Department of Chemistry[1], Kahramanmaras Sutcu Imam University, Faculty of Science and Arts, Campuse of Avsar, Kahramanmaras; Department of Analytical Chemistry[2], Ankara University, Faculty of Pharmacy, Tandogan, Ankara, Turkey

Electroanalytical determination of donepezil HCl in tablets and human serum by differential pulse and osteryoung square wave voltammetry at a glassy carbon electrode

A. Golcu[1], S. A. Ozkan[2]

Received September 10, 2005, accepted December 16, 2005

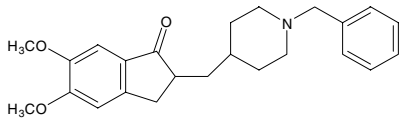
Prof. Dr. Sibel A. Özkan, Department of Analytical Chemistry, Ankara University, Faculty of Pharmacy, 06100 Tandogan, Ankara
ozkan@pharmacy.ankara.edu.tr

Pharmazie 61: 760–765 (2006)

Donepezil hydrochloride (DNP) is used for the treatment of mild to moderate dementia of the Alzheimer's type. The voltammetric behavior of DNP was studied at a glassy carbon electrode using cyclic, linear sweep, differential pulse (DPV) and square-wave (OSWV) voltammetric techniques. DNP exhibited irreversible anodic waves within the pH range 1.80 and 9.00 in different supporting electrolytes. The peak was characterized as being irreversible and diffusion-controlled. The possible mechanism of the oxidation process is discussed. The current-concentration plot was rectilinear over the range from 1×10^{-6} to 1×10^{-4} M in Britton-Robinson buffer at pH 7.0 with a correlation coefficient between 0.997 and 0.999 in supporting electrolyte and human serum samples using the DPV and SWV techniques. The repeatability and reproducibility of the methods for both media (supporting electrolyte and serum sample) were determined. Precision and accuracy of the developed methods were demonstrated by recovery studies. The standard addition method was used for the recovery studies. No electroactive interferences were found in biological fluids from endogenous substances or additives present in tablets. The methods developed were successfully applied to the determination of DNP in tablets and in spiked human serum.

1. Introduction

Donepezil (DNP) is used for the treatment of mild to moderate dementia of the Alzheimer's type. Current theories on the pathogenesis of the cognitive signs and symptoms of Alzheimer's disease attribute some of them to a deficiency of cholinergic neurotransmission. DNP is postulated to exert its therapeutic effect by enhancing cholinergic function (PDR 2003). The chemical name for DNP is [(±)-2,3-dihydro-5,6-dimethoxy-2-[[1-(phenylmethyl)-4-piperidinyl]methyl]-1H-inden-1-one hydrochloride.



DNP is well absorbed with a relative oral bioavailability of 100% and reaches peak plasma concentrations in 3 to 4 h. The elimination half-life of DNP is about 70 h. Therefore, development of a more effective analytical method is required for the routine analysis of DNP in biological fluids and pharmaceutical dosage forms (PDR 2003).

A survey of the literature revealed that very few methods have been proposed for its determination in biological fluids and pharmaceutical dosage forms. The analysis of DNP in human plasma and tablet dosage forms using HPLC-UV (Yasui-Furukori et al. 2002; Adrisano et al. 2001; Farger and Gartner 2002; Pappa et al. 2002) and mass spectrometric detection (Matsui et al. 1999; Lu et al. 2004) including a time consuming sample preparation step have been reported in the literature.

Electroanalytical methods have been developed to the point where they are highly sophisticated and flexible in application. However, they are not as widely used as their potential might suggest. In particular, electroanalytical methods allow the determination of electroactive analytes even at very low levels of concentration. A method which has a shorter run time and is fully validated is particularly useful for routine analysis. Electroanalytical techniques have been used for the sensitive determination of a wide range of pharmaceuticals, with the advantages that in most instances there is no need for derivatization, extraction or evaporation steps, and that these techniques are less sensitive to matrix effects than other analytical techniques (Wang 2000; Smyth and Vos 1992).

