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Research Article

NOVEL APPLICATION OF MIXED SOLVENCY CONCEPT USING POORLY WATER SOLUBLE DRUG DICLOFENAC SODIUM

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ABSTRACT

Poor water solubility of drugs often causes significant problems in producing formulations of sufficiently high bioavailability, preventing effective use of the drugs. '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 diclofenec sodium was selected as a model drug for the enhancement of aqueous solubility by mixed –solvency concept. It was achieved by making blends of randomly selected water-soluble substances from among the hydrotropic (urea, sodium citrate); water soluble solutes (PEG400, PEG6000); and co-solvents (PEG200, PEG4000). The aqueous solubility of diclofenac sodium was observed at room temperature in the randomly selected blends of solubilizers containing different combinations keeping total concentration 40%w/v constant. Diclofenec sodium have λmax 276 nm and obeys Beers Law in concentration range of 10-60 µg/ml. The results suggest that solubility of the diclofenac sodium containing urea, PEG and sodium acetate (blends) was enhanced significantly using mixed solvency approach.

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

INTRODUCTION

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. Some authors presented detailed review on different drug solubilization techniques. They are 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 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. Purified water was used to prepare the solutions of solubilizers. A spectrophotometer (UV-1700 Shimadzo) was used for quantitative analysis.

Methods

Diclofenac sodium (40 mg) was accurately weighed and transferred to 50 ml volumetric flask. To this 40 ml of distilled water was added. The flask was shaken to dissolve 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 10-60 µg/ml. Absorbance was noted at 276nm against reagent blanks to get the calibration curve. The Solubility of diclofenec sodium in distilled water was observed and shown in Table (1).

Analysis of Diclofenac sodium (API) by proposed method

A blend (40%w/v constant) of solubilizers was prepared by 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.

BLEND-1

HYDROTROPE	PERCENTAGE
Urea	15%
PEG-400	10%
PEG-6000	7.5%
Sodium acetate	7.5%

BLEND-2

HYDROTROPE	PERCENTAGE
Urea	12%
PEG-4000	8%
PEG-200	15%
Sodium acetate	5%

BLEND-3

HYDROTROPE	PERCENTAGE
Urea	18%
PEG-200	7%
PEG-400	7%
Sodium acetate	8%

BLEND-4

HYDROTROPE	PERCENTAGE
Urea	20%
PEG-400	8%
PEG-6000	7%
Sodium acetate	5%

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 i.e. blend2, blend3 and blend4 respectively and absorbance were 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 (2). From the table it is evident that there was improvement in the solubility of diclofenac sodium in 40% blend containing urea, PEG-200, PEG-400, PEG-4000, PEG-6000 and sodium acetate in varying concentrations. On comparing Table-1 and Table-2 the drug solubility was found to be enhanced by 1.7, 3.03, 3.4 and 3.6 folds with blend-1, blend-2, blend-3 and blend-4 respectively. The greatest enhancement in solubility was observed in case of Blend 4 and least in case of Blend 1.

These results demonstrate the principle of mixed-solvency concept that water soluble substances whether hydrotropic or solvents or water-soluble solids can be combined randomly in varying concentrations to give a desired solubility to poorly water-soluble drugs. Blends of water soluble substances can be prepared in safe level of concentrations of individual solubilizers to give a concentrated solution to act as solubilizing system for development of their different dosage forms.

Table 1: Solubility of Diclofenac sodium in water

S. No.	Concentration	Absorbance
1	10µg/ml	0.27
2	30µg/ml	0.75
3	60 µg/ml	0.85

Table 2: Solubility of Diclofenac sodium in different blends

S. No.	Blend	Absorbance	Saturated solubility
1	Blend-1	1.132	102 µg/ml
2	Blend-2	1.595	182 µg/ml
3	Blend-3	1.831	204 µg/ml
4	Blend-4	1.881	218 µg/ml

CONCLUSION

The solubility of the diclofenac sodium containing different combinations of urea, PEG-200, PEG-400, PEG-4000, PEG-6000 and sodium acetate in varying concentrations 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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