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MOTHER THERESA INSTITUTE OF PHARMACEUTICAL EDUCATION & RESEARCH

miperknlapindia@gmail.com

PHYSICAL PHARMACEUTICS - I
LAB MANUAL

(B. Pharm 2nd Year- 3rd Semester)

INDEX

EXERCISE NO – 1

Aim - To determine the solubility of drug at different temperature,

Reference – R.S. Gaud and G.D. Gupta; Practical Physical Pharmacy; CBS Publication & Distributer Pvt.; First Edition, (2019) pp110-111

Requirements

Chemicals/reagents

• Pure inorganic salts (KCI, NaCl, NaNO,,K,SO, etc.)
• Distilled water

Equipments/Glasswares

• Thermostat
• Thermometer
• Porcelain dishes or watch glasses
• Beaker (50 ml, 100 ml, and 250 ml)
• Pipette (10 ml)
• Hot plate

Procedure

1. Clean all glasswares using detergent solution and chromic acid solution.
2. Wash two to three times using purified water.
3. Take 50 ml of distilled water in a beaker (100 ml).
4. Add some amount of salt like potassium chloride or sodium chloride in distilled water and stir using glass rod or by an electric motor driven shaker.
5. Increase the temperature to 85°C with contineous stirring.
6. Maintain this temperature for few minutes and then cool down the solution.
7. Take sample at 80°C using a pipette with a piece of filter paper, tie at the tip of the pipette.
8. Remove the piece of filter paper from the tip of pipette and transfer 10 ml of this solution in weighed porcelain dish or watch glass.
9. Allow the temperature to fall down slowly to 70°, 60°, 40°, 30°C and then to room temperature.
10. At each temperature take sample of the solution and repeat the step 7 and step8
11. Evaporate the solution of each porcelin dish or watch glass using direct heat or on the water bath or put in the oven.
12. Dry the solution till constant weight.
13. Take weight of the dish using double pan balance or Chernical balance and excite weight of the powder
14. Record all the parameter in the form of table or in proper way so that it was easy to understand the concept of solubility,

Observations

Observation table –

Sl. No.	Temperature (^oC)	Weight of of empty dish w_1g	Weight of empty dish + solution w_2g	Weight dish + residue W_3g	Weight of residue $W_3 - W_1$g	Weight of solvent $W_2 - W_3$g	Solubility in g/100g
1	80						
2	70						
4	60						
5	50						
6	30						
7	RT						
8	20						
9	10						
10	5						

Calculations

Solubility of salt in solvent at temperature (°C) is calculated by the following formula in g/100g

Solubility of salt at 80°C = $\frac{W3 - W1}{W2 - W3g} \times 100$

Result

Solubility of the given salt at room temperature (considering the saturated solutions at room temperature) ---- %. Plot the graph between solubility and temperature. The graph will show a smooth curve without any break.

Experiment No. 2

Aim – To determine the pka value of a weak acid by titrating it against base potentiometrically (using a pH meter)

Theory – When acitic acid is titrated against strong base it forms a mixture of acid and its salt. The mixture acts as a buffer solution. During the course of titration acid concentration decreases and salt concentration goes on increasing. During any stage of titration the pH of buffer solution is explained by the Henderson – Hasselbalch equation.

$$pH - pK_a - \log [Salt][Acid] \ldots\ldots\ldots\ldots (1)$$

Where, $pK_a = - \log K_a$ and K_a = dissociation constant of the acid

[Salt] = concentration of salt CH_3COONa

[Acid] = concentration of acid CH_3COOH

At the half neutralization point [Salt] - [Acid]

And equation (1) above gives $pH = pK_a$

Requirements –

Chemicals – 0.04N acetic acid
0.04N NaOH (Standard)
Buffer solution of known pH

Apparatus – Burette
Beakers
Stirrer
pH meter

Procedure –

Standardize the pH meter by the use of buffer solution of known pH. Pipette out 25ml of 0.04N acetic acid solution in a dry beaker. Dip the electrode into the acid. Measure the pH. Add from the burette 1ml of 0.04N NaOH and stir. Measure the pH (do not remove the glass rod used for stirring). Continue addition of 1ml of NaOH till there is sudden change in pH and thereafter take at least three more readings. After each addition measure the pH.

