentration of single suspending agent bentonite has more physical stable

8. DETERMINATION OF VISCOSITY OF SEMISOILD BY USING BROOKEFIELD VISCOMETER

AIM: To determine the viscosity of semisolid by using Brooke field viscometer

REQUIREMENTS:

Chemicals : Any semisolid material.

Glassware and apparatus: Brookfield viscometer

PRINCIPLE: Newton was the first to study the flow properties of liquids in quantitative terms liquids that obey newton's law of flow are called as Newtonian fluids.

F= ɳG, Shear stress- shear rate

Relationship is normally in the form of a curve rheogram or consistency curve. When data are plotted by taking "F" on x-axis and "G" on y-axis, a flow curve is obtained. The rheogram passes through the origin and the slope given the coefficient of viscosity system that follow this linear relationship are called as Newtonian fluids. This class includes liquids such as water, glycerine, chloroform, solutions of syrups, very dilute colloidal solution. Simple liquids exhibit Newtonian flow. Rheological properties of heterogeneous dispersions such as emulsions, suspensions and semisolid are more complex and do not obey newton's equation of flow based on the pattern of consistency curve, Non-Newtonian fluids are categorized as

- Plastic flow
- Pseudo plastic flow
- Dilatant flow

PROCEDURE:

- Prepare bentonite magma (5%w/v), methyl cellulose (2%w/v) and mineral oil. They show Non-Newtonian rheological profile
- Measure the viscosity of these liquids using a Brookfield viscometer and observe the thixotrophy phenomenon
- Place the spindle with the correct number listed in the data sheet in each liquid and rotate the spindle at the speeds indicated. Once the dial reading has stabilized, record the values of

viscosity in (cps).

CALCULATION:

Viscosity in cps= dial reading x factor

S. No	**Spindle Speed**	**Factors**	**Dial Reading**	**Viscosity** **(F × Dial reading)**
1.	6	1000		
2.	12	500		
3.	30	200		
4.	60	100		
5.	30	200		
6.	12	500		
7.	6	1000		

REPORT:

The viscosity of the given sample was found to be= ……centipoise (cps)

9. DETERMINATION OF REACTION RATE CONSTANT FIRST ORDER

AIM: To determine the reaction rate constant and half life of ester (methyl acetate or number of globules) at 0.5M HCL at room temperature

APPARATUS AND CHEMICALS REQUIRED:

- Conical flask (250 ml)
- 10 ml volumetric pipette
- Burette
- Ethyl acetate or methyl acetate
- Test tube
- 0.5 N HCL solution
- 0.25 N NAOH solution
- Phenolphthalein indicator
- Ice cold water

PROCEDURE:

Preparation of hydrochloric acid solution (0.5N) IP

Solutions of any normality XN may be prepared by diluting 85 x ml of HCL to 1000ml with water. Measure 850 ml of distilled water into a 1000ml volumetric flask. Add 42.5 ml of conc. HCL and slowly added. Finally make up the water in 1000ml.

Preparation of NAOH solution (0.25 N) IP:

Solutions of any normally XN may be prepared by dissolving 40 x gm of NAOH in water and diluting to 1000ml. weigh 10gm of NAOH and transferred into 1000ml volumetric flask. Add water slowly with stirring finally makeup the water into 1000ml.

PROCEDURE:

KINETIC METHOD

- 100ml of 0.5N HCL solution is measured and transferred into a 250ml conical flask
- It should be kept in the water bath for equilibrium (do not heat)
- 10ml of the given ester it transfer into the test tube and kept in the water bath for equilibrium.Normally it takes 10minutes
- The acid solution its mix ester sample thoroughly and kept in water bath
- Immediately after mixing 5ml of the mixer is withdrawn using the pipette and transferred in to a conical flask containing 10ml ice water

- The few drops of phenolphthalein indicator is added to the mixture
- The reaction mixer is titrated against 0.25N NAOH solution. This value of alkaliconsumed represents V0.
- 5ml samples by periodically at 10, 20, 30, 40, 50, 60, 75minutes. the volumeconsumed at each time interval represent Vt
- The reaction mixture is heated at water bath at the 60^0c at 20 minutes
- The mixture cooled to room temperature
- 5ml of sample by withdrawn at transfer into the conical flask containing 10 ml ice cold water.The titration is repeated and this value represents Vα.