Electroanalytical techniques have been used for the determination of a wide range of drug compounds (Uslu and Özkan 2002, 2004; Uslu et al. 2005). Additionally, the application of electroanalytical techniques includes the determination of the electrode reaction mechanism. Redox properties of drugs can give insights into their metabolic fate or their *in vivo* redox processes or pharmacological

activity. No electroanalytical methods for the determination and oxidation mechanism of DNP, in bulk form, pharmaceutical dosage forms and biological fluids, appear to have been reported to date. Therefore the aim of this study was to establish the experimental conditions to investigate the oxidation behaviour of DNP, and to optimize the conditions for determination of this compound in pharmaceutical dosage forms and human serum samples using cyclic, linear sweep, differential pulse (DPV) and square wave (OSWV) voltammetric techniques.

2. Investigations, results and discussion

DNP is electrochemically oxidizable on a glassy carbon electrode in all media studied and at all pH values from 1.8–9.0. DNP is precipitated at pH $\geq$ 10.0. For this reason, only the range between pH 1.8 and 9.0 was investigated in all supporting electrolytes. DNP is characterised on current-voltage curves recorded by CV at a glassy carbon electrode by one anodic peak and one wave depending on pH (Fig. 1). The peak and wave were shifted to less positive potentials by increasing the pH value. All anodic responses will be discussed in this contribution.

The reversibility of the anodic process was studied using cyclic voltammetry. As shown in Fig. 2, scanning was started at -0.3 V in the positive direction. At pH 7.0, DNP oxidation occurs at about $+0.9$ V. After the first peak at $+0.9$ V **(I)**, one additional wave **(II)** was obtained at about $+1.4$ V (Fig. 2). On reversing at $+1.6$ V, no reduction peak or wave corresponding to the anodic peak and wave was observed on the cathodic branch. On the second and third sweep, no new anodic and cathodic peak appeared. The initial potential variation was studied in supporting electrolytes between -0.30 and 0.0V, and it was observed that the initial potential had no effect on either the peak potential or the peak current for the main peak. Cyclic voltammetric measurements showed the irreversible nature of the oxidation process. It was observed that the DNP peak and waves decreased at the second and higher cycles (Fig. 2). This phenomenon may be partly attributed to the consumption of adsorbed DNP on the electrode surface.

The effect of the potential scan rate between 5 and 500 mVs^{-1} on the peak current and potential of DNP was evaluated. The first oxidation peak was split by raising the scan rate (above 500 mVs^{-1}). A 99 mV positive shift in the peak potential confirmed the irreversibility of the oxidation process. Scan rate studies were carried out to assess whether the processes at the glassy carbon electrode were under diffusion or adsorption control. When the scan rate was varied from 5 to 500 mVs^{-1} in 1×10^{-4} M solution of DNP, a linear dependence of peak intensity i_p (μA) on the square root of the scan rate $\nu^{1/2}$ (mVs^{-1}) was

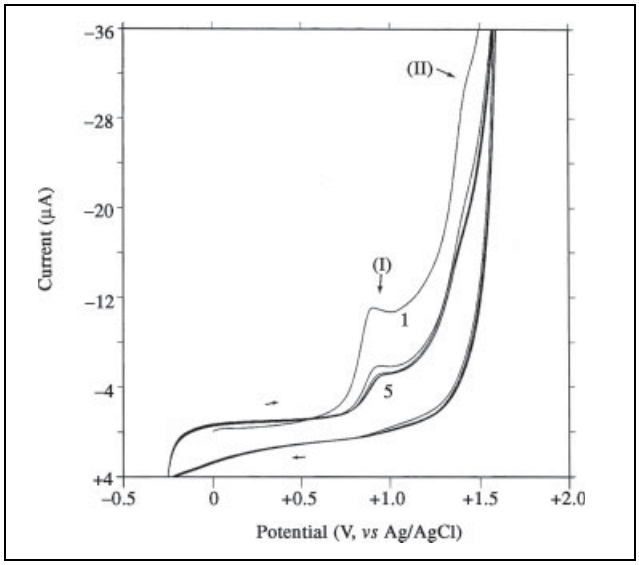


Fig. 2: Multisweep cyclic voltammograms of 1×10^{-4} M DNP solutions in Britton-Robinson buffer at pH 7.00. Scan rate, 100 mV/s. The numbers indicate the number of scans. First peak and second wave are indicated with arrows and shown as (I) and (II), respectively

