Department of Applied Chemistry, Cochin University of Science and Technology, Kochi, India

Voltammetric studies of sparfloxacin and application to its determination in pharmaceuticals

K. Girish Kumar, P. Augustine, R. Poduval, S. John

Received May 24, 2005, accepted May 31, 2005

Dr. K. Girish Kumar, Reader in Analytical Chemistry, Department of Applied Chemistry, Cochin University of Science and Technology, Kerala, India
giri@cusat.ac.in

Pharmazie 61: 291–292 (2006)

A detailed study of the electrochemistry of sparfloxacin at a glassy carbon electrode was carried out in the pH range 2.0–10.0 in aqueous solution using cyclic and differential pulse voltammetry. Influence of different supporting electrolytes, pH, scan rate and concentrations were studied on the voltammetric response. The studies revealed the irreversible oxidation of sparfloxacin at basic pH in a diffusion controlled manner. In addition, a differential pulse voltammetric method was proposed for the determination of the drug in different pharmaceutical formulations.

1. Introduction

Sparfloxacin, 5-amino-1-cyclopropyl-7-(*cis*-3,5-dimethylpiperazin-1-yl)-6,8-difluro-1,4-dihydro-4-oxoquinoline-3-carboxylic acid and it is not yet official in any Pharmacopoeia. It is an antibacterial agent against gram positive and gram negative bacteria (Marona et al. 2001; Chin et al. 1991; Miyamoto et al. 1990).

Analytical methods for the determination of sparfloxacin in pure form and dosage forms include HPLC (Marona et al. 1999a; Borner et al. 1992; El-Sayed et al. 1995), UV-spectrophotometry (Marona et al. 1999b) and microbiological assay. The microbiological assay is the most commonly used routine method. However, it is slow, inaccurate and subject to interference with other antibiotics (Reeves et al. 1975). The major disadvantages of the HPLC method include the requirement for the complex and expensive equipment, provision for the use and disposal of solvents, a labour-intensive sample preparation procedure and personnel skilled in chromatographic techniques. Hence, it is worth to develop some novel methods for the determination of the drug.

In continuation of our studies on the analysis of drugs (Girish Kumar et al. 2001; Girish Kumar et al. 2000), a differential pulse voltammetric method has been developed for the determination of sparfloxacin in pure form and in dosage forms. Furthermore, cyclic, linear and differential pulse voltammetric studies have been carried out on the drug on bare and modified glassy carbon electrode to study the electrochemical reactions of the drug.

2. Investigations, results and discussion

Voltammetric studies of sparfloxacin on a glassy carbon electrode in acid, neutral and alkaline conditions at different sweep rates ranging from 50 mVs^{-1} to 1000 mVs^{-1} were carried out. For all concentrations and sweep rates studied, one anodic peak around 700 mV was observed. The oxidation peak may be due to the irreversible oxidation of the primary amino group present in the drug, and the overall reaction is found to be diffusion controlled. Differential pulse and square wave studies also led to the same conclusion. Glassy carbon electrodes modified with mercaptopropionic acid, mercaptobenzothiazole and thioglycolic acid (self assembled monolayer) were also used for carrying out the electrochemical studies but the modification did not offer additional advantage.

The effect of scan rate on peak current and peak potential of sparfloxacin has been evaluated. It is seen that as the scan rate increased, the peak potential is shifted to more positive values, which confirms the irreversibility of the process. The peak current increased linearly with the scan rate. The linear increase in peak current with the square

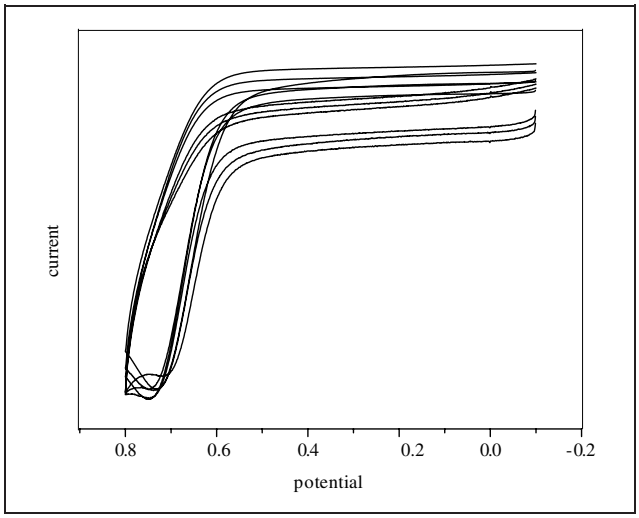

Fig.: Overlays of cyclic voltammograms of sparfloxacin at different concentrations in 0.1 M NaOH supporting electrolyte, scan rate – 100 mV/s

Table: Differential pulse voltammetric determination of sparfloxacin

Substance taken	Range studied (M)	Present method*			Comparison method*		
		Average recovery	SD	CV %	Average recovery	SD	CV %
Sparfloxacin	1×10^{-5}–1×10^{-4}	0.964	0.0096	0.99	0.95	0.009	0.16
Tablet (Sparta) specification 200 mg/tablet)		200.3 (mg/tablet)	1.01	0.50	198.1 (mg/tablet)	0.98	0.49

* Average of six replicates

root of scan rate, in the range 50 mVs^{-1} to 600 mVs^{-1} with a slope of 7.6 showed the diffusion controlled nature of the electro-oxidation.

The plot of peak potential $(Ep)_a$ vs the logarithm of scan rate also gave straight line as needed for a diffusion controlled process.

The studies have been carried out with different supporting electrolytes such as 0.1 N HCl, tetrabutylammonium chloride, KCl and 0.1 N NaOH. A well defined anodic peak has been obtained in the case of 0.1 N NaOH as supporting electrolyte and hence throughout the investigations, NaOH was used as the supporting electrolyte.

Influence of pH was studied in the pH range 2.0 to 10.0. The peak potential was found to have lower values at alkaline pH and increased with decrease in pH. Also the peak intensity was found to decrease in acidic media and was not seen below pH 7.0. Using the optimum conditions described above, typical cyclic voltammograms are obtained at various concentrations of sparfloxacin (Fig.).

On the basis of these investigations, an analytical method was suggested. Since the differential pulse voltammetry showed a much more intense oxidation peak than the linear and cyclic voltammetry, the quantitative technique was developed based on this technique. The optimum concentration range was found to be 1×10^{-4} to 1×10^{-5} M, with a lower detection limit of 1×10^{-5} M. The average error and the precision factor are highly satisfactory (Table). The method has been compared with the established spectrophotometric method (Marona et al. 1999b) and the results presented in the Table reveal the accuracy and precision of the presently developed method. The method has been applied for the determination of the drug in a commercially available tablet (SPARTA-Alembic Limited, India) and the results show that the technique is precise and accurate (Table).

The major advantage of the proposed method over the existing methods is that it is accurate, selective, precise and cost effective. The electrochemical studies reveal the irreversible oxidation pattern of the drug in basic medium.

3. Experimental

3.1. Apparatus

Electrochemical measurements were made on a BAS Epsilon Electrochemical analyzer (Bioanalytical System, USA) interfaced to a PC. For voltammetric measurements a commercial glassy carbon working electrode (∅: 3 mm, BAS), a platinum wire auxiliary electrode and Ag/AgCl (NaCl 3 M, BAS) reference electrode were used. Before each experiment the glassy carbon electrode was polished manually with alumina (∅: 0.01 μm) in the presence of double distilled water on a smooth polishing cloth.

3.2. Reagents and materials

Sparfloxacin tablets were purchased from the local market. All the chemicals used were of reagent grade quality and they were employed without further purification. Sparfloxacin stock solutions were prepared daily by direct dissolution in the selected supporting electrolytes. Three different electrolytes viz., HCl (0.1 M), tetrabutyl ammonium chloride (0.1 M), and NaOH (0.1 M) were used as the supporting electrolytes. All solutions were protected from light and were prepared in doubly distilled water.

3.3. Procedures

3.3.1. Calibration graphs

A stock solution of the drug (1×10^{-3} M) was prepared in methanol. Standard solutions of the analyte (1×10^{-4}–1×10^{-5} M) were prepared by serial dilution of stock solution and adding the appropriate supporting electrolyte. The stock solutions were prepared daily and protected from light. Cyclic, linear and differential pulse voltammetric measurements were conducted on the samples. The calibration curve was prepared by plotting the differential pulse voltammetric current vs concentration.

3.3.2. Procedure for tablets

Ten tablets were weighed and ground to a fine powder. An adequate amount of this powder corresponding to a stock solution of concentration 1×10^{-3} M was weighed and transferred to a beaker. The powder was dissolved in methanol and filtered to a volumetric flask (100 ml) through a Whatman 41 filter paper. The beaker was washed several times and the washings were collected in the standard flask and then it was quantitatively diluted. Solutions of different concentrations were prepared by the general procedure after adding the supporting electrolyte. Differential pulse voltammetric currents were measured and the concentrations have been determined from the calibration curve.

References

Borner K, Borner E, Lode H (1992) Determination of sparfloxacin in serum and urine by high-performance liquid chromatography. J Chromatogr Biomed Appl 579: 285–289.

Chin NX, Gu JW, Yu KW, Zhang YX, Neu HC (1991) *In vitro* activity of sparfloxacin. Antimicrob Agents Chemother 35: 567–571.

El-Sayed YM (1995) A simple high-performance liquid chromatographic assay for sparfloxacin in human plasma. Anal Lett 28: 279–293.

Girish Kumar K, Chowdary KPR, Devala Rao G (2000) spectrophotometric method for the determination of nimodipine in pharmaceutical dosage forms. Ind J Pharm Sci: 316–318.

Girish Kumar K, Chowdary KPR, Devala Rao G (2001) A new spectrophotometric method for the determination of nitrendipine. The Antiseptic 98: 453–454.

Marona HRN, Schapoval EES (1999a) A high performance liquid chromatographic assay for sparfloxacin. J Pharm Biomed Anal 20: 413–417.

Marona HRN, Schapoval EES (1999b) Spectrophotometric determination of sparfloxacin in tablets. J Antimicrob Chemother 44: 136–137.

Marona HRN, Schapoval EES (2001) Spectrophotometric determination of sparfloxacin in pharmaceutical formulations using bromothymol blue. J Pharm Biomed Anal 26: 501–504.

Miyamoto T, Matsumoto JI, Chiba K, Egawa H, Shibamori K, Minamida A. et al. (1990) Synthesis and structure activity relationships of 5-substituted 6,8 fluoroquinolones, including sparfloxacin, a new quinolone antibacterial agent with improved potency. J Med Chem 33: 1645–1656.

Reeves DS, Bywater MJ (1975) Quality control of serum gentamycin assays-experience of national surveys. J Antimicrob Chemother 1: 103–116