

APPLICATION OF HYDROTROPIC SOLUBILIZATION PHENOMENON IN SPECTROPHOTOMETRIC ESTIMATION OF LEVOFLOXACIN IN TABLET DOSAGE FORM

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ABSTRACT: Several techniques are used to increase the aqueous solubility of poorly water soluble drugs. Hydrotropic solubilisation technique is one of them. In the present investigation hydrotropic solution of urea (4M) has been employed as solubilizing agent to solubilization poorly water soluble drug Levofloxacin, from fine powder of its tablet dosage form for spectrophotometric determination in ultraviolet region. Levofloxacin shows maximum absorbance at 289 nm. Beer's law was obeyed in the concentration range of 2-12 µg/ml. Results of analysis were validated statistically and by recovery studies. The proposed method is new, simple, environment friendly, accurate and cost-effective and can be successfully employed in routine analysis of levofloxacin in tablets. Hydrotropic agent urea did not interfere in spectrophotometric estimation.

Key words: - levofloxacin, Hydrotropic solubilization

INTRODUCTION

The term hydrotropic has been used to designate the increase in solubility of poorly water soluble drugs in concentrated solutions of hydrotropic agents. A huge number of poorly water soluble drugs have been solubilized by use of various hydrotropic solutions.¹⁻²⁴ Sodium salicylate, Sodium benzoate, nicotinamide, urea, sodium ascorbate, sodium ascorbate, sodium citrate, sodium acetate are the most commonly used hydrotropic agents. Maheshwari has analyzed various poorly water soluble drugs viz. frusemide¹, cefixime², salicylic acid³, ketoprofen⁴, tinidazole⁵, aceclofenac⁶ and amoxicillin⁷ using hydrotropic solubilisation technique. Maheshwari *et al.* have estimated a large number of poorly water soluble drugs viz. hydrochlothiazide⁸, tinidazole⁹, metronidazole⁹, nalidixic acid⁹, ibuprofen¹⁰, naproxen¹⁰, flurbiprofen¹⁰, aceclofenac¹¹, aspirin¹², cephalixin¹³, paracetamol¹⁴ and piroxicam¹⁵, norfloxacin and tinidazole¹⁶. Benzodiazepine¹⁷, nimesulide¹⁸, nifedipine¹⁹, riboflavin²⁰, etodolac²¹, rapamycin²², indomethacin²³ using hydrotropic agents. Levofloxacin, (-)-(S)-9-fluoro-2,3-dihydro-3-methyl-10-(4-methyl-1-piperazinyl)-7-oxo-7H-pyrido(1,2,3-de)-1,4-benzoxazine-6-carboxylic acid hemihydrate

is a quinolone anti-microbial agent which exhibits broad spectrum in-vitro bactericidal activities against gram positive and gram negative aerobes. There was tremendous increase in aqueous solubility of levofloxacin in 4M urea solution (more than 10 fold enhancement in aqueous solubility as compared to solubility in distilled water). Thus, it was thought worthwhile to solubilize the poorly water soluble, levofloxacin, from fine powder of its crushed tablets by 4 M urea solution to carry out spectrophotometric estimations. In most of the hydrotropic solubilization studies it was assumed that the enhancement in solubility of drugs was due to "salting-in" effect or due to change in solvent character.

METHODOLOGY

INSTRUMENT: Shimadzu UV visible recording spectrophotometer (model UV-1700) with 1cm matched silica cells was employed.

Chemicals: Levofloxacin drug sample was supplied as gift sample by Cipla Pvt. Ltd. Mumbai. Commercial tablet of levofloxacin were procured from the market. All other chemical used were of analytical grade.

Preliminary solubility studies of levofloxacin:

Solubility of levofloxacin were determined at $28 \pm 1^\circ\text{C}$ in 4M urea solution, distilled water and buffer of pH^8 . Sufficient excess amount of drug was added to screw capped glass vials of 30 ml capacity, containing distilled water, buffer of pH^8 and 4 M urea solution. The vials were shaken mechanically for 12 hours at $28 \pm 1^\circ\text{C}$ in orbital flask shaker (Khera Instrument Pvt. Ltd, India) the solution were allowed to equilibrate for next 24 hours and then centrifuge for 5 min. at 2000 rpm. The supernatant of each vial was filtered through whatman filter paper #41. Filtrates were diluted suitably and analyzed spectrophotometrically against corresponding solvent blanks.

Analysis of levofloxacin tablet using 4 M urea solution:

Twenty tablets of formulation I was weighed and powdered. Powder equivalent to 100 mg levofloxacin was transferred to a 50ml volumetric flask containing 40 ml of 4 M urea solution. The flask was shaken for about 5 minutes to solubilise the drug.

Then volume was made up to the mark with distilled water solution was filtered through whatman filter paper no 41. Filtrate was divided in 2 parts, A & B part A was kept at room temperature for 48 hours to check the effect on stability of drug in presence of urea and also to not precipitation, if any during this period.

