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New spectrophotometric analysis of gatifloxacin tablets utilizing mixed solvency concept (at 288 nm)

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ABSTRACT

A new, simple, safe, accurate and reproducible spectrophotometric analytical method was developed for the quantitative estimation of gatifloxacin in solid dosage form by mixed hydrotropic agents. 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 gatifloxacin was more than 4 fold in one blend containing Propylene glycol, PEG400, PEG4000 and Sodium citrate (10% w/v each) as compared to solubility in distilled water. In the present study mixed blend were employed for the spectrophotometric estimation of gatifloxacin at 288nm. The results of the analysis were validated statistically and by recovery studies. The drug follows Beer's law in concentration range of 4-20 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, Gatifloxacin, Propylene glycol, Sodium citrate, PEG4000.

INTRODUCTION

Gatifloxacin is a second generation fluoroquinolone. Quinolones, a commonly used term for the quinolonecarboxylic acids or 4-quinolones, are a group of synthetic antibacterial agents containing a 4-oxo-1,4-dihydroquinolineskeleton. In general, quinolones can act as antibacterial drugs that effectively inhibit DNA replication and are commonly used as treatment for many infections. In comparison with first- (nalidixic acid, cinoxacin) and second- (norfloxacin, enoxacin, ofloxacin, and ciprofloxacin) generation, third-generation quinolones (gatifloxacin,

and moxifloxacin) show a much broader spectrum of activity providing expanded gram-negative and gram-positive activity coverage as well as expanded activity against atypical pathogens. Gatifloxacin is a third-generation quinolone antimicrobial drug mainly used for the treatment of acute exacerbations of chronic bronchitis and community-acquired pneumonia. It inhibits the bacterial enzymes DNA gyrase and topoisomerase IV. It has excellent activity against Streptococcus pneumoniae, many atypical respiratory pathogens & certain anaerobes[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[3-14.]

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 increase the solubility of Gatifloxacin in water soluble solubilizer which are present in the blends at the safe level. Thus it was thought to solubilize the poorly water soluble Gatifloxacin from fine powder of its tablets using mixed blends to carryout spectrophotometric estimation, precluding the use of organic solvent.

MATERIALS AND METHODS

1. Preparation of calibration curve –100 mg of Gatifloxacin bulk drug was solubilized with 20 ml of mixed hydrotropic solution containing propylene glycol, PEG-400, PEG-4000 & sodium citrate (10% w/v each) and then diluted to 50 ml with distilled water to obtain various dilution (4, 8, 12, 16, 20 µg/ml). Absorbance were measured at 288 nm against corresponding reagent blanks. Linear relationship was observed.

2. Preliminary solubility studies of drug – Solubility of Gatifloxacin was determined in distilled water and mixed hydrotropic solution containing propylene glycol, PEG-400, PEG-4000 & sodium citrate (10% w/v each) at room temperature. Enhancement in the solubility of Gatifloxacin in mixed hydrotropic blend was more than 4 -fold as compared to solubility in distilled water.

3. Analysis of Gatifloxacin tablets using mixed hydrotropic solution - Twenty tablets of Gatifloxacin (formulation-I) were weighed and ground to fine powder. Accurately weighed powder sample equivalent to 100 mg of Gatifloxacin was transferred to 100 ml volumetric flask

containing 20 ml of mixed hydrotropic solution containing propylene glycol, PEG-400, PEG-4000 & sodium citrate (10% w/v each). 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 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 20 to 40 mg of Gatifloxacin pure drug was added to the pre-analyzed tablet powder equivalent to 100 mg Gatifloxacin. Procedure of analysis was same using mixed hydrotropic solution. Percent recoveries were calculated.

RESULTS AND DISCUSSION

Solubility determination studies indicated that enhancement in aqueous solubility of Gatifloxacin in mixed hydrotropic solution were more than 4 fold as compared to solubility in distilled water. It is evident from Table-1 that the mean percent label claim estimated were 97.82 and 97.57 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 Gatifloxacin with statistical Evaluation (n=3).

Tablet Formulation	Label claim (mg/tablet)	% drug estimated (mean ± SD)	% Coefficient of variation	Standard error
I	400	97.82 ± 0.627	0.641	0.961
II	400	98.57 ± 1.629	1.653	0.768

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 98.85 to 100.59. 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 tablet powder with stastical evaluation (n=3).

Tablet Formulation	Drug present in preanalyzed tablet powder (mg)	Pure drug added(spiked) (mg)	% Recovery estimated (mean ± SD)	% Coefficient of variation	Standard error
I	100	20	100.59 ± 1.200	1.193	0.693
I	100	40	98.91 ± 1.287	1.301	0.743
II	100	20	98.85 ± 0.545	0.551	0.315
II	100	40	98.99 ± 0.796	0.804	0.460

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 Gatifloxacin tablets. Mixed hydrotropic solution containing propylene glycol, PEG-400, PEG-4000 & sodium citrate (10% w/v each) does not interfere in the spectrophotometric estimation above 288 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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