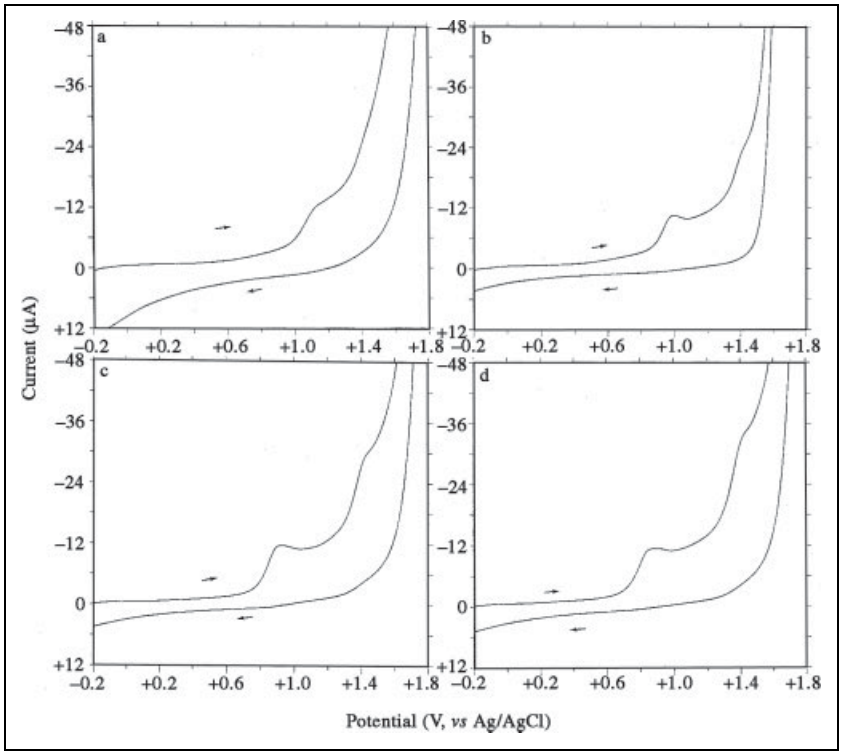


Fig. 1:
Cyclic voltammograms of 1×10^{-4} M DNP in phosphate buffer at pH 3.00 (a); acetate buffer at pH 4.60 (b); Britton-Robinson buffer at pH 7.00 (c); Britton-Robinson buffer at pH 8.00 (d). Scan rate 100 mVs^{-1}

found, demonstrating diffusional behavior. The equation is given below in Britton-Robinson buffer at pH 7.0:

$$ip\ (\mu A) = 0.53\nu^{1/2}\ (mVs^{-1}) - 1.05$$
$$r = 0.995\ (n = 8) \quad (1)$$

A plot of logarithm of peak current versus logarithm of scan rate gave a straight-line with a slope of 0.65, close to the theoretical value of 0.5, which applies to a diffusion controlled electrode process (Laviron et al. 1980). The equation obtained is:

$$\log i_p\ (\mu A) = 0.65 \log \nu\ (mVs^{-1}) - 0.70$$
$$r = 0.997\ (n = 8) \quad (2)$$

Due to the poorly resolved signal obtained by cyclic voltammetry (CV) when pH decreased below 3.0, the effects of pH on peak potential and peak intensity were studied using CV, DPV and SWV techniques. The peak potential of the oxidation process moved to a less positive potential. All the graphs obtained were found to be similar. For this reason, only the SWV graph for the first peak is given as Fig. 3a and 3b. The plot of the first peak potential versus pH showed a linear decrement between 1.8 and 7.0. At pH $\geq$ 10.0 the DNP become a turbid solution and then precipitated.

