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NEW SPECTROPHOTOMETRIC ESTIMATION OF GATIFLOXACIN IN THE TABLETS USING MIXED SOLVENCY APPROACH

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ABSTRACT

On the basis of a large number of solubilization experiments on poorly water-soluble drugs, the author is of the opinion that hydrotropy is another type of co-solvency and all water soluble substances whether liquids or solids may act as solubilizers for poorly water-soluble drugs. In the present investigation, mixed-solvency concept has been utilized for solubility enhancement of poorly water-soluble drug, gatifloxacin. One blend containing mixed solvent system of sodium citrate, sodium benzoate, glycerin and PEG-4000 (ten percent each) was made to study the influence on solubility of gatifloxacin. The blend was found to increase the solubility of gatifloxacin synergistically. This concept shall prove a boon in pharmaceutical field (and also in non-pharmaceutical field viz. chemical engineering etc.). In the present investigation, the mixed-solvency concept has been employed to analyze gatifloxacin in the bulk drug sample precluding the use of organic solvents (a way towards green chemistry).

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KEYWORDS

Gatifloxacin, Mixed solvency, Solubility enhancement, UV-Visible Spectrophotometry.

INTRODUCTION

In the Pharmaceutical analysis and formulation development fields, it is most often required to increase the aqueous solubility of poorly water soluble drugs. Most of the newly developed drug molecules are lipophillic in nature and poor solubility is one of the most difficult problems of these drugs.

Several hydrotropic agents[1-23] and co-solvents have been observed to enhance the aqueous solubilties of poorly water soluble drugs. Maheshwari[10] has demonstrated the synergistic solubilizing capability due to mixed hydrotropy concept. Same concept has been applied to analyze the poorly water-soluble drug, aceclofenac, titrimetrically, precluding the use of organic solvent. Author has carried out a good amount work on hydotropy. He has nicely applied the application of hydrotropy in titrimetric and spectrophotometric estimation of a large number of poorly water–soluble drugs[1-14] precluding the use of organic solvents. He is of the opinion that hydrotropy is another type of co-solvency. This gave a new thought that like mixed-hydrotropy, a mixed –solvency concept may be tried to observe the effect on solubility of poorly water –soluble drugs.

UV/Visible is an absorption spectrophotometic method for the estimation of poorly water-soluble drug of gatifloxacin in pharmaceutical formulations has been developed. Aqueous solubility of the selected drug was enhanced to a great extent (more than 24 fold) in 10% each solution of sodium citrate, sodium benzoate, glycerin and PEG-4000. The primary objective of the present investigation was to employ the hydrotropic solutions to extract the drug from their dosage forms precluding the use of costlier organic solvents. The selected λ- max for gatifloxacin was 333 nm.

Sodium citrate, sodium benzoate, glycerin and PEG-4000 they does not show any absorbance above 333 nm and therefore no interference in the estimation were observed. The results of analysis have been validated statically and by recovery studies. Proposed method is new, simple, economic, accurate, safe and precise.

MATERIALS AND METHODS

All chemicals and solvents used were of analytical grade. A spectrophotometer (Model UV-160A) (Shimadzu, Kyoto, Japan) with 1 cm matched silica cells was used for spectrophotometric analysis. Gatifloxacin was obtained as a gift sample from M/s Ranbaxy Laboratories Ltd., Dewas; and gatifloxacin tablets were purchased from the local market.

Preparation of calibration curve of gatifloxacin: Accurately weighed 50 mg of gatifloxacin was solubilized by 20 ml of mixed hydrotropic solution of sodium citrate, sodium benzoate, glycerin and PEG-4000 (ten percent each) in a 100 ml volumetric flask, and distilled water was added to make up the volume. This stock solution was further diluted with distilled water to get various dilutions containing 20, 40, 60, 80, 100 and 120, µg/ml of drug. Absorbances were noted at 333 nm against corresponding reagent blanks.

Preliminary solubility studies of gatifloxacin: Solubility of gatifloxacin was determined in distilled water and mixed hydrotropic solution of sodium citrate, sodium benzoate, glycerin and PEG-4000 (ten percent each) at 28°C ± 1°C. There was more than 24-fold enhancement in the solubility of drug in the

mixed hydrotropic solution, as compared with the solubility in distilled water.

Analysis of gatifloxacin tablets by the proposed method: Twenty tablets of gatifloxacin (formulation-I and -II) were weighed and finely powdered. Powder equivalent to 50 mg of gatifloxacin was taken in a 100 ml volumetric flask. Forty milliliters of mixed hydrotropic solution of sodium citrate, sodium benzoate, glycerin and PEG-4000 (ten percent each) was added and the flask was shaken properly for 10 min. to solubilize the drug; and the volume was made up to the mark with distilled water. After filtration through a Whatmann filter paper no. 41, the filtrate was appropriately diluted with distilled water for spectrophotometric estimation against reagent blank to calculate the drug content. (Table-1)

Recovery studies: To evaluate the validity and reproducibility of the proposed method, recovery experiments were carried out. For recovery studies, in pre-analyzed tablet powder equivalent to 100 mg gatifloxacin, bulk drug samples 20 and 40 mg were added as spiked concentrations and drug contents were determined by the proposed analytical method. The results of analysis of recovery studies are presented in (Table-2).

RESULTS AND DISCUSSION

Results of solubility studies of gatifloxacin revealed that enhancement in solubility in a mixed hydrotropic solution of sodium citrate, sodium benzoate, glycerin and PEG-4000 (ten percent each) was more than 24-fold as compared with its solubility in distilled water. It is evident from Table-1 that the values of mean percent drug (gatifloxacin) estimated by proposed spectrophotometric method for formulation I and II are 99.41 and 98.14, respectively.

Table - 1

Result of analysis of commercial tablets of gatifloxacin with statistical evaluation. (n=3)

Tablet formulation	Label claim per tablet (mg/tablet)	Percentage drug estimated mean±SD	Percentage coefficient of variation	Standard error
I	400	99.41 ± 1.499	1.508	0.865
II	400	98.14 ± 0.888	0.905	0.513

The values of mean percent drug estimated, by the proposed method for both formulations are very close to 100.0, indicating the accuracy of the proposed method of analysis. Low values of standard deviation, percent coefficient of variation and standard error (Table-1) further validated the proposed method.

The values of the mean percent recoveries estimated ranged from 99.53 to 101.41. The values are very close to 100 indicating the accuracy of the proposed method. The values of standard deviation, percent coefficient of variation and standard error are satisfactorily low and thus validate the proposed method (Table-2).

Table - 2
Results of recovery studies with statistical evaluation. (n=3)

Tablet formulation	Drug present in pre-analyzed tablet powder(mg)	Pure drug added (spiked) (mg)	Percent recovery estimated (mean ± SD)	Percent coefficient of variation	Standard error
I	100	20	100.75± 1.555	1.543	0.898
I	100	40	99.53 ± 1.229	1.235	0.710
II	100	20	99.86 ± 0.921	0.922	0.532
II	100	40	101.41± 0.867	0.855	0.501

CONCLUSIONS

It is, thus, concluded that the proposed method is new, simple, environment friendly, accurate and reproducible. The proposed method can be successfully employed in the routine analysis of gatifloxacin in tablets. Like this method, other solubilizers can also be tried by combining them to improve the solubility of poorly water soluble drugs to be applied in different fields of analysis. Mixed solvency may find wide use in development of aqueous formulations of poorly water soluble drugs in future.

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