Observations –

Room temprature =-------^{O}C

Vml of 0.04N	pH	dpH	dV	$\frac{dpH}{dV}$	Total volume ml	dB	$\beta = dB/dpH$

Graph

- Plot the graph of pH V3 volume of 0.04N NaOH 'V'.
- To determine exact end point plot $\frac{dpH}{dV}$ vs V
- Plot a graph of β vs pH. Find the pH at which β is Maximum.

Calculation –

Read the end point of the titration from graph (2). Let it be x ml of 0.04N NaOH; Now from graph (1) read the pH for V = $\frac{x}{2}$, i.e. read the pH of the half neutralization stage at which [salt] =[Acid] and equation (1) pH = pKa

Therefore Ka =

Calculation of dB-

Since 1000ml of NaOH = 1 equivalent of NaOH

Therefore 2ml of 0.04N NaOH = (2x1x0.04)(25x1000) equivalent of NaOH

If 'x' ml of 0.04N NaOH is added to 25ml of 0.04N acetic acid solution, the total volume of the solution is (25 - x) ml and gram equivalent of NaOH per liter of solution added per 2ml increment in NaOH is,

dB = (2x1000){(25x 1000) (25-x)}=2/25 x total volume

Result

The buffer capacity (β_{max}) at room temprature

pKa of acetic acid = --------at room temprature

Ka for acetic acid = ------- at room temprature

EXERCISE NO. – 3

Aim – To determine the partition coefficient of Succinic acid between benzene and water

Requirements

Chemicals/reagents

- Benzene & Succinic acid
- 0.05 M sodium hydroxide

Equipments/glasswares

Separating funnel
Conical Flask
Burette
Pipette
Reagent Bottles

Procedure

1. Take three reagent bottles and clean these bottles by reagent and rinse through the distilled water.
2. Prepare composition of the solution as given in the table.
3. Transfer these solution in clean and dry reagent bottles and fix the label A, B, and C respectively.
4. Place the stopper on each bottle and shake it for 30 min.
5. Place the stopper on each bottle and shake it for 30 min. or shake using wrist action shaker and rotatary shaker.
6. Variability of the result depends on the shaking hence more and effective shaking is essential for reproducible results.
7. Now take this mixture in separating funnel and keep aside for about to 30 min.
8. Separate carbon tetrachloride and aqueous layer in two conical flasks:
9. Intermediate liquid cannot be collected as it contain little of both liquids.
10. Put the label on both conical flasks with the samples taken originally.
11. Pipette out 10 ml of the aqueous layer and transfer in another conical flask.
12. Separate two layers by separating funnel.
13. Withdraw 10 ml sample of organic layer in conical flask.
14. Add 2 to 3 drops of phenolphthalein as an indicator and titrate it using 0.05 M NaOH.
15. Repeat the above three steps and similarly titrate with Benzoicacid layer.
10. Withdraw 10 ml of aqueous layer and follow steps 15 - 16.
11. Record all estimation values carefully.

Observations

Table A. - Titration of aqueous layer

S. No.	Container	Volume (ml)	Burette reading		Volume used of 0.05M Sodium hydroxide (ml)
			Initial	Final	
1.					V_1
2.					V_2
3.					V_3

Table B. Titration of of organic layer

S. No.	Container	Volume (ml)	Burette reading		Volume used of 0.05M Sodium hydroxide (ml)
			Initial	Final	
1.	A'				V_1'
2.	B'				V_2'
3.	C'				V_3'

Calculation

(a) For aqueous layer

Concentration of Succinic acid in container A

$$N_1V_1 = N_2V_2$$

$$N_1 = 0.01xV_2/10$$

Concentration of Succinic acid in water layer (C_1)

$$C_1 = (0.01xV_2 x127)/10 \text{mole/liter}$$

Similarly calculate the concentration of Succinic acid in other flask (B and C)

