ing suitable aliquots of the clear supernatant liquor and diluting with the selected supporting electrolyte. DPV and SWV curves were recorded. In order to know whether the excipients show any interference with the analysis, known amounts of the pure drug were added to the different pre-analysed formulations of CIS and the mixtures were analysed by the proposed methods.

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Determination of the antihypertensive drug lacidipine in pharmaceuticals by differential pulse and square wave voltammetry

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Lacidipine (LCD) is, like other dihydropyridine calcium channel blockers [1, 2], widely used in the treatment of hypertension, Angina pectoris and in the therapy of cerebrovascular spasm of various origins.

Several articles describe HPLC methods for the determination of LCD in plasma [3–5]. Also micellar electrokinetic chromatography has been used for the determination of plasma levels of LCD [6]. However, to our knowledge at present no information about the electrochemical redox properties of LCD and its analytical applications have appeared in the literature. The only work that involves electrochemical aspects has been published recently [7]. It deals with the voltammetric behaviour of LCD and its determination by differential pulse voltammetry.

Electrochemistry has a distinct advantage compared to most analytical techniques. Many studies have demonstrated that the electroanalytical techniques – voltammetry and various pulse methods – are useful for making concentration measurements as well as for studying reaction mechanisms of electroactive compounds in pharmaceuticals [8–12].

The purpose of the present study was to carry out a detailed investigation on the electrochemical behaviour of LCD at a glassy carbon electrode using cyclic, differential pulse (DPV) and square wave voltammetry (SWV) and performed a study concerning the determination of LCD in pharmaceutical dosage forms using DPV and SWV.

The oxidation of LCD was studied by cyclic, DPV and SWV using methanol as solvent and sulphuric acid, phosphate and Britton-Robinson buffers as supporting electrolytes. LCD was oxidized at the glassy carbon electrode, producing only one anodic peak. The electrochemical oxidation can be represented by the following equation [7, 13, 14]:

$$\text{Dihydropyridine} \rightarrow \text{pyridine} + 2e^- + 2H^+$$

LCD is oxidized in an alcoholic medium (30% methanol; v/v) in the pH range 1.5–11.04 at a glassy carbon electrode in sulphuric acid, Britton-Robinson and phosphate buffers as supporting electrolytes giving rise to voltammetric peaks whose potentials and currents are pH dependent. Cyclic voltammetric measurements performed on 1×10^{-4} M LCD solutions show the irreversible nature of the oxidation peak at the glassy carbon electrode in the range of scan rates comprised of between 15 and 750 mVs^{-1} and in the entire pH range investigated. A 152 mV positive shift in the peak potential was observed, which confirms the irreversibility of the process, with the simultaneous increase in peak current when the scan rate was increased. Scan rate studies were then carried out to assess whether the processes on the glassy carbon electrode were under diffusion or adsorption control. When scan rate is varied from 5 to 750 mVs^{-1} in a 1×10^{-4} M LCD, a linear dependence of the peak intensity upon the square root of the scan rate is found, demonstrating a diffusional behaviour (correlation coefficient 0.997). Plotting log i vs log v, a straight line was obtained

