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Research Article

NEW SPECTROPHOTOMETRIC ESTIMATION OF PRULIFLOXACIN USING NEUBERG'S HYDROTROPIC SALT

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ABSTRACT

A new, simple, safe, accurate and reproducible spectrophotometric analytical method was developed for the estimation of Prulifloxacin, from its tablet dosage form. In the present investigation, 2.0 M Sodium benzoate solution also known as Neuberg's hydrotropic salt was employed as hydrotropic solubilizing agent to solubilize poorly water-soluble drug Prulifloxacin for its spectrophotometric analysis. The primary objective of the present investigation was to employ this hydrotropic solution to extract the drug from its dosage form, precluding the use of costlier organic solvents. Aqueous solubilities of this selected model drug was to a great extent in 2.0 M sodium benzoate solutions. Various organic solvents like methanol, chloroform, ethanol, acetonitrile, hexane and toluene are widely used to conduct the spectrophotometric analysis, but higher cost and toxicity prevents their frequent use. The results of the analysis were validated statistically and by recovery studies. The λ max was observed at 296nm.The drug follows Beer's law in concentration range of 15-60 mcg/ml with coefficient correlation value of 0.992. The mean percent recovery was 100.49%.

Keywords: Prulifloxacin, Neuberg's hydrotropic salt, validation, Beer's law.

INTRODUCTION

Prulifloxacin[1-2] is an older synthetic chemotherapeutic antibiotic of the fluoroquinolone drug class. It is a prodrug which is metabolized in the body to the active compound ulifloxacin. It has been approved for the treatment of uncomplicated and complicated urinary tract infections, community-acquired respiratory tract infections and gastroenteritis, including infectious diarrhoeas. The chemical name of Prulifloxacin is (*RS*)-6-Fluoro-1-methyl-7-[4-(5-methyl-2-oxo-1,3-dioxolen-4-yl)methyl-1-piperazinyl]-4-oxo-4*H*-[1,3]thiazeto[3,2-*a*]quinoline-3-carboxylic acid, as shown in chemical structure of Prulifloxacin in figure 1.

Literature surveys have revealed a number of methods for the estimation of Prulifloxacin depending on different analytical techniques, LC-MS/MS[3], RPHPLC[4] HPLC[5-6], UV Spectrophotometric methods[7-9]. The drug Prulifloxacin is hydrophobic in nature. Various techniques have been employed to enhance the aqueous solubility of poorly water soluble drugs such as alteration in pH of solvent, co-solvents, complexation, hydrotropic solubilization etc.

The term "hydrotrophy" originally put forwarded by Neuberg[10] to describe the increase in the solubility of the solute by the addition of fairly high concentration of alkali metal salts of various organic acids. According to Neuberg, the solublizing agent, are anionic organic salts. Saleh and El-Khordagui[11] made an attempt to extent the definition of the term hydrotropic agent to include cationic and nonionic organic compounds bearing the essential structural features of Neuberg's hydrotropes. Cationic compounds such as p-amino benzoic acid hydrochloride, procaine hydrochloride and neutral molecules such as resorcinol and pyrogallol confer typical hydrotropic properties.Winsor[12] considered hydrotrophy as a solubilization phenomenon; with the solute dissolved in oriented clusters are the hydrotropic agents. Sodium salicylate, sodium benzoate, sodium lauryl sulphate, sodium glycinate, sodium gentisate, nicotinamide, urea, sodium acetate, sodium citrate and niacinamide have been employed as a hydrotropic agents[13-18]. A successful attempt have been made by using this phenomenon for the analysis of

various poorly water soluble drugs viz. frusemide, cefixime, hydrochlorothiazide, ketoprofen, bulk sample of ketoprofen and salicylic acid, norfloxacin in combination with tinidazole and metronidazole[19-25].Various organic solvents like methanol, chloroform, alcohol, dimethyl formamide and benzene have been employed for the solubilization of poorly water soluble drugs for spectrophotometric estimations. None of these methods are without their limitations so the need was felt to develop new, accurate, environmental friendly, cost effective, safe, sensitive spectrophotometric methods for estimation of prulifloxacin in tablet dosage form by using aqueous solution of 2.0 M sodium benzoate solution, as a hydrotropic agent.

MATERIALS AND METHODS

Instrumentation

A double beam UV/visible spectrophotometer, lab India 3000 make with 1cm quartz cells was used for the absorbance measurements. Instrument used was calibrated.

Chemicals

All the reagents used for the analysis were of analytical grade. Distilled water was used throughout the study. Standard Prulifloxacin was obtained as a gift sample from Micro labs, Bangalore .The tablet Percin of strength 600 mg were produced from the market manufactured by Lupin Pharma.