(b) For organic layer

Concentration of Succinic acid in container A

$$N_1'V_1' = N_2'V_2'$$

$$N_1' = 0.01xV_2'/10$$

Concentration of Succinic acid in water layer (C_1)

$$C_2 = (0.01xV_2' x127)/10 \text{mole/liter}$$

Similarly calculate the concentration of Succinic acid in other flask (B' and C')

Partition Coefficient $K = C_2/C_1$

Result

The partition coefficient of succinic acid between in and distilled water = ----

EXERCISE NO. 4

Aim - To determine the partition coefficient of iodine between carbon tetrachloride and distilled water

Requirements

Chemicals/reagents

- Carbon tetrachloride
- Iodine
- Distilled water

Equipments/glasswares

- Separating funnel
- Conical flask
- Burette
- Pipette
- Reagent bottles

Procedure

1. Prepare a saturated solution of iodine in carbon tetrachloride (stock solution).
2. Take three reagent bottles and clean these bottles by reagent and rinse with it distilled water.
3. Prepare composition of the solution as given in the table.
4. Transfer these solution in clean and dry reagent bottles and be it as A, B, and C respectively.
5. Place the stopper on each bottle and shake it for 30 min. or shake using wrist action shaker and rotatory shaker.
6. Variability of the result depends on the shaking hence more and effective shaking is essential for reproducible results.
7. Now take this mixture in separating funnel and keep aside for about to 30 min.
8. Separate carbon tetrachloride and aqueous layer in two conical flasks:
9. Intermediate liquid cannot be collected as it contain little of both liquids.
10. Put the label on both conical flasks with the samples taken originally.
11. Pipette out 10 ml of the aqueous layer and transfer in another conical flask.
12. Add 2 to 3 drops of starch solution and titrate it against 0.01sodium thiosulphate solution
13. Record the titration value and repeat the steps10 and 11
14. Similarly, titrate the aqueous layer from other containers
15. Pipe 10 ml of carbon tetrachloride layer in a dry and dean comical flask
16. Add starch solution 2 to 3 drops as an indicator and estimate concentration of iodine by time with 0.01N sodium thiosulphate solution
17. Repeat the step 15 and 16 till get constant burette reading.
18. Similarly, titrate other cartoon tetrachloride solution as step 15 to 17
19. Take all readings carefully
20. Calculate concentration of iodine in both phases i.e. aqueous and organic phase.

Table- A Preparation of solution

S. No.	Container	Composition
1.	A	25ml stock solution + 100ml distilled water
2.	B	15ml stock solution + 10ml pure CCl_4 ++ 100ml distilled water
3.	C	5ml stock solution +20ml pure CCl_4 ++ 100ml distilled water

Observations

Table A. - Titration of aqueous layer

S. No.	Container	Volume (ml)	Burette reading		Volume used of 0.05M Sodium hydroxide (ml)
			Initial	Final	
1.					V_1
2.					V_2
3.					V_3

Table B. Titration of of organic layer

S. No.	Container	Volume (ml)	Burette reading		Volume used of 0.05M Sodium hydroxide (ml)
			Initial	Final	
1.	A'				V_1'
2.	B'				V_2'
3.	C'				V_3'

Calculation

(c) For aqueous layer

Concentration of Succinic acid in container A

$$N_1V_1 = N_2V_2$$

$$N_1 = 0.01xV_2/10$$

Concentration of Succinic acid in water layer (C_1)

$$C_1 = (0.01xV_2 x127)/10 \text{mole/liter}$$

Similarly calculate the concentration of Succinic acid in other flask (B and C)

(d) For organic layer

Concentration of Succinic acid in container A

$$N_1'V_1' = N_2'V_2'$$

$$N_1' = 0.01xV_2'/10$$

Concentration of Succinic acid in water layer (C_1)

$$C_2 = (0.01xV_2' x127)/10 \text{mole/liter}$$

Similarly calculate the concentration of Succinic acid in other flask (B' and C')

Partition Coefficient $K = C_2/C_1$

Result

The partition coefficient of iodine between carbon tetrachloride and distilled water = ------

EXERCISE NO. 5

Aim - To determine surface tension of liquid using stalagmometer.

