Experiment 1

Hydrotropy Studies

A hydrotrope is a compound that solubilises hydrophobic compounds in aqueous solutions (by means other than micellar solubilization). The term *hydrotropy* was originally put forward by Carl Neuberg to describe the increase in the solubility of a solute by the addition of fairly high concentrations of alkali metal salts of various organic acids. However, the term has been used in the literature to designate non-micelle-forming substances, either liquids or solids, organic or inorganic, capable of solubilizing insoluble compounds. The chemical structure of the conventional Neuberg's hydrotropic salts (proto-type, sodium benzoate) consists generally of two essential parts, an anionic group and a hydrophobic aromatic ring or ring system. The anionic group is involved in bringing about high aqueous solubility, which is a prerequisite for a hydrotropic substance. The type of anion or metal ion appeared to have a minor effect on the phenomenon. Additives may either increase or decrease the solubility of a solute in a given solvent. These salts that increase solubility are said to 'salt in' the solute and those salts that decrease the solubility 'salt out' the solute. The effect of an additive depends very much on the influence it has on the structure of water or its ability to compete with the solvent water molecules. A convenient quantitation of the effect of a solute additive on the solubility of another solute may be obtained by the Setschetow equation:

$$\text{Log } \frac{S_o}{S} = K.Ca$$

where

S_o = solubility in the absence of additive

S = solubility in the presence of additive

C_a = concentration of additive

K = salting coefficient, which is a measure of the sensitivity of the activity coefficient of the solute towards the salt.

The study on solubility yields information about the structure and intermolecular forces of drugs. Use of the solubility characteristics in bioavailability, pharmacological action and solubility enhancement of

various poorly soluble compounds is a challenging task for researchers and pharmaceutical scientists. Hydrotropy is one of the solubility enhancement techniques which enhance solubility to many folds with use of hydrotropes like sodium benzoate, sodium citrate, urea, niacinamide etc. and have many advantages like; it does not require chemical modification of hydrophobic drugs, use of organic solvents, or preparation of emulsion system etc. Solubility enhancement of various poorly soluble compounds is a challenging task for researchers and pharmaceutical scientists. The study on solubility yields information about the structure and intermolecular forces of drugs. Drug efficacy can be severely limited by poor aqueous solubility and some drugs also show side effects due to their poor solubility. There are many techniques which are used to enhance the aqueous solubility. The ability to increase aqueous solubility can thus be a valuable aid to increase efficiency and/or reduce side effects for certain drugs. This is true for parenterally, topically and orally administered solutions.

Object

Study of effect of solvent / cosolvent hydrotropic agents on solubility of given drug.

References

1. Maheshwari, RK., Solubilization of ibuprofen by mixed solvency approach, The Indian Pharmacist, 2009, vol VIII, No.87; 81-83.
2. Maheshwari RK, Chavada V, Sahoo K, and Varghese S., Novel application of hydrotropic solubilization in the spectrophotometric analysis of diclofenec sodium in solid dosage forms, Asian Journal of Pharmaceutics, 2006, vol I, Issue; 30-33.

Principle

Development of drug formulations for poorly soluble drugs is undoubtedly very important for producing patient-friendly formulations with high bioavailability. The bioavailability may be enhanced by increasing the solubility of the drug. There are different drug solubilization techniques. Such as, pH adjustment, micronization, micellar solubilization, co solvency and salting in, hydrotropy etc. Hydrotropes, co-solvents and water soluble solutes have been observed to enhance the aqueous solubility of poorly water soluble drugs. It has been demonstrated that synergistic effect can be obtained by mixed solvency concept. The use of hydrotropy can be utilized in titrimetric and spectrophotometric estimation of a large number of poorly water soluble drug substances. The mixed solvency approach discourages the use of organic solvents in large concentration (which may prove toxic) for development of a dosage form.

Requirements

Apparatus: UV Spectrophotometer, Beaker, Measuring cylinder, Volumetric flask & Stirrer.

Chemicals: Distilled water, Urea, PEG-400, PEG-6000, PEG-200 & PEG-4000.

Procedure

1. Accurately weigh 40 mg of Diclofenec sodium and transfer to 50 mL volumetric flask.
2. To this, add 40 mL of distilled water.
3. Shake the flask to dissolve the drug and make up the volume with distilled water.
4. Dilute the stock solution with distilled water to obtain various dilutions containing between 10-60 µg/mL.
5. Note absorbance at 276nm against reagent blanks to get the calibration curve.
6. Prepare blend (40%w/v constant) of solubilizers using varying concentrations of the solvents as shown below for Blends (1-4). Blend-1 containing urea, PEG400, PEG6000 and Sodium acetate, Blend- 2 contains urea, PEG4000, PEG200 and Sodium acetate, Blend -3 contains urea, PEG200, PEG400 and Sodium acetate and Blend- 4 contains urea, PEG400, PEG6000 and Sodium acetate.

Table 1 Blends and their Compositions

S. No.	Ingredients	% used in Blends			
		1	2	3	4
1	Urea	15	15	10	10
2	Sodium acetate	10	10	15	15
3	PEG 200	---	15	---	15
4	PEG 400	15	10	15	---
5	PEG 4000	---	---	10	---
6	PEG 6000	10	---	---	10

Observations

Table 2 Solubility of Drug in Purified Water.

S. No.	Concentration	Absorbance
1	10 ug/mL	
2	20 ug/mL	
3	30 ug/mL	
4	40 ug/mL	
5	50 ug/mL	

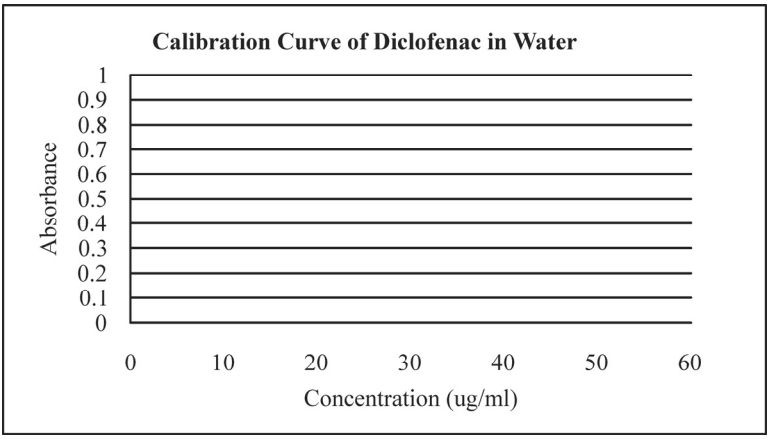

Fig. 1 Calibration curve of Diclofenac sodium in water.

Table 3 Solubility of Diclofenac Sodium in Different Blends.

S. No.	BLEND NO.	Absorbance	Saturated Solubility
1	BLEND NO. 1		
2	BLEND NO. 2		
3	BLEND NO. 3		
4	BLEND NO. 4		