The linear segment can be expressed by the following equation in all supporting electrolytes when using the SWV technique.

$$Ep\ (mV) = 1380.66 - 79.39\ pH$$
$$r: 0.918\ (\text{between pH 1.5 and 7.0}) \quad (3)$$

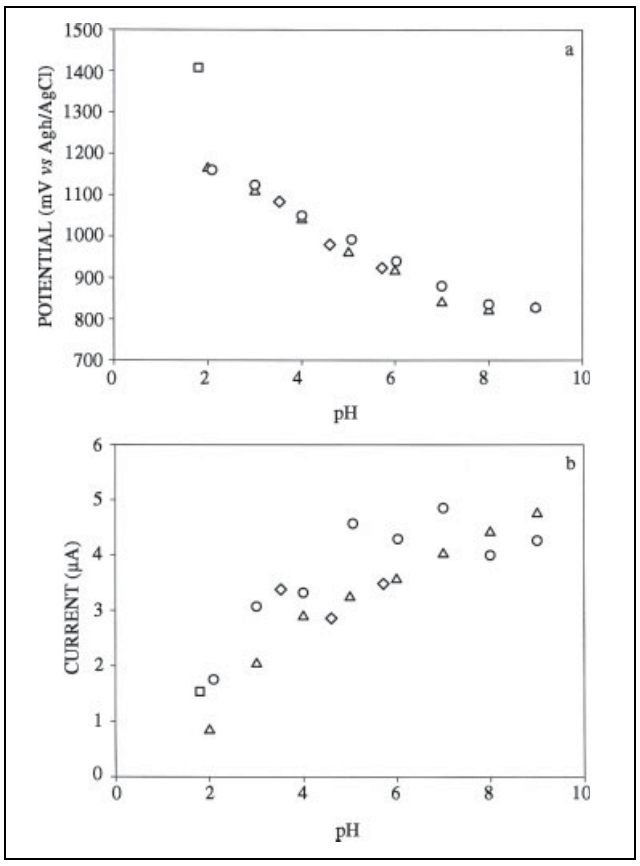


Fig. 3: Effects of pH on DNP anodic peak potential (a) and peak current (b); DNP concentration 1×10^{-4} M. 0.1 M H_2SO_4 (□); 0.04 M Britton-Robinson (○); 0.2 M acetate (◇) and 0.2 M phosphate (△) buffers

As can be seen from the second equation, and Fig. 3a, the peak potential becomes nearly pH independent above pH 7.0.

The influence of pH on the DNP current at a glassy carbon disc electrode was also studied. The i_p vs. pH plot (Fig. 3b) shows that peak current is maximum in neutral media. The experimental results show that the shapes of the curves were better in Britton-Robinson buffer at pH 7.0 than for other supporting electrolytes and pH values. Britton-Robinson buffer at pH 7.0 was chosen with respect to the sharp response and better peak shape for the calibration curve for pharmaceutical dosage form and human serum samples. For this reason Britton-Robinson buffer at pH 7.0 was chosen for calibration and analysis of the serum samples and tablets. A buffer concentration of 0.04 M was selected to obtain an adequate buffering capacity.

Even though the exact oxidation mechanism was not determined, some conclusions about the potentially electroactive centers under working conditions could be reached. The electrochemical oxidation of DNP appears to be a complex process and different reaction pathways are possible. Taking into account all the electrochemical studies performed, we considered the electrochemical behavior of DNP at glassy carbon electrode, and suggest that the first main anodic reaction could be attributed to the oxidation of the nitrogen atom on the piperidinyl moiety in the molecule. The second anodic oxidation step of DNP appears to be related to the oxidation of alkoxybenzene, which was reported in our previous study and in the literature (Demircigil et al. 2002; Grimshow 2000; Bermejo et al. 2000). Our results revealed a good agreement with the redox mechanism postulated for similar compounds such as formoterol fumarate, mefexamide, sulpiride and tamsulosin and suggested that the second anodic step of DNP can be determined electrochemically by oxidation of alkoxybenzene groups. Taking into account all the studies performed, we suggest that the oxidation processes may be occurring on the nitrogen atom of the piperidinyl moiety and alkoxybenzene groups of the molecule, respectively, which is electroactive in both acidic and basic media.

