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A Novel Application of Hydrotropic Solubilization in the Spectrophotometric Analysis of Gatifloxacin in Solid Dosage Form

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In the present investigation, hydrotropic solubilization technique has been employed to solubilize the poorly water-soluble fluoroquinolone antibiotic gatifloxacin. There was more than 18-fold enhancement in aqueous solubility of gatifloxacin in 1.5 M metformin hydrochloride (MH) and more than 230 times enhancement in 2.0 M sodium benzoate (SB) as compared to aqueous solubility. The selected λ_{max} for spectrophotometric estimation was 333 nm. The hydrotropic agent and the additive used in the manufacture of tablet did not interfere in the analysis. Statistical data proved the accuracy, reproducibility and precision of proposed method.

Key Words: Hydrotropy, Gatifloxacin, Sodium benzoate, Metformin hydrochloride, Spectrophotometry.

INTRODUCTION

Increasing the aqueous solubility of insoluble and slightly soluble drug is of major importance. In hydrotropic solubilization phenomenon, addition of large amount of a second solute results in an increase in the aqueous solubility of another solute. Concentrated aqueous hydrotropic solutions of sodium benzoate, urea, nicotinamide, sodium salicylate, sodium acetate and sodium citrate have been observed to enhance the aqueous solubility of many poorly water-soluble drugs. Maheshwari has developed new analytical method based on hydrotropic solubilization phenomenon for poorly water soluble drugs frusemide[1], cefixime[1], ketoprofen[2], salicylic acid[3], tinidazole[2] and aceclofenec[2]. Maheshwari *et al.* have analyzed ofloxacin[4], metronidazole[5], nalidixic acid[5], tinidazole[5,6], norfloxacin[5,6] and cephalexin[7] by spectrophotometry using hydrotropic solubilization technique.

There was considerable increase in the solubility of gatifloxacin in 1.5 M metformin hydrochloride solution and in 2 M sodium benzoate solution (as compared to aqueous solubility). Thus, it was thought worthwhile to solubilize the poorly water-soluble gatifloxacin from fine powder of its tablets by these hydrotropic solutions to carry out spectrophotometric estimation.

EXPERIMENTAL

Gatifloxacin was gifted by Alkem Lab., Mumbai (India). All chemicals used were of analytical grade. A Shimadzu UV-visible recording spectrophotometer (model-UV 160 A) with 1 cm matched silica cells was used for spectrophotometric analysis. Commercial tablets of gatifloxacin were procured from market.

Calibration curve: 100 mg of gatifloxacin bulk drug was solubilized with 5 mL of 1.5 M metformin hydrochloride solution and 5 mL of 2 M sodium benzoate solution separately and diluted to 100 mL with distilled water to obtain stock solutions (1000 mg/mL). The stock solution was diluted with distilled water to obtain various dilutions (5, 10, 15, 20, 25, 30 μg/mL). A linear relationship was observed over the range of 5 to 30 μg/mL of gatifloxacin (λ_{max} 333 nm), after measuring their absorbances at 333 nm against respective reagent blanks.

Preliminary solubility studies of drugs: Solubility of gatifloxacin was determined in distilled water, 1.5 M metformin hydrochloride solution and 2 M sodium benzoate solution at 27 ± 1ºC. Enhancement in the solubility of gatifloxacin in 1.5 M metformin hydrochloride solution and 2 M sodium benzoate solution were more than 18-fold and 230-fold, respectively (as compared to aqueous solubility in distilled water).

Analysis of gatifloxacin tablet using 1.5 M metformin hydrochloride solution: 20 Tablets of gatifloxacin (formulation-I) were weighed and ground to fine powder. An accurately weighed powder sample equivalent to 100 mg of gatifloxacin was transferred to a 100 mL volumetric flask containing 5 mL of 1.5 M metformin hydrochloride solution. The flask was shaken for about 10 min to solubilize the drug and then volume was made up to mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. The filtrate was divided in to two part A and B. Part A was kept at room temperature for 24 h to check its chemical stability and precipitation, if any. Part B was diluted sufficiently with distilled water and analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table-1). After 24 h, the part A solution was analyzed in same way as the part B solution. Same procedure was followed for formulation-II.

Analysis of gatifloxacin tablets using 2 M sodium benzoate solution: An accurately weighed powder sample equivalent to 100 mg of gatifloxacin was transferred to a 100 mL volumetric flask containing 5 mL of 2 M sodium benzoate solution. The flask was shaken for about 10 min to solubilize the drug and then volume was made up to mark with distilled water. The solution was filtered through Whatmann filter paper No. 41. The filtrate was divided into two parts A and B. Part A was kept at room temperature for 24 h to check its chemical stability and precipitation, if

any. Part B was diluted sufficiently with distilled water and analyzed on UV spectrophotometer against reagent blank. Drug content of tablet formulation was then calculated (Table-1). After 24 h, the part A solution was analyzed in same way as the part B solution. Same procedure was followed for formulation-II.

