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Quantitative estimation of Ciprofloxacin in marketed formulation by hydrotropic techniques

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Abstract

An accurate, precise, sensitive and economical procedure for the determination of ciprofloxacin hydrochloride in tablet dosage form has been developed. In the present investigation, 2.0 M urea solution (hydrotropic solubilizing agents was employed to solubilize, Ciprofloxacin (a poorly water soluble drug) from fine powder of its tablets to carryout spectrophotometric analysis. The result showed that Beer's law was obeyed in concentration range of 5-50 µg/ml with good linearity (r^2>0.99) for both the drugs in both methods. The recoveries were within 98.62 -101.27% for Ciprofloxacin hydrochloride. Precision was good with acceptable limits of detection (LOD) and quantitation (LOQ) for both compounds. The average content of the compound was 101.23 for Ciprofloxacin hydrocloride.The optimized methods showed good reproducibility and recovery with standard deviation of < 1.0% and percent relative standard deviation less then 2.0%.

Key-Words: Ciprofloxacin hydrochloride, Spectrophotometric method, Hydrotropic agent

Introduction

The term hydrotropy has been used to designate the increase in solubility of various substances in water due to the presence of large amounts of additives[1,2]. Various organic solvents have been employed for the solubilization of poorly water soluble drugs for spectrophotometric estimations. Drawbacks of organic solvents include higher cost, toxicity, pollution and error in analysis due to volatility. The primary objective of this study was to employ hydrotropic solubilizing agents for the selected drugs to preclude the use of organic solvents. Chemically Ciprofloxacin Hydrochloride (CPH) is (1-cyclopropyl-6-fluoro-1, 4-dihydro-4-oxo-7-(1-piperazinyl)-3-quinolinecarboxylic acid) is fluoro quinolones and antimicrobials with potent activity against a broad spectrum of bacteria[3,4,5]. Literature survey revealed that chromatographic method was reported for its estimation from tablet formulation[6,7] and spectrophotometric methods for estimation in combined dosage forms[8].

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Material and Methods

Instrumentation

UV-Visible double beam spectrophotometer, Shimadzu model-1700 having spectral bandwidth 3nm and of wavelength accuracy ±1nm, with 1cm quartz cells was used. All weighing were done on electronic balance (Shimadzu, Model AY - 120).

Reagents and Chemicals

Analytically Pure samples of CPH were obtained as gift sample from Zest Pharma Pvt. Ltd, Indore (MP), India and were used as such without further purification. The tablet dosage form(Cipro 500), was procured from the local market, Indore, India. 2.0 M urea was selected as hydrotropic solubilizing agent. All other material used was of analytical reagent grade.

Preliminary solubility studies of drug[15]

Solubility of both drugs was determined at 28 ± 2 ^{0}C. An excess amount of drug was added to two screw capped 30ml glass vials containing different aqueous systems viz distilled water, buffer of pH 6.4, buffer of pH 8.2, and 2.0 M urea. The vials were shaken mechanically for 12 h at 28+1˚ in a mechanical shaker. These solutions were allowed to equilibrate for next 24 h and then centrifuged for 5 min at 2000 rpm. The supernatant liquid was taken for appropriate dilution after filtered through whatmann filter paper # 41 and analyzed spectrophotometrically against corresponding solvent blank. After analysis, it was found that the enhancement in the solubility of CPH was found to be

more than 30 folds in 2.0 M urea as compared to solubility studies in other solvents.

Preparation of standard stock solution and calibration curves of CPH

About 50mg each of CPH was accurately weighted and transferred to 50ml of volumetric flask separately. 40 ml, 2.0 M urea was used to solubilize after shaking for 10 to 15 minutes. Rest of the volume was made up with distilled water to get solution of 1000µg/ml. Stock solutions of 100µg/ml of each drugs were prepared by further dilution and scanned over the range of 400nm-200nm in the spectrum mode to get the overlain spectra of both drugs. The spectra exhibit major absorbance maxima at 272 nm for CPH. Beers-Lambert law obeyed in the range of 5-50 µg/ml for CPH. Six mixed standards 5, 10, 15,20,25,30 for CPH; was prepared from stock solutions of CPH for further study.

Analysis of Tablet Formulation

Twenty tablets were taken and their average weight was determined, they were crushed to fine powder. Then powder equivalent to 50 mg (101.91 mg) of CPH was taken in 50ml volumetric flask and 40 ml, 2.0 M urea was used to solubilize after shaking for 10 to 15 minutes. Rest of the volume was made up with distilled water to get solution of 1000µg/ml. Stock solutions of 100µg/ml of each drugs were prepared by further dilution. The supernatant liquid was transferred to 50ml of volumetric flask through a whatman No-41 filter paper. The residue was washed twice with water and the combined filtrate was made up to 50ml mark with water. The above solution was further diluted to get a solution containing 10 µg/ml of CPH. CPH was determined from their calibration curve plotted between absorption difference and concentration. The results of analysis were given in Table 1.

Recovery studies

To check the accuracy of the developed methods and to study the interference of formulation additives, analytical recovery experiments was carried out by standard addition method. From that total amount of drug found and percentage recovery was calculated. The results were reported in Table 2.

Validation of the developed methods

The developed methods for estimation of CPH validated as per ICH guidelines.

Accuracy

To check the accuracy of the developed methods and to study the interference of formulation additives, analytical recovery experiments was carried out by standard addition method. Total amount of drug found and percentage recovery was calculated and results were reported in Table 2.

Precision

Precision of the method was verified by repeatability and intermediate precision studies.

Repeatability

To check the degree of repeatability of the methods, suitable statistical evaluation was carried out. Five samples of the tablet formulations were analyzed for the repeatability study. The standard deviation, coefficient of variance and standard error was calculated. The results were reported in Table 1.

Results and Discussion

All UV spectrophotometric methods were found to be simple, accurate, economic and rapid for simultaneous estimation of CPH in tablet dosage form. By performing these methods it was found that both drugs shown good regression value at their respective wavelengths and the recoveries were within 99.42 - 101.27% for CPH. The optimized methods showed good reproducibility and recovery with standard deviation of < 1.0% and percent relative standard deviation less then 2.0%.

Since urea do not interfere above 245 nm, therefore other poorly water-soluble drugs can also be estimated above 245 nm by hydrotropy avoiding the use of organic solvents.There was no interference of urea and commonly used additives present in tablet formulations. A critical evaluation of the proposed methods was performed by statistical analysis of the experimental data. In order to demonstrate the validity and applicability of the proposed methods, recovery studies were performed by analyzing synthetic mixture of CPH.

Hence, the proposed methods could be successfully applied to the determination of CPH in the commercially available bulk and tablet dosage form. Thus, it may be concluded that the proposed methods of analysis are new, simple, cost-effective, environmentally friendly, safe, accurate and reproducible. Definitely, there is further scope of 2.0 M urea solution as solubilizing agent for other poorly water-soluble drugs. There was no interference of urea in the estimation. The proposed method can be successfully employed in the routine analysis of CPH containing dosage forms.

Conclusion

It is thus concluded that the proposed method is new, simple, cost effective, accurate, safe, free from pollution and precise and can be successfully employed in the routine analysis of poorly water soluble drugs in pharmaceutical dosage forms.

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Table 1: Result of Pharmaceutical Formulation Analysis

Parameters	Brand- A CPH	Brand -B CPH
Label claim (mg/Tab)	500	500
Found (mg/Tab)	498.33	499.02
Drug content[a]	101.42	99.64
±S.D	0.304	0.132
%COV	0.291	0.581
SE	0.103	0.521

Value for drug content (%) are the mean of six estimation, S.D: Standard deviation, COV: Coefficient of variance and S.E: Standard error

Table 2: Result of Recovery studies

Method	Drug	Labelclaim (mg/tab)	Amount (mg/ml) taken	added	% Recovery±S.D	COV%
Brand-A	CPH	500	30	5	100.32±0.642	0.421
			60	10	100.63±0.820	0.421
			90	15	99.83±0.101	0.152
Brand-B	CPH	500	30	5	101.01±0.282	0.513
			60	10	100.18±0.307	0.133
			90	15	98.99±0.482	0.212

%Recovery is mean of three estimation, S.D is standard deviation and COV is coefficient of variance