Part B filtrate was appropriately diluted with distilled water and absorbance was noted at 289 nm (λ_{max}) against solvent blank and drug content was calculated (table 1).After 48 hour , filtrate of part A was appropriately diluted with distilled water and analyzed for drug content. There was no precipitation in the filtrate in 48 hours. Similar procedure was adopted in cases of formulation II and formulation III.

Recovery studies: In order to check the accuracy, reproducibility and precision of the proposed method, recovery studies were conducted. Preanalyzed tablet powder (formulation I) equivalent to 100 mg levofloxacin was transferred with 50 ml volumetric flask. Pure levofloxacin drug sample (5mg) was added in the same volumetric flask. Now 40 ml of 4 m urea solution the flask was shaken about 5 min to solubilise the drug then the volume was made up to the mark with distill water then solution was filtered in whatman filter paper no. 41 the filtrate was diluted with distill water appropriately and absorbance was noted at 289 nm against corresponding reagent blank . Drug content was calculated and % recovery was estimated (table 2). Similar procedure was repeated during 10 mg

and 15 mg of pure levofloxacin as spiked concentration (in place of 5 mg) Recovery studies using formulation II and formulation III were repeated

in the same way. The drug content were determined in % recovery were estimated (table 2)

RESULT AND DISCUSSION:

The solubility of levofloxacin in 4 M urea solution was found to be more than 10 fold as compare to its solubility in distilled water. The pH of 4 M urea solution was 8. To check the effect of pH on solubility of drug, its solubility was also determined in buffer of pH 8. Solubilities of levofloxacin in distilled water and buffer pH 8 were almost same thus it is concluded that enhancement in solubility of levofloxacin in 4 M urea solution was due to hydrotropic solubilization only. As evident from table 1, % label claim estimated using the proposed method ranged from 98.73 ± 1.261 to 101.34 ± 0.943 since the % label claims are close to 100, the proposed method is accurate and get further validated statistically by low values of standard deviation, % coefficient of variation and standard error.

Fresh filtrate and 48 hours aged filtrate (kept at room temperature) of drug in 4M urea solution were found to have same drug contents. Also there was no precipitation within 48 hours this indicates that analysis can be accurately performed within 48 hour of extraction of the drug from tablet powder.

The result of recovery studies (presented in table 2) indicates that % recovery estimated ranged from 98.46 ± 1.049 to 100.50 ± 1.121 by use of proposed method. Since the percent recovery values are close to 100, this indicates the accuracy of the proposed method. Values of standard deviation, % coefficient of variation and standard error are satisfactorily low and confirm further the accuracy, reproducibility, precision of the proposed method.

Methanol, ethanol, chloroform, hexane, acetonitrile, acetone, diethyl ether, toluene and carbon tetra chloride are widely used in spectrophotometric estimation of poorly water soluble drug. Most of these organic solvents are toxic, costlier and source of pollution. Inaccuracy of spectrophotometric estimations due to volatility is another drawback of these solvents. Urea does not interfere above 250 nm just like levofloxacin as model drug (poorly water soluble) other poorly water soluble drugs may be studied for the enhancement effect in solubility in 4 M urea solution. If the λ_{max} of such drug is above 250 nm and there is significant enhancement in solubility in hydrotropic solution the drug can be easily estimated like the proposed method avoiding the use of organic solvents.

CONCLUSION

It is thus concluded that the proposed method is new, simple, cost effective, safe, accurate, precise and

environmentally friendly. The proposed method can successfully employed in the routine analysis of levofloxacin in tablet dosage forms.

Acknowledgement

The author is thankful to Copal Pvt. Ltd. Mumbai for generous gift of levofloxacin drug sample and The Principal Dr.S.B. Bhise of Government College of pharmacy, Karad for providing necessary facilities to carry out the research work.

Table 1: Results of analysis of commercial tablets of levofloxacin

Tablet formulation	Label claim (mg)	% label claim estimated * (mean $\pm$ S.D)	% coeff. of variation	Standard error
I	250	99.60 $\pm$ 1.452	1.502	0.751
II	250	98.73 $\pm$ 1.261	1.270	0.635
III	250	101.34 $\pm$ 0.943	0.934	0.473

* Average of six determinations

Table 2: Recovery study for spiked concentration of drug added to the preanalyzed tablet powder with statistical evaluation

Tablet formulation	Amount of levofloxacin in tablet powder taken (mg)	Amount of standard drug added (mg)	% recovery estimated * (mean $\pm$ S.D)	% coeff. of variation	Standard error
I	100	5	99.21 $\pm$ 0.638	0.642	0.312
	100	10	98.99 $\pm$ 1.245	1.248	0.632
	100	15	100.02 $\pm$ 0.480	0.475	0.2364
II	100	5	98.89 $\pm$ 1.025	1.005	0.5001
	100	10	98.56 $\pm$ 0.982	0.986	0.479
	100	15	98.99 $\pm$ 1.222	1.208	0.599
III	100	5	99.14 $\pm$ 0.873	0.881	0.4105
	100	10	100.50 $\pm$ 1.121	1.132	0.546
	100	15	98.46 $\pm$ 1.049	1.062	0.491

*Average of six determinations

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