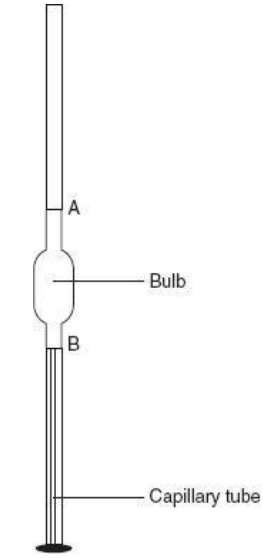
Requirements

Chemicals/reagents

- Distilled water
- Ethyl acetate
- or benzene
- or nitrobenzene
- or toluene
- or carbon tetrachloride

Equipments/glasswares

- Pycnometer
- Thermometer
- Beaker 100 ml, and 250ml
- Burette stand
- Weight box
- Weighing balance



stalagmometer.

Procedure

1. Thoroughly clean the pycnometer and stalagmometer using chromic acid and purified water or as because surface tension is highly affected with grease or other lubricants
2. Stalagmometer must be mounted in the vertical plane using burette stand.
3. Fill the purified water in the instrument and count the number of drops falling down between two points of the instrument as shown in Fig.
4. Repeat the step-3 at least three times.
5. Rinse the stalagmometer using the same liquid of which surface tension is to be determined.
6. Fill the stalagmometer by liquids and count the number of drops formed between two points as step 3
7. Repeat the steps 6 at least three times for accuracy.
8. Density of the liquid is determined using pycknometer as given in experiment 2.2 at the same temperature

Observations

(a) Temperature (room temperature)= t°C
(b) Weight of empty pycnometer= Wi
(c) Weight of pycnometer + distilled water= W2
(d) Weight of pycnometer + liquid= W3

Observation table

Liquid	Number of drops				Specific gravity	Surface tension
	(i)	(ii)	(iii)	Mean		
Water				n_1		
Liquid				n_2		

Calculation

(a) Weight of liquid =W_3 - W_1

(b) Weight of distilled water = W_2 - W_1

(c) Specific gravity of liquid (P2/P1) = ($W3 - W_1$)/($W_2 - W_1$)

$$\gamma_2 = \frac{f_2\, n2}{f_1\, n1} \times \gamma_1$$

Calculate the surface tension of liquid by this equation, yi is the surface tension of water obtain from the table (appendix)

Result

Surface tension of given liquid at room temperature (t°C) = -------- dynes/cm

Experiment No. 6

Aim- To determine the composition of NaCl in a solution using phenol – water system by critical solution temperature (CST) method

Requirements –

Chemicals: Phenol in liquid state
Sodium chloride

Apparatus: Test tube
Thermometer
Beaker
Stirrer
Water bath

Procedure –

1. Weigh accurately 1gm of NaCl for making the stock solution.
2. Take clean test tube and transfer the NaCl solution 0.0ml, 0.2ml, 0.4ml, 0.6ml, 0.8ml and 1.0ml solution in different test tube.
3. Makeup the volume upto 10ml each test tube by adding distilled for making the concentration of 0.0%, 0.2%, 0.4%, 0.6%, 0.8% and 1.0%.
4. Take pure phenol in the liquid form concentration of 80%v/v.
5. In another test tube add 2.5ml liquid phenol and add 2.5ml of different concentration of NaCl solution in each test tube.
6. The two layers will form.
7. Heat the test tube in a water bath, for measuring the temperature put the thermometer in the test tube.
8. Record the temperature at which the layers of liquid disappears

Observations-

Sl. No.	Conc. of NaCl w/v	Temp. at which the layer disappear (t_1)	Temp. at which the layer reappear (t_2)	$CST = (t_1 + t_2)/2$
	0.0			
	0.2			
	0.4			
	0.6			
	0.8			
	1.0			
	Unknown			

Graph – plot a graph of transition temperature vs concentration of NaCl find the conc. of unknown sample.

Result – Critical temperature of NaCl unknown concentration solution for phenol water system is -----.