2.1. Analytical parameters and validation of the proposed methods

DPV and OSWV are effective and rapid electroanalytical techniques with well-established advantages, including good discrimination against background currents and low detection limits (Wang 1996; Kissinger and Heineman 1996). The peak current-potential curve is the most useful analytical signal for both techniques. Its peak height is usually proportional to concentration.

Quantitative evaluation is based on the linear correlation between the peak current and concentration. Good correlations were obtained in DPV and OSWV of DNP in a supporting electrolyte consisting of 0.04 M BR buffer at pH 7.0 for concentrations between 1×10^{-6} and 1×10^{-4} M; then the plot leveled off at higher concentrations, as expected for a process that is limited by adsorption of the compound. The characteristics of the calibration plots including necessary validation parameters for both techniques are summarized in Table 1. The detection (LOD) and quantification limits (LOQ) of both procedures are also shown in Table 1, which were calculated on the peak current using the following equations:

$$LOD = 3\ s/m\,; \quad LOQ = 10\ s/m \quad (4)$$

Table 1: Regression data of calibration lines for quantitative determination of DNP by DPV and OSWV in supporting electrolyte and human serum sample

	DPV		OSWV	
	Supporting electrolyte	Serum	Supporting electrolyte	Serum
Measured potential (V)	0.79	0.81	0.82	0.83
Linearity range (M)	1×10^{-6}–1×10^{-4}	1×10^{-6}–1×10^{-4}	1×10^{-6}–1×10^{-4}	1×10^{-6}–1×10^{-4}
Slope (μAM^{-1})	2.77×10^{4}	1.96×10^{4}	4.11×10^{4}	3.22×10^{4}
Intercept (μA)	0.106	0.108	0.191	0.0334
Correlation coefficient	0.997	0.997	0.999	0.999
SE of slope	5.31×10^{2}	3.52×10^{2}	8.72×10^{2}	2.03×10^{2}
SE of intercept	2.39×10^{-2}	1.58×10^{-2}	3.9×10^{-2}	9.47×10^{-3}
LOD (M)	2.90×10^{-7}	2.34×10^{-7}	2.63×10^{-7}	1.51×10^{-7}
LOQ (M)	9.66×10^{-7}	7.80×10^{-7}	8.77×10^{-7}	5.04×10^{-7}
Repeatability of peak current (RSD%)	0.884	0.224	0.158	0.292
Repeatability of peak potential (RSD%)	0.566	0.273	0.399	0.213
Reproducibility of peak current (RSD%)	0.780	0.474	1.425	0.713
Reproducibility of peak potential (RSD%)	0.752	0.901	0.782	0.401

Where s, the noise estimate, is the standard deviation of the peak currents (four runs) of the sample, and m is the slope of the related calibration graphs (Riley and Rosanske 1996; Swartz and Krull 1997).

Performing replicate analyses of the standard solutions assessed the accuracy, precision and reproducibility of the proposed methods. The selected concentrations within the calibration range were prepared in the supporting electrolytes and analyzed with the relevant calibration curves to determine intra-day and inter-day variability. The intra- and inter-day precision were determined as the RSD %. Precision, accuracy and reproducibility results shown in Table 1 demonstrate good precision, accuracy and reproducibility.

Stability studies of DNP in supporting electrolyte indicated that no significant changes in sample concentrations occurred on storage of samples over a 1-week period in a refrigerator at 4 °C.

2.2. Determination of DNP in film-coated tablets

On the basis of the above results, the proposed DPV and OSWV methods were applied to the direct determination of DNP contents in film-coated tablet dosage forms using the relevant calibration straight lines without any sample extraction or filtration and after adequate dilution. Each tablet for oral administration contains 5.0 mg donepezil HCl, and the following inactive ingredients: lactose monohydrate, cornstarch, microcrystalline cellulose, hydroxypropyl cellulose and magnesium stearate. The film coating contains talc, polyethylene glycol, hydroxypropyl methylcellulose and titanium dioxide (PDR 2003). The proposed methods could be successfully applied to DNP assay in film-coated tablet dosage forms without any interference. The assay showed the drug content