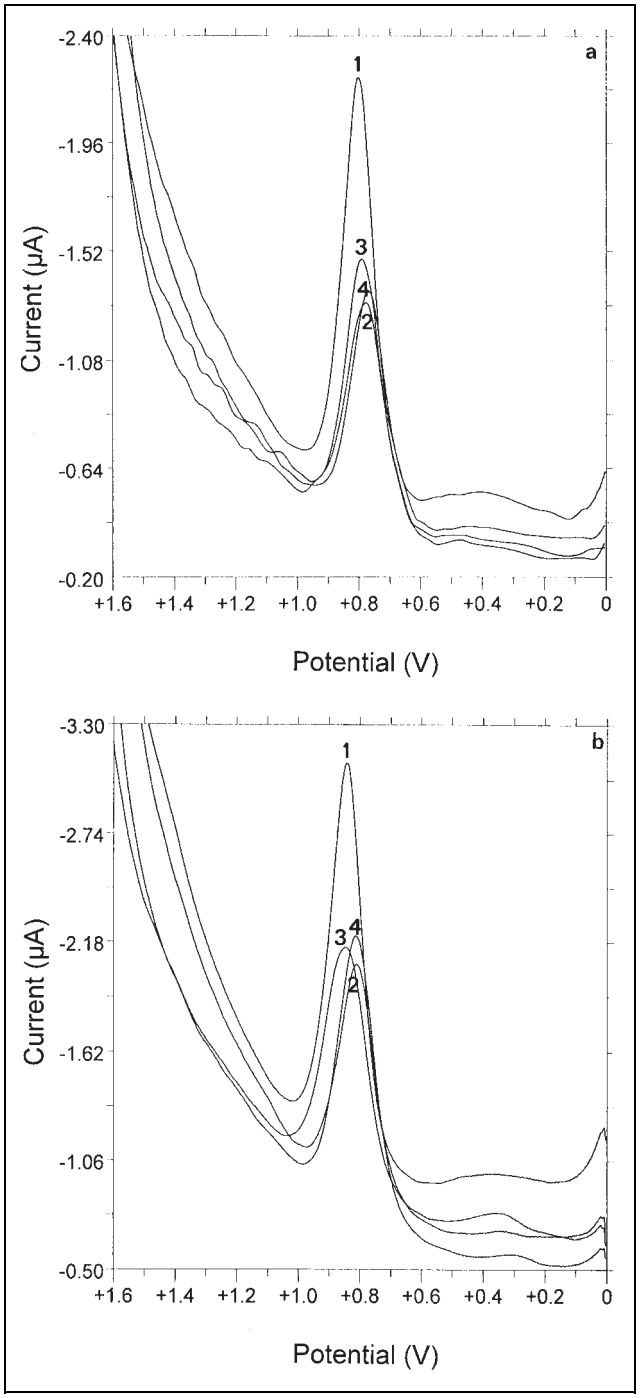

Fig.. Differential pulse (a) and square wave (b) voltammograms of 1×10^{-4} M LCD in different supporting electrolytes (30% methanol). 0.5 M H_2SO_4 (1); phosphate buffer at pH 2.5 (2); Britton-Robinson buffer at pH 2.06 (3); Britton-Robinson buffer at pH 3.0 (4)

$\log i = -1.13 + 0.97 \log v$, with a slope very close to one, which is the expected value for an ideal reaction of surface species [15]. The effect of pH on the peak current shows a maximum at pH 1.5 (0.5 M H_2SO_4) thus this pH value and this supporting electrolyte was chosen to carry out the electroanalytical study. 0.5 M H_2SO_4 was selected for further work because it not only gave the highest peak current but also gave the best peak shape (Fig.). For quantitation the calibration curve method, with a concentration range between 2×10^{-6} and 1×10^{-4} M was used. The characteristics of the calibration curves were described in the Table. The detection (LOD) and quantitation (LOQ) limits were also given in the Table. The LOD and LOQ

Table: Statistical analysis of LCD using both of the proposed voltammetric methods and assay of LCD in commercial tablets using the proposed methods and mean recoveries of LCD in spiked Lacipil® tablets