OBSERVATIONS :

1. Water bath temperature =_____________℃
2. Titre reading at t=0, (Vo)=_____________ml 0.1 N NaOH
3. Infinity reading (Vα)=___________________ml 0.1 N NaOH.
4. Initial Concentration of ester= a =Vo-Vα =_____________ml 0.1 N NaOH.

OBSERVATION TABLE :

Time (t) (min)	V_t (ml)	X= (V_t-V_0) (ml)	(a-x) = (Vα- Vo) (ml)	Log (a-x)	K=2.303/t. log10a/a-x
0	—	0			
10					
20					
30					
40					
50					

Vt = Volume (ml) of 0.1 N NaOH required at

time t.k= Reaction rate constant

x= Change in concentration of methyl acetate a-x = Concentration of methyl acetate remaining at time (t).

Calculations:

1. Determination of k by substitution: Calculate values of k by substituting titre readings at differenttime interval in equation of reaction rate constant for first order reaction.

$$k=2.303/t \log10 a/a-x$$

2. Determination of k from graph: Find values of '*k*' from slope of the graph as given below. Inlogarithmic form, the rate constant equation for first order is written as

$$\text{Log}(a-x) = -k/2.303t + \log a$$

Plot the graph of log (a-x) vs. time for first order reaction.

Precautions:

1. Maintain temperature of reaction mixture constant during reaction.
2. Shake reaction mixture after every withdrawal.
3. Use dry pipette to withdraw reaction mixture samples.
4. Withdraw samples at right time interval and use ice or cold water to arrest reaction.
5. Judge the end point accurately.

REPORT:

The reaction rate constant (k) of the given data (methyl acetate or ethyl acetate) in 0.5NHCL acid is: From graphical method= ______minutes and From substitution method= _________minutes.

The half -life ($t_{1/2}$) of the given ester (methyl acetate or ethyl acetate) in 0.5N HCL acid is

From graphical method=

From substitution method=

10. DETERMINATION OF REACTION RATE CONSTANT SECOND ORDER

AIM: To determine the reaction rate constant and half-life period of ethyl acetate in 0.025N sodium hydroxide solution at room temperature.

PRINCIPLE:

The alkaline hydrolysis of an ester (ethyl acetate) is irreversible and follows the secondorder kinetics.

$$\underset{\text{Ethyl acetate}}{CH_3COOC_2H_5} + \underset{\text{sodium hydroxide}}{NaOH} \longrightarrow \underset{\text{Sodium acetate}}{CH_3COONa} + \underset{\text{ethyl alcohol}}{C_2H_5OH}$$

The molecularity of the reaction is two and the order is also two. Second order reaction isdefined as the reaction in which the rate of reaction depends upon the concentration of two reactants with each term raised to the first power.

Apparatus and chemicals:

- Conical flask (250 ml)
- Water bath
- Pipette
- Burette (50 ml)
- Ethyl acetate solution (0.05N)
- Hydrochloric acid solution
- Ice cold water
- Phenolphthalein indicator

PROCEDURE:

Preparation of ethyl acetate solution (0.05N)

The molecularity weight of ethyl acetate is 88.10 density is 0.90g/ml. percentage purity is 99%. Measure 50 ml of Ethyl acetate and transfer into 1000ml volumetric flask dilute to 1000ml with distilled water.

Preparation of hydrochloric acid solution (0.02N)

Solutions of any normality XN may be prepared by diluting 85 xml of hydrochloric acid to

1000ml with water. Measure 850 ml of distilled water into 1000ml volumetric flask. Add 1.7ml of concentrated hydrochloric acid slowly and shake. Finally make up the volume to the mark.

Preparation of sodium hydroxide solution (0.05N)

Weigh 2.0gm of sodium hydroxide in water and transfer into 1000ml volumetric flask. Add water slowly with continuous stirring, while cooling the flask under running tap water. Add sufficient water to make 1000ml. allow it to stand overnight and pour off the clear liquid into a bottle. This clear solution is used.