Recovery studies: For recovery studies 20 and 40 mg of gatifloxacin pure drug was added to tablet powder equivalent to 100 mg gatifloxacin. Procedure of analysis was same using 2 M sodium benzoate solution and 1.5 M metformin hydrochloride solution. Per cent recoveries were calculated and reported in Table-2.

RESULTS AND DISCUSSION

Result of solubility determination studies indicated that enhancement in aqueous solubility of gatifloxacin in 2 M sodium benzoate solution was more than 230 times and in 1.5 M metformin hydrochloride solution was more than 18-fold as compared to solubility in distilled water. Therefore, these solutions were employed to extract out gatifloxacin from fine powder of tablets. It is evident from Table-1 that per cent label claim-ranged from 98.52 ± 0.885 to 99.89 ± 1.821 in case of proposed method employing 2 M sodium benzoate solution. Per cent label claim in case of 1.5 M metformin hydrochloride solution ranged from 99.79 ± 1.442 to 100.85 ± 1.391. Per cent label claims are very close to 100 with low values of standard deviation, per cent coefficient of variation and standerd error showing accuracy of proposed methods.

TABLE-1
ANALYSIS OF COMMERCIAL TABLET FORMULATIONS WITH STATISTICAL EVALUATION

Tablet formulation	Label claim per tablet (mg)	Method	% Label claim estimated* (mean ± SD)	Coefficient of variation (%)	Standard error
I	100	SBM	99.89 ± 1.821	1.832	0.743
	100	MHM	99.79 ± 1.442	1.445	0.589
II	100	SBM	98.52 ± 0.885	0.898	0.361
	100	MHM	100.85 ± 1.390	1.379	0.568

*Average of three determinations, SBM-Sodium benzoate method, MHM-Metformin hydrochloride method

Accuracy, reproducibility and precision of proposed methods were further confirmed by per cent recovery values. As evident from Table-2 per cent recovery values ranged from 98.76 ± 1.228 to 100.74 ± 1.003 with 2 M sodium benzoate solution and 98.77 ± 0.880 to 100.72 ± 0.608 with 1.5 M metformin hydrochloride solution. Per cent recovery values are very close to 100 with low values of standard deviation, coefficient of variation and standard error. These results validated the proposed methods.

TABLE-2
RECOVERY STUDIES FOR SPIKED CONCENTRATION OF DRUG ADDED TO PREANALYSED TABLET POWDER WITH STATISTICAL EVALUATION

Tablet formulation	Drug present in pre-analyzed tablet powder taken (mg)	Pure drug added (mg)	Method	% Recovery estimated* (mean ± SD)	Coefficient of variation (%)	Standard error
I	100	20	SBM	98.76 ± 1.228	1.243	0.507
	100	40	SBM	100.32 ± 0.667	0.665	0.272
	100	20	MHM	99.07 ± 0.976	0.985	0.398
	100	40	MHM	100.72 ± 0.608	0.604	0.248
II	100	20	SBM	99.33 ± 1.236	1.244	0.505
	100	40	SBM	100.74 ± 1.003	0.996	0.409
	100	20	MHM	98.77 ± 0.880	0.891	0.359
	100	40	MHM	99.81 ± 0.761	0.762	0.311

*Average of three determinations, SBM -Sodium benzoate method
MHM-Metformin hydrochloride method

The drug contents in extracts of hydrotropic solutions (2 M sodium benzoate) and (1.5 M metformin hydrochloride) were nearly same during 24 h and there was no precipitation in 24 h. This indicates that extracts can be analyzed with sufficient accuracy.

Conclusion

It is concluded that the proposed methods are new, simple, cost-effective, accurate, safe and precise and can be successfully employed in the routine analysis of gatifloxacin. Metformin hydrochloride does not interfere in the spectrophotometric estimation above 250 nm. Thus, other poorly water-soluble drugs can be checked for their solubilities in this hydrotropic solution. If they have good solubilities in metformin hydrochloride solution, they can be easily estimated excluding the use of organic solvents provided their λ_{max} value is above 250 nm. Sodium benzoate does not absorb above 300 nm and can be employed to estimate drugs having λ_{max} above 300 nm. Both hydrotropic agents are economic.

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