International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 29-10-2024, Accepted: 28-11-2024, Published: 13-12-2024
Volume 9, Issue 4, 2024, Page No. 53-55

Spectrophotometric determination of PK_a of Cefotoxime sodium

Mamatha Kola[1*], N Raju[2], Sabavat Anjali[3], Mukalla Uha[3], Phani Vennela Mudunuri[3] Mohammad Bakhatwar[1]
[1] Assistant Professor, Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Osmania University, Hyderabad, Telangana, India
[2] Department of Pharmaceutics, Pramog Labs Private Limited, Hyderabad, Telangana, India
[3] Department of Pharmaceutics, Gokaraju Rangaraju College of Pharmacy, Osmania University, Hyderabad, Telangana, India

Abstract
Acid dissociation constant is very important parameter during drug development and to understand mechanism of drug action. The pKa influence physiochemical properties of drug substance such as solubility and dissolution rate. The Amount of drug that exists in unionized form and in ionized form is a function of pKa of drug & pH of the fluid at the absorption site. In the HPLC method development the knowledge of pka of chemical species is very useful to choose appropriate buffer, as the retention time of ionized and unionized form of chemical substance is different. In this study, a simple cost-effective method to determine the pKa value of cefotaxime sodium was proposed. The pKa value was found in good agreement with the reported values.

Keywords: Cefotaxime sodium, Spectrophotometric method, pK_a

Introduction

Cefotaxime sodium, CFT is a third-generation cephalosporin antibiotic belonging to the class of semi-synthetic antibiotics of the β-lactam family. Which is chemically (6R,7R)-3-(acetoxymethyl)-7-((Z)-2-(2 aminothiazol-4-yl)-2-(methoxyimino) acetamido)-8-oxo-5-thia-1-azabicyclo [4.2.0] oct-2-ene-2-carboxylic acid. The acid dissociation constant (pK_a) of a drug influences lipophilicity, solubility, protein binding and permeability which in turn directly affects pharmacokinetic (PK) characteristics such as absorption, distribution, metabolism and excretion (ADME)[1–6]. A detailed mining through literature reveals that there are several methods to determine the dissociation constant (pka). NMR-pH is also excellent technique for determining pK_a [7]. The pK_a value determination of by means of LC is also widely used [8,9]. The pK_a value determination by Capillary electrophoresis (CE) is based on effective mobility of ionizable compound in a series of electrolyte solution of constant ionic strength and various pH [10]. In recent years, a new procedure has been developed where LC and CE methodologies are used for pK_a determination in combination with a diode-array detector (DAD) for absorbance measurements [11]. Theoretical pK_a values can be calculated by computational methods (e.g., SPARC [12] and ACD/Lab [13]. In the compounds with acid or basic functionality, their ionization state is controlled by solution pH, these different chemical species (cationic, neutral, or anionic) often have vastly different properties with respect to UV absorption. CFT has acidic functionalities.

Based on this behavior of cefotaxime a simple and accurate spectrophotometric method was proposed to determine the pK_a value of CFT in buffer media of varying pH with uniform concentration.

Material& methods

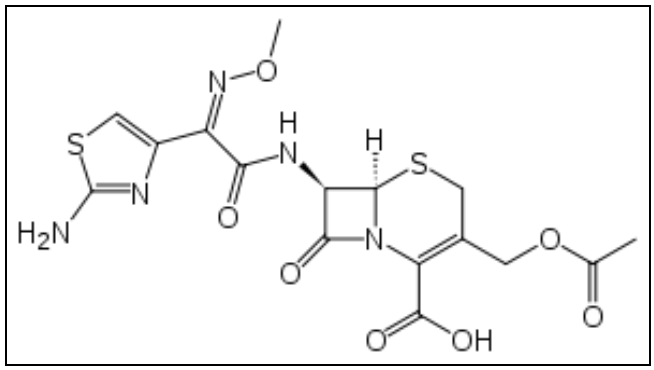
Apparatus

Shimadzu UV-1800 double beam spectrophotometer with 1 cm quartz cell was used to record electronic spectrum of CFT in buffer medium of varying pH's. Citizen model CTG 302B digital balance used to weigh the samples and Elico LI 615 pH-meter was used to measure the buffer pH.

Reagents and solutions

All the chemicals and reagents were of analytical grade and double distilled water was used for dilution of reagents and sample. CFT sample was procured as gift sample from Aurobindo Pharma, Hyderabad.

All the buffers prepared as per the procedure [14]. CFT stock solution was prepared by dissolving 56.8 mg in 250 ml water. The stock solution was stored in cool dry place, protected from light and this stock solution is further diluted with buffer. The structure of CFT is shown below.



Procedure

The Uv-visible spectra of cefotaxime was recorded in methanol solution and also recorded in aqueous buffer media pH ranging from 1.5 to 10.5 at a uniform concentration. The collective spectra's of CFT in the pH range 1.5 to 10.5 are shown in Fig 1**.** The difference in the absorbance at different wave length with respect to pH can be used to determine the value of the pK_a of CFT. The graphical plot of absorbance of CFT at a wavelength (λ1) and wavelength (λ2) against the pH solutions will give two

sigmoid plots, the inflection point of sigmoid plot will be the pK_a of CFT.

Results and discussion

The Uv-visible spectra's of CFT in methanol, acid and basic buffers are found to be different. The variation in spectral profile of CFT with respect to pH of buffer indicates that the electronic structure of CFT in pH sensitive and pH induce change in its electronic structure. The Fig 1 shows the collective spectra of CFT in the pH range 1.5 through 10.5. From the Fig, it is clear that CFT exhibits two isosbestic points, one at ~ 254 and the other at ~ 300 nm with a general hypsochromic shift of the spectral profile in the pH range 1.5-4.4. This spectral behavior is due the fact that deprotonation of carboxylic acid site of CFT. The protonation or deprotonation on the other active site will not much influence the electronic structure of CFT hence, it is not considered for studies.

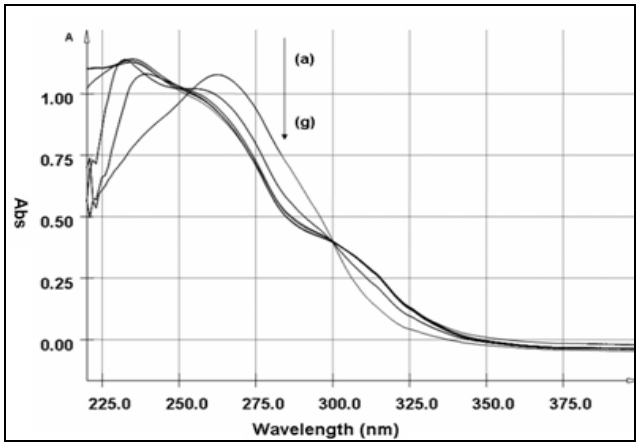


Fig 1: Electronic spectra of CFT (5 x10^{-5} M) in buffer media of varying pH (a) 1.5, (b) 2.5, (c) 3.2, (d) 4.4, (e) 6.8, (f) 8.4 and (g) 10.50

The presence of the isosbestic point is an indication of the presence of two absorbing species during acid-base equilibrium. The plots of Absorbance vs pH at both λ_{max} 238 and 260 nm are shown in **Fig 2** and the respective absorbance values at 238 nm and 260 nm at different pH's are collected in

Table 1

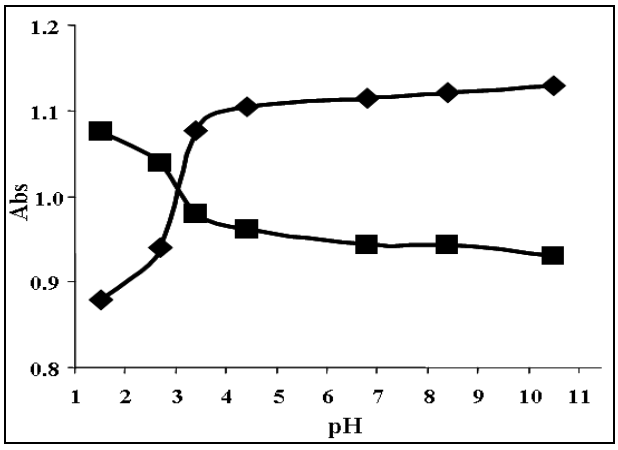


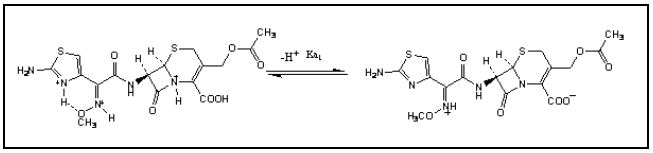
Fig 2: Plot of Absorbance vs pH at 238 (◆) and 260 (■) nm

The intercept of the two sigmoid plots is equal to the pK_a of CFT and it is found to be 3.5 from Fig 2.

Table 1: Absorbance values of CFT (5 x10^{-5} M) at 238 and 260 nm

pH	Abs 238 nm	Abs 260 nm
1.5	0.879	1.075
2.5	0.940	0.998
3.2	1.077	0.980
4.4	1.105	0.962
6.8	1.115	0.944
8.4	1.121	0.943
10.5	1.130	0.93

The experimental value is in good agreement with reported values[15]. The possible protonation and deprotonation mechanism is shown Scheme 1.



Scheme 1: Protonation-deprotonation of CFT

Conclusion

A simple method for the determination of pK_a of CFT is described. The method is based on the acid-base chemistry of carboxylic acid group of CFT. This method is suitable to the chemical having acid-base functionalities or having similar structure to CFT.

References

1. Kerns EH, Di L. Physicochemical pro filing: overview of the screens. Drug Discov Today Technologies,2004:1:343.
2. Avdeef A. Physicochemical profiling (solubility, permeability and charge state). Curr. Top. Med. Chem,2001:1:277–351.
3. Vieira DCM, Ricarte PC, Salgado HRN. Development and Validation of the Quantitative Analysis of Cefuroxime Sodium in Powder for Injection by Infrared Spectroscopy. Adv. Anal. Chem,2012:6:80–87.
4. Consortti LP, Salgado HRN. A Critical Review of Analytical Methods for Quantification of Cefotaxime. Crit. Rev. Anal. Chem,2017:47:359–371.
5. Manfio ML, Agarrayua DA, Machado JC, Schmidt CA. A Fully Validated Microbiological Assay to Evaluate the Potency of Ceftriaxone Sodium. Braz. J. Pharm. Sci,2013:49:4.
6. Ali SM, Elbashir AA, Aboul-Enein HY. Spectroscopic Methods for Analysis of Cephalosporins in Pharmaceutical Formulations. World J. Anal. Chem,2015:3:21–32.
7. Lee AC, Crippen GM. Predicting pKa. J Chem Inf Model,2009-2013:49:1033.
8. Katzung BG. Basic Pharmacology & Clinical, 9th ed; Guanabara Koogan S.A. Rio de Janeiro, Brazil, 2005.
9. Spillane WJ. Reactions of acids and their derivatives, Organic Reaction Mechanisms, 1984, 10.1002/9780470066713.ch2, (33-85), (2007).
10. Lin CE, Chen HW, Lin EC, Lin KS, Huang HC. Optimization of separation and migration behavior of

cephalosporins in capillary zone electrophoresis. J Chromatogr A,2000:879:197–210.
Journal of the Serbian Chemical Society,2014:79(5):579- 586
11. Blasioli S, Martucci A, Paul G, Gigli L, Cossi M, Johnston CT, *et al*. Colloid Interface Sci,2014:419:148–159.
12. Yang G, Zhao F, Zeng B. Biosense. Bioelectron,2014:53:447–452.
13. Shah R, Jat R. Reverse phase high performance liquid chromatographic method for the quantification of cefotaxime sodium in pharmaceutical dosage form. J. Drug Delivery and Therap.,2015:5(3):96-100.
14. The United States Pharmacopeia (USP 32). TheNational Formulary (NF 34). By authority of United States Pharmacopeial Convention. Rockville, MD: United States Pharmacopoeial Convention, INC, 2011b, 683.