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Research Article

NEW SPECTROPHOTOMETRIC ESTIMATION OF NAPROXEN TABLETS FORMULATIONS EMPLOYING MIXED SOLVENCY CONCEPT (AT 331NM)

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Abstract

The present investigation illustrates the application of mixed solvency. There was a synergistic effect on enhancement in solubility of poorly water soluble drug naproxen by mixing hydrotrops. Various organic solvents like methanol, chloroform, ethanol, acetonitrile, hexane, toluene are widely used to conduct the spectrophotometric analysis, But higher cost and toxicity prevents their frequent use. The enhancement of solubility of naproxen was more than 79 fold in one blend containing Sodium benzoate - 8% w/v, PEG300 - 3% w/v, PEG6000 - 7% w/v, Glycerin -7% w/v, Propylene glycol - 3% w/v and Niacinamide - 2% w/v as compared to solubility in distilled water.

In the present study mixed blend were employed for the spectrophotometric estimation of naproxen at 331nm. The results of the analysis were validated statistically and by recovery studies. The drug follows Beer's law in concentration range of 50-300 mcg/ml. The percent label claims and percent recoveries estimated were close to 100 with low values of standard deviation. Thus the statistical data proved the accuracy, reproducibility and precision of the proposed method. The mixed solvency concept used in the present study did not interfere in the analysis.

Key Words: Mixed solvency, Salicylic acid, PEG 400, PEG 4000, Propylene glycol.

Introduction

Naproxen sodium (NAS) is a non-steroidal anti-inflammatory drug used to relieve moderate to severe aches and pains. Most of its therapeutic activity is probably mediated through prostaglandin synthesis inhibition[1].

Mixed solvency is the term originally put forward by Neuberg[2] 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. Mixed solvency process involves cooperative intermolecular interaction with several balancing molecular forces, rathe than either a specific complexation event or a process dominated by a medium effect, such as co-solvency or salting-in. Mixed solubilizers have been observed to enhance the aqueous solubility of poorly water-soluble drugs[4-14].

Mixed solvency technique is the phenomenon to increase the solubility of poorly water-soluble drugs, using blends of hydrotrops[15]. This technique can provide additive or synergistic enhancement effect on solubility of poorly water-soluble drugs. Utilization of this method in the formulation of dosage forms made of water insoluble drugs can also reduce the concentration of individual hydrotropic agents, in order to minimize the side effects (in place of using a large concentration of one hydrotrope, a blend of several hydrotropes can be employed in much smaller concentrations, reducing their individual toxicities).

The objective of the present study is to explore the application of mixed hydrotropic solubilization technique to analyze bulk sample salicylic acid using spectrophotometrically. In the present work, salicylic acid, a non-steroidal anti-inflammatory agent was selected as a model drug which is a BCS class II drug (highly permeable and low soluble).

Materials and Methods

All chemicals and solvent used were of analytical grade. Naproxan was obtained as gift sample from Alkem Lab. Ltd., Mumbai.

1. Preparation of calibration curve

50 mg of naproxen bulk drug was solubilized with 40 ml of mixed hydrotropic solution, Sodium benzoate - 8% w/v, PEG300- 3% w/v, PEG6000 – 7% w/v, Glycerin – 7% w/v, Propylene glycol – 3% w/v and Niacinamide

2% w/v and then diluted with 50 ml distilled water to obtain various dilution (50, 100, 150, 200, 250, 300 µg/ml). Absorbance were measured at 331 nm against corresponding reagent blanks. Linear relationship was observed.

2. Preliminary solubility studies of drug: Solubility of naproxen was determined in distilled water and mixed hydrotropic solution, Sodium benzoate - 8% w/v, PEG300- 3% w/v, PEG6000 – 7% w/v, Glycerin – 7% w/v, Propylene glycol – 3% w/v and Niacinamide 2% w/v at room temperature. Enhancement in the solubility of naproxen in mixed hydrotropic blend was more than 79 fold as compared to solubility in distilled water.

3. Analysis of Naproxen tablets using mixed hydrotropic solution

Twenty tablets of naproxen (formulation-I) were weighed and ground to fine powder. Accurately weighed powder sample equivalent to 50 mg of naproxen was transferred to 50 ml volumetric flask containing 40 ml of mixed hydrotropic. The flask was shaken for about 10 min & volume was made up to the mark with distilled water. The solution was filtered through Whattman filter paper No.41. The filtrate was diluted with distilled water and analyzed on UV spectrophotometer at 331 nm against reagent blank. Drug content of tablet formulation was then calculated. Same Procedure was followed for formulation-II.

4. Recovery studies

To evaluate the validity and reproducibility of the proposed method, recovery experiments was carried out. For recovery studies 15 to 30 mg of Naproxen pure drug was added to the pre-analyzed tablet powder equivalent to 50 mg naproxen. Procedure of analysis was same using mixed hydrotropic solution. Percent recoveries were calculated.

Result and Discussion:

Solubility determination studies indicated that enhancement in aqueous solubility of naproxen in mixed hydrotropic solution were more than 79 fold as compared to solubility in distilled water. It is evident from Table-1 that the mean percent label claim estimated were 99.81 and 98.08 for formulation I & II respectively. The mean percent label claim are very close to 100 with low value of standard deviation, percent coefficient of variation and standard error showing the accuracy of the proposed method.

Table-1: Analysis of marketed tablets of Naproxen with statistical evaluation (n=3).

Tablet Formulation	Label claim(mg/tablet)	% Drug estimated(mean ±SD)	% coefficient of variation	Standard Error
I	250	99.81 ± 1.254	1.256	0.724
II	250	98.08 ± 0.888	0.905	0.513

Accuracy, reproducibility and precision of proposed method were further confirmed by percent recovery value. As evident from Table-2, the mean percent recovery values ranged from 99.48 to 101.92. The values are very close to 100, indicating the accuracy of the proposed method.

Table-2: Recovery studies for spiked concentration of drug added to preanalyzed tablets powder with stastical evaluation (n=3).

Tablet Formulation	Drug present in preanalyzed tablet powder (mg)	Pure drug added (spiked in mg)	% Recovery estimated (mean ±SD)	% coefficient of variation	Standard Error
I	50	15	100.41 ± 1.189	1.184	0.686
II	50	30	100.21 ± 0.917	0.915	0.529
III	50	15	101.92 ± 1.541	1.512	0.890
IV	50	30	99.48 ± 1.202	1.208	0.694

The values of standard deviation, % coefficient variation and standard error were satisfactorily low which further validated the method.

Conclusion:

The proposed method is new, simple, cost-effective and precise and can be employed in the routine analysis of naproxen tablets. Mixed hydrotropic solution Sodium benzoate, PEG300, PEG6000, Glycerin, Propylene glycol and Niacinamide does not interfere in the spectrophotometric estimation above 331 nm. Thus the poorly water-

soluble drugs can be checked for their solubilities in this mixed hydrotropic solution. If there is sufficient solubility, the solution can be used to solubilize the drug for spectrophotometric analysis.

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