Primary solubility studies

Solubility of drug was determined at 25 ±1 °C. Different aqueous systems used were Distilled Water, pH 7, 8M Urea, 2M Nicotinamide and 2M Sodium benzoate. Solutions were thus analysed spectrophometrically against corresponding solvent blank.

Preparation of standard stock

Accurately weighed 100mg of Prulifloxacin was solubilized by 50 ml of 2.0M sodium benzoate solutions and final volume was adjusted with distilled water in 100 ml of volumetric flask. From the above solution 1ml of solution was taken and diluted to 10 ml with distilled water to get a solution containing 100 µg/ml.

Working standard solutions were scanned in the entire UV range of 400-200 nm to determine the λ max of drugs. The λ max of Prulifloxacin was found to be 296 nm in figure: 2. The standard solutions were diluted with distilled water to obtain various dilutions (15, 20, 25, 30,35,40,45,50,55,60 µg/ml). The linear relationship was observed over the range of 15-60 µg/ml. Absorbance was noted at 296 nm against corresponding reagent.

Preparation of sample solution

Twenty tablets of Prulifloxacin marketed formulation was weighed and ground to fine powder. An accurately weighed powder sample equivalent to 100 mg of Prulifloxacin was transferred in to a 100 mL volumetric flask. 50 mL of 2M Sodium Benzoate solution was added and the flask was shaken for about 20 minutes to dissolve the drug. Then the volume was made up to the mark with distilled water. The solution was filtered through Whatman filter paper No.41. The above sample stock solution was diluted with distilled water to get the concentration of 50 µg/ml. The absorbance was measured at 296 nm and the drug content of the tablet formulation was then calculated.

VALIDATION [26]

Linearity and range

Linearity plot is shown in figure 3. The response for prulifloxacin was linear in the concentration range of 15 µg/ml – 60 µg/ml. The regression equation calculated by least square method was $y = 0.012x + 0.067$ with coefficient of correlation $R^2 = 0.992$. Spectral characteristics of the method as shown in Table no 1.

Accuracy

Accuracy studies were done as percent recovery; it was performed by adding constant amount of the standard drug to the sample at levels of 80%, 100% and 120% of the test concentration. The results are tabulated in Table no 2.

Precision

Data obtain from precision experiments are given in Table no 3. Precision was calculated for Interday. The data obtained shows that method is sufficiently precise. Precision is calculated as % Relative Standard Deviation.

RESULTS AND DISCUSSION

Results of solubility studies indicated that enhancement in aqueous solubility of Prulifloxacin in 2.0 M Sodium benzoate solution was more as compared to its solubilities in Distilled water, 8M Urea, 2M Nicotinamide. Therefore, this solution was employed to extract Prulifloxacin from the fine powder of tablet formulation. The pH of hydrotropic solution was found to be 7. Therefore, in order to study the influence of pH on solubilities, buffer solution of pH 7 was made, and the solubility of the drug was determined. This study proves that increase in solubilities of hydrotropic solutions are not

due to alteration in pH, but are due to hydrotropic phenomenon. This indicates that the enhancement in the aqueous solubility of Prulifloxacin in 2.0 M Sodium benzoate hydrotropic solutions was largely due to hydrotropy.

Beer's law is obeyed in concentration range of 15 - 60 µg/ml with correlation coefficient of 0.992 and regression equation of y = 0.012x + 0.067. The method was validated for linearity, accuracy and precision.

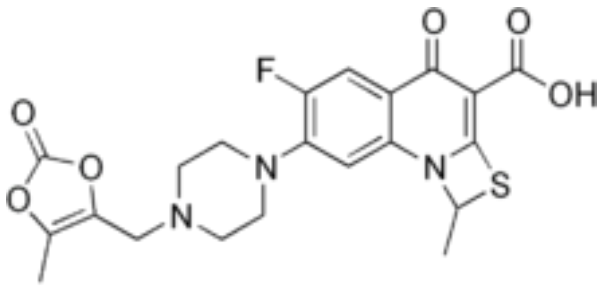

Fig. 1: Chemical Structure of Prulifloxacin

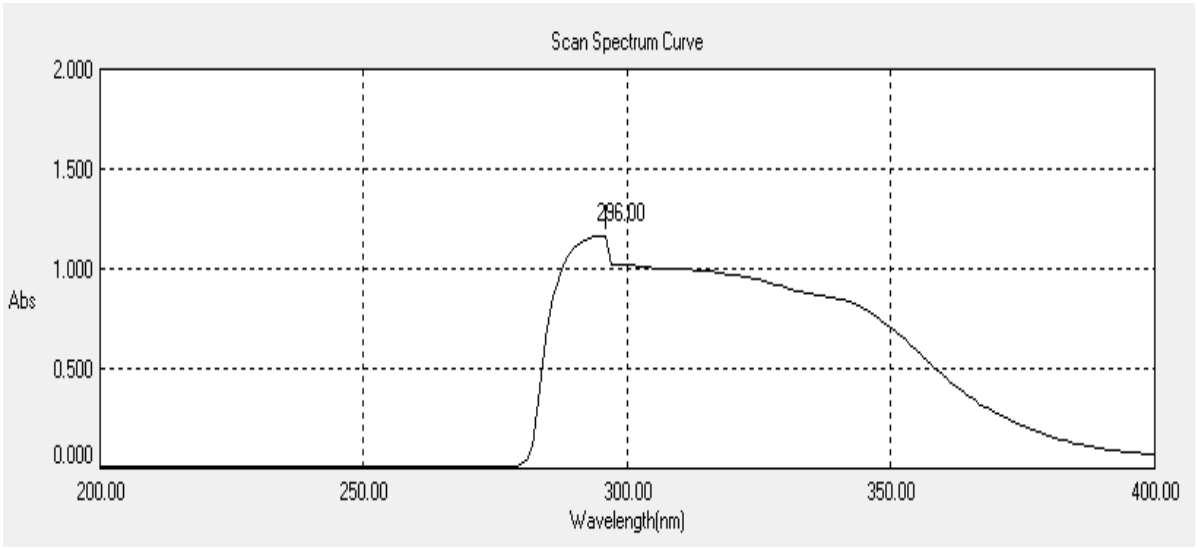

Fig. 2: Spectra of Prulifloxacin. (λmax: 296 nm)

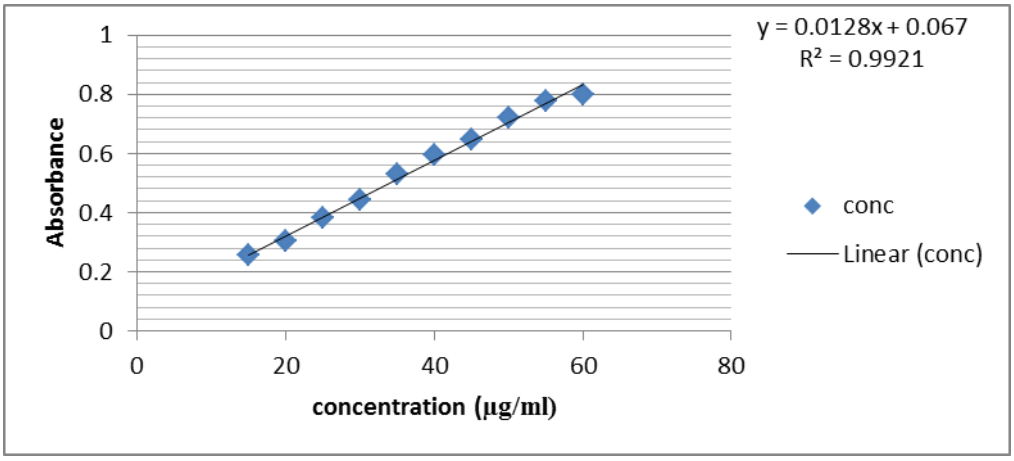

Fig. 3: Calibration curve of Prulifloxacin

Table 1: Spectral characteristic of method

parameters	value
Concentration range	15-60 µg/ml
Equation of the line	y = 0.012x+0.067
Correlation coefficient	0.992
Slope	0.012
Intercept	0.067

Table 2: Result of accuracy by Recovery studies

Conc. Of sample added (µg/ml)	Level of addition (%)	Conc. Of standard added (µg/ml)	Total Conc. (µg/ml)	Absorbance at 296 nm *	Conc. Obtained from graph. (µg/ml)	% recovery
15	80	12	27	0.389	26.83	98.58
	100	15	30	0.429	30.16	101.06
	120	18	33	0.467	33.33	101.83
					Mean	100.49
					SD	1.386
					%RSD	1.37

*Average of three absorbances

Table 3: Result of Precision

Conc. Of solution (µg/ml)	Absorbance			Average	% RSD (%)	Conc. From graph (µg/ml)
	Day 1	Day 2	Day 3			
15	0.247	0.249	0.251	0.249	0.65	15.16
30	0.437	0.427	0.425	0.429	1.2	30.16
60	0.787	0.781	0.761	0.776	1.43	59.08

CONCLUSION

It has been observed that 2M Sodium benzoate can be used as hydrotropic reagent for solubilising Prulifloxacin. The proposed method described is simple, rapid, accurate, environment friendly with no toxic effect for the routine analysis of Prulifloxacin from its pharmaceutical formulations over a concentration range of 15-60 µg/ml without interference from common excipients. Moreover it exhibits advantage of being convenient, fast, and safe and eco- friendly.

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