Kinetic method:

- ✓ Measure 50ml of 0.05N sodium hydroxide solution and transfer into a conical flask. Keep it in a water bath for equilibrium at room temperature.
- ✓ Measure 50ml of 0.05N of the given ester and transfer into a conical flask. Keep it in above water bath for equilibrium. Normally it takes about 10 minutes.
- ✓ Mix the alkali and ester solution thoroughly and keep in same water bath.
- ✓ Immediately after mixing, withdrawn a 10ml sample of the mixture with pipette and transfer into a conical flask containing 10ml ice cold water
- ✓ Add few drops of Phenolphthalein indicator
- ✓ Titrate against 0.02N hydrochloric acid. This titter value times t=0 corresponds to the original concentration “a” report the results.
- ✓ Periodically withdrawn samples at 5, 10, 15, 20, 25, 30 minutes time periods. Repeat the steps 4 to 6. These titter values denote the amount of sodium hydroxide or ethyl acetate remain unreacted ie, (a-x) at time. Record the results
- ✓ Substitute the values in integral equation and calculate the reaction rate constant (K_2). These values will more or less constant
- ✓ Calculate the average of the reaction rate constant (K_2)
- ✓ Draw a plot by taking x/a (a-x) on y-axis and time on x-axis
- ✓ Estimate the slope. This slope same as K_2 value.

CALCULATION:

time (min)	**volume of HCL consumed**		**volume of HCL (ml)**	**concentration in mol/liter a or (a-x)**	**x= a(a-x)**	**x/a(a-x)**	**K_2= x/at (a-x) liter/mol**
	initial (ml)	final (ml)					
00							
5							
10							
15							
20							
25							
30							

REPORT:

The reaction rate constant (K_2) of the given ester (methyl acetate or ethyl acetate) in 0.025N NAOH at room temperature

From graphical method= minutes

From substitution method= minutes

The half -life ($t_{1/2}$) of the given ester (methyl acetate or ethyl acetate) in 0.025N NAOH at room temperature

From graphical method=

From substitution method=

11. ACCELERATED STABILITY STUDIES

AIM:

To determine the shelf-life of the product. If stored at 25^0C from the given data.

- A pharmaceutical product needs to be physically, chemically, therapeutically, toxicologically and microbiologically stable throughout its shelf-life. The pharmaceutical companies do stability testing for estimating the shelf-life and based on this the expiry date is given for the product.
- The real time studies at recommended condition are ideal method for predicting shelf- life often the studies are designed to increase the rate of chemical degradation or physical change of pharmaceutical products by using exaggerated storage conditions. This is known as accelerated stability testing. The pharmaceutical products are subjected to higher temperature and humidity conditions for accelerating the degradation. However the results of accelerated testing are not always predictive of physical changes and potency.
- The pharmacopoeia specifies certain storage conditions. The following table gives the details as specified in Indian pharmacopoeia.

Storage Condition	**Meaning**
Cold	any temperature not exceeding 8^0C (2-8^0C)
Cool	any temperature between 8-25^0C
Warm	any temperature between 30-40^0C
Excessive Heat	any temperature above 40^0C

PRINCIPLE:

Though the medicinal products needs to be physically, chemically, therapeutically, toxicologically and microbiologically stable. The chemical instability is most often the main consideration for determining the shelf-life or expiry date. The medicinal products are stored at higher teperatureconditions to accelerate the degradation rate. This is known as accelerated stability taesting. The rate of chemical reaction increases by 2-3 folds for every rises in 10^0C at room temperature.The Arrhenius equation plot (log k vs 1/t) from the equation.

$\log k = \log A - K/2.303\,RT$

Where,

K= rate constant, R= gas constant, T= absolute temperature

E= energy of activation is used to find out the reaction rate constant at 25^0C.

PROCEDURE:

- The order of drug decomposition reaction is determined first by plotting curve. Percent potency retained versus time. Here it is first order
- The k value is determined for each temperature curve.
- The Arrhenius plot is drawn log k vs 1/t
- The value at desired temperature is determined by extrapolating Arrhenius equation
- The value of k is placed in the first order rate equation and is calculated.

  Three drug products were kept at 4^0C ± 2^0C/ 75% RH ± 5% RH

Storage Period In Months	Potency Retained Product-I	Potency Retained Product-II	Potency Retained Product-III
0			
3			
6			

REPORT:

The shelf-life of the medicinal product is

Product-I K=

Product-II K= Product –

III K=

The best product is=