	DPV	SWV
Working potential, V (vs Ag/AgCl)	0.81	0.84
Linearity range (M)	2×10^{-6} to 1×10^{-4}	2×10^{-6} to 1×10^{-4}
Slope (μAM^{-1})	1.06×10^4	9.6×10^3
Intercept (μA)	0.033	0.073
Correl. Coeff.	0.999	0.999
RSD of slope	1.19	0.46
RSD of intercept	0.97	0.36
LOD	1.42×10^{-7}	3.12×10^{-7}
LOQ	4.73×10^{-7}	1.04×10^{-6}
Repeatability of peak current (RSD %)	0.71	0.72
Repeatability of peak potential (RSD %)	0.74	0.30
Reproducibility of peak current (RSD %)	0.58	0.86
Reproducibility of peak potential (RSD %)	0.57	1.01
Labelled claim (mg)	4.0	4.0
Amount found (mg)[a]	3.97	3.99
RSD %	0.76	0.70
Added (mg)	1.0	1.0
Found (mg)	0.99	1.00
Recovered %[b]	99.73	100.1
RSD % of recovery	0.81	0.69

[a] Each value is the mean of five experiments.
[b] Recovery value is the mean of five results

values were calculated as the blank response plus three times or ten times, respectively the blank standard deviation divided by the slope of the calibration curve. The repeatability (intra-day) and the reproducibility (inter-day) of the peak potential and peak currents were calculated from four independent runs of a 4×10^{-5} M LCD solutions. The results were shown in the Table.

The proposed methods were further applied to the determination of the compound in its tablet dosage form. Well defined DPV and SWV peaks were obtained and no interferences were observed. There is no need for any extraction procedure before voltammetric analysis. The proposed methods could be applied with great success to LCD assay in tablets without any interferences.

There are no official methods in any pharmacopoeias for the determination of LCD from tablets. For this reason, both the proposed voltammetric techniques were checked by performing recovery tests. Moreover, in order to know whether the excipients in the tablets show any interference with the analysis and the accuracy of the proposed methods were evaluated by recovery studies after addition of known amounts of pure LCD to various pre-analyzed formulations of the drug (Table). The results demonstrate the validity of the proposed methods for the determination of LCD in pharmaceutical dosage forms. The proposed methods proved to have precision and accuracy adequate for a reliable analysis of LCD. From all of the results obtained it can be concluded that DPV and SWV are adequate voltammetric techniques for the determination of LCD. Both techniques are remarkable regarding reproducibility and speed. The recoveries obtained from tablet dosage forms show the applicability of these techniques to quality control analysis of this drug. According to the obtained results, the LOD and LOQ values were lower and linearity range was wider than with previously published voltam-

metric techniques [7]. The advantages of the proposed methods for analytical purposes lie in the rapid determination of LCD in pharmaceutical dosage forms, easy preparation of the sample, fair enough reproducibility, use of inexpensive instrumentation. It does not require separation procedures such as filtration, extraction and expensive grades of solutions.

Experimental

1. Apparatus and reagents

The voltammetric experiments were performed using a Bioanalytical System (BAS 100W) electrochemical analyser. A glassy carbon working electrode (BAS), a Ag/AgCl reference electrode (NaCl 3M, BAS), a platinum wire auxiliary electrode (BAS) and a standard one-compartment three-electrode cell of 10 ml capacity were used in all experiments. Before each experiment the glassy carbon electrode was polished manually with alumina ($\phi = 0.01$ μm), in the presence of bidistilled water on a smooth polishing cloth. Operating conditions for differential pulse voltammetry (DPV) were: pulse amplitude 50 mV; pulse width 50 ms; scan rate 20 mVs^{-1} and for square wave voltammetry (SWV); pulse amplitude 25 mV; frequency, 15 Hz; potential step 4 mV.

LCD and its pharmaceutical formulation were kindly provided by Glaxo Smith-Kline Pharm. Ind. (Istanbul, Turkey). A stock solution of LCD (1×10^{-3} M) was prepared in methanol and kept in the dark in a refrigerator. The working solutions for the voltammetric investigations were prepared by dilution of the stock solution by the selected supporting electrolytes, namely sulphuric acid (0.5 M), phosphate buffer (0.2 M; pH 2.5–11.0) and Britton-Robinson buffer (0.04 M; pH 2.06–11.04) were used.