Experiment No. 7

Aim – To determine the HLB number of surfactant by saponification method.

Theory – The hydrophilic-lipophilic balance of a surfactant is a measure of the degree to which it is hydrophilic or lipophilic, determination by calculating values for the different religions of the molecule, as described by ***Griffin*** in 1949 and 1954.

Griffin's Method

Griffin's Method for non – ionic surfactants as described as described in 1954 work as follows:

$$HLB = 20\ (1 - \frac{S}{A})$$

Where S = saponification number
A = Acid number

$$HLB = 20 \times \frac{Mh}{M}$$

Where Mh is the molecular mass of the hydrophilic portion of the molecule and M is the molecular mass of the hole molecule, giving a result on a scale of 0 to 20. An HLB value of 0 corresponds to a completely lipophilic/ hydrophobic molicule and a value of 20 corresponds to complete hydrophilic/ lipophobic molicule.

Chemicals – Distilled water,
Fatty acid ester e.g. Glyceryl monostearate (GMS),
0.5N Alcoholic Potassium hydroxide (KOH)
Stearic Acid, ether,
0.5N Hydrochloric Acid (HCl)
0.1N Sodium Hydroxide (NaOH)
Phenolphthalein indicator.

Apparatus – Round bottom flask
Reflex Condenser
Beakers
Burette
Pipette
Conical Flask.

Procedure –

1. ***Prepararion of 0.5N alcoholic KOH***
   Dissolve around 4gm of KOH in 3-5ml distilled water in a volumetric flask and make up total volume to 100ml with alcohol. Allow it to stand for about 24 hours and separate out clear liquid by decantation. Use this solution for experiment. Alcoholic KOH is used

because surfactents are freely soluble in alcohol than in water. The solubility improved by alcohol hydrolysis is effective one.

2. ***Determination of saponification number –***
   Weigh accurately 0.5g of Glyceryl monostearate (GMS) and transfer into round bottom flask, add 15ml of alcoholic potassium hydroxide to it and reflux on boiling water both for about half an hour.
   Reflux seperately 15ml of alcoholic potassium hydroxide (without GSM) on boiling water bath for about an hour blank reading.
   Cool both the solution to room temprature and titrate separately against 0.5N hydrochloric acid using phenolphthalein as the indicator.
   (End point: pink to colourless or slightly yellowish)
   Let the titer reading for sample (GMS) be V_1 and blank be as V_2.

3. ***Determination of acid number –***
   Weigh accurately 0.5g of stearic acid, add it to a mixture of 10ml of alcohol. If stearic acid does not dissolve in the solvent mixture, warm it on water bath until it dissolves.
   (Note – take care while warming, since alcohol are highly inflamable liquid).
   Titrate solution of stearic acid against 0.1N sodium Hydroxide using phenophthalein as the indicator.
   Let the titrate reading be V_3.

Observations

1. Saponification number = _____
   (i) Volume of 0.5N HCl consumed by sample (V_1) =_____ml
   (ii) Volume of 0.5N HCl consumed by sample (V_2) =_____ml

2. Acid number =
   Volume of 0.1N sodium hydroxide consumed (V_3) =_____ml

Calculations

1. ***Calculation for saponification number:***

   1000ml of 1N KOH = 56000mg of KOH

   ($V_2 – V_1$) ml of 0.5N KOH mg of KOH/0.5g GMS

   Substute values of V1 and V2 to determine saponification number mg of KOH/g of GMS saponification value -------

2. ***Calculation for acid number:***
   V_3 ml of 0.1N NaOH 0.5g of stearic acid

   $2V_3$ ml of 0.1N NaOH 0.5g of stearic acid

(1000ml of NaOH = 1000ml of KOH 56000mg of KOH)

$2V_3$ ml of 0.1N KOH

Substitute value of V_3 and calculate the acid number.

Acid number = --------

3. ***Calculation of HLB Value:***

$$HLB = 20\ (1 - \frac{S}{A})$$

Where S = saponification number

A = Acid number

Result -

The HLB Value of given surfactant was found to be_____.