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SHORT COMMUNICATION

NOVEL APPLICATION OF MIXED SOLVENCY CONCEPT IN ECOFRIENDLY QUANTIATIVE ANALYSIS OF BULK DRUG OF DICLOFENAC SODIUM

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ABSTRACT

'Mixed-solvency ' concept is the phenomenon to increase the solubility of poorly water-soluble drugs in the aqueous solution containing blends of hydrotropic agents, co-solvents and water soluble solutes which may give synergistic enhancement effect on solubility of such drugs. In the present study mixed –solvency concept has been applied for the enhancement of aqueous solubility of a poorly water-soluble drug diclofenec sodium(selected as a model drug) by making blends of randomly selected water-soluble substances from among the hydrotropes (urea, sodium citrate) ; water soluble solutes(PEG4000, PEG6000); and co-solvents(PEG300,PEG400). The aqueous solubility of diclofenac sodium was observed at room temperature in the randomly selected blends of different combinations keeping total concentration 30%w/v constant. Quantitative analysis of bulk drug diclofenec sodium was done by u.v. spectrophotometric estimation at λmax at 276 nm in concentration range of 15-90 µg/ml . The results suggests significant enhancement in the solubility of the poorly water soluble drug sample containing different combinations of such substances (blends).

Key words: poorly water-soluble drugs, solubility, mixed solvency.

INTRODUCTION

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 spectrophometric 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 forms. A number of solubilizers may be taken in small concentration curtailing their toxic levels and shows significant improvement in the solubility of the of poorly water soluble drugs[1-9].

MATERIALS UNDER METHODS

Gift sample of drug Diclofenac sodium was procured from M/s Aerrow pharmaceuticals, Indore, M.P. All the chemicals and solvents used were of analytical grade. Distilled water was used to prepare the solutions of solubilizers. A spectrophotometer (UV-1700 Shimadzo) was used for quantitative analysis.

METHODS

Preparation of calibration curve of Diclofenac sodium: 40 mg of Diclofenac sodium was accurately weighed and transferred to 50 ml volumetric flask. To this 40 ml of distilled water was added. The flask was shaken to solubilize the drug and volume was made upto the mark with distilled water. The stock solution was further diluted with distilled water to obtain various dilutions containing between 15-90 µg/ml. Absorbance was noted at 276nm against reagent blanks to get the calibration curve. The Solubilityof diclofenec sodium in distilled water was observed and shown in Table (1).

ANALYSIS OF DICLOFENAC SODIUM (API) BY PROPOSED METHOD:

A blend (30%w/v constant) of solubilizers was prepared by using varying concentrations of the solvents as shown below for Blends (1-4)

Blend 1

Solvent	Concentration
Urea	7.5%
PEG 4000	7.5%
Sodium acetate	7.5%
PEG 300	7.5%

Blend 2

Solvent	Concentration
Urea	10%
PEG 6000	8%
PEG4000	6%
PEG 400	6%

Blend 3

Solvent	Concentration
Ureat	10%
Sodium acetate	4%
PEG 6000	12%
PEG 300	4%

Blend 4

Solvent	Concentration
Urea	12%
PEG300	8%
PEG400	5%
Sodium acetate	5%

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Bulk drug was first dissolved in 10ml of blend 1.The solution was vigorously shaken for a definite time with regular intervals until a supersaturated solution is obtained. The resulting solution was diluted upto 1000ml with the blend. Absorbance of this solution was noted at 276nm against the solvent blend. The same procedure was followed with the other blends (2-4) and absorbance was noted at the same wavelength. The corresponding concentration gives the solubility of the drug and thus the enhanced solubility of the drug was calculated by comparing the solubility of the drug in water.

RESULTS AND DISCUSSION

The results obtained are shown in Table (1) for Solubility of diclofenec sodium in water as well as in Table (2) Solubility of diclofenec sodium in different blends (1-4). It is evident that there was improvement in the solubility of diclofenac sodium in (30% blend) containing different combinations of urea, PEG4000, PEG6000, PEG300, PEG400 and sodium acetate. On comparing Table-1 and Table-2, the drug solubility was found to be enhanced by 1.83, 2.57, 3.08 and 3.2 folds with blend-1, 2, 3 and 4 respectively. The greatest enhancement in solubility was observed in case of Blend 4 and least in case of Blend 1.

Table 1: Solubility in distilled water

S. N.	Solvent system (Distilled water)	Absorbance
1	30µg/ml	0.72
2	60 µg/ml	0.86
3	90 µg/ml	0.98

Table 2: Solubility in blends

S.No.	Blend number	Absorbance	Saturated solubility
1	Blend 1	1.176	110µg/ml
2	Blend 2	1.463	154µg/ml
3	Blend 3	1.692	185µg/ml
4	Blend 4	1.731	192µg/ml

These results demonstrate the principle of mixed-solvency concept that water-soluble substances whether hydrotropes or solvents or water-soluble solids combined randomly gives a desired solubility for a poorly water-soluble drugs. The results also suggests that in developing liquid dosage forms, blends of solubilizers can be employed to reduce the toxicities of solubilizers by reducing the individual concentration of solubilizers (instead of employing one solubilizer in higher concentration which may be toxic for same solubility enhancement).Blends of water soluble substances can be made in safe level of concentrations of individual solubilizer to give a concentrated solution to act as solubilizing system for development of liquid syrups or topical solutions or injections etc.

CONCLUSION

The solubility of the Diclofenac Sodium containing different combinations of urea, PEG4000, PEG6000, PEG300, PEG400 and sodium acetate was enhanced significantly, using this mixed-solvency approach. Therefore the results suggest that mixed –solvency approach for the enhancement of solubility of poorly water-soluble sample drug can also be used successfully for other poorly-water soluble drugs.

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