2. Analysis of tablets

Ten tablets were throughly ground and mixed. An amount of powder equivalent to 1×10^{-3} M of LCD was accurately weighed and transferred into a 25 ml calibrated flask and completed to the volume with methanol. The contents of the flask were sonicated for 10 min to effect complete dissolution. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant liquor and diluting with the selected supporting electrolyte.

In order to know whether the excipients show any interference with the analysis, known amounts of the pure drug were added to the different preanalysed formulations of LCD and the mixtures were analysed by the proposed methods.

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Preparation and characterization of sparfloxacin-β-cyclodextrin complexes

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Sparfloxacin, (*cis*)-5-amino-1-cyclopropyl-7-(3,5-dimethyl-1-piperazinyl)-6,8-di-fluoro-1,4-dihydro-4-oxo-3-quinoline carboxylic acid, is a fluoroquinolone antibacterial reported to have a low aqueous solubility [1]. It has been reported that the absorption of sparfloxacin after oral administration is a long process and peak concentrations are generally not observed before 3 to 5 hours which leads to interpatient variability [2, 3]. Cyclodextrins by virtue of formation of water soluble inclusion complexes have been known to increase the solubility and dissolution rate of poorly water soluble drugs [4–6].

The present study was an attempt to improve the solubility, dissolution rate and bioavailability of sparfloxacin by forming inclusion complexes with β-cyclodextrin (β-CD). Inclusion complexes of sparfloxacin with β-CD were prepared by kneading and solid dispersion techniques in molar ratio of 1 : 1 and evaluated by differential scanning calorimetry, powder X-ray diffractiometry, fourier transform infrared spectroscopy, phase solubility and dissolution studies.

Solubility of SFLX increased linearly with increasing concentration of β-CD, showing a typical A_L-type phase solubility curve [7], characteristic of complexation with a stoichiometric ratio of 1 : 1. The apparent 1 : 1 stability constant, K_c, was found to be 57.33 M^{-1}.

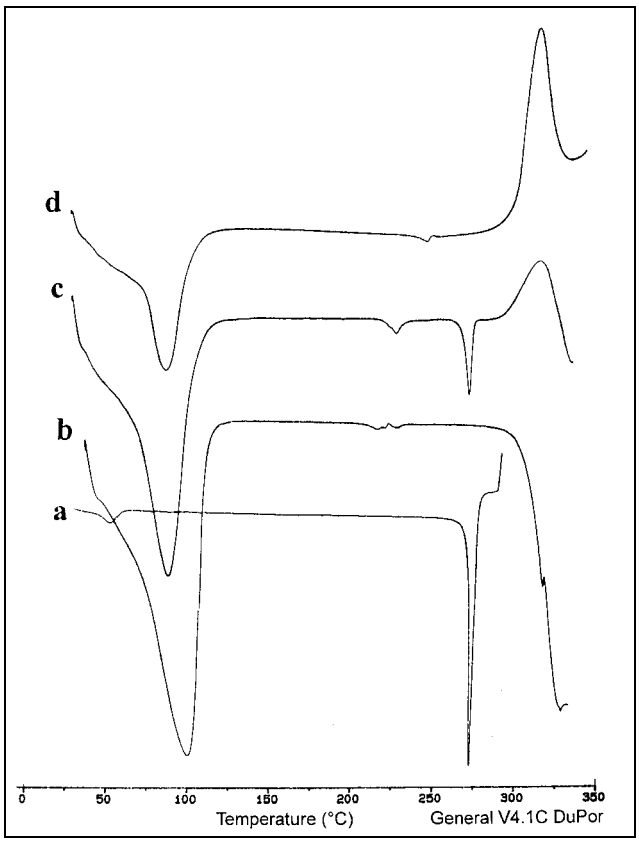

Fig. 1: DSC thermograms of the sparfloxacin-β-cyclodextrin system. a: sparfloxacin, b: β-cyclodextrin, c: 1:1 complex by solid dispersion d: 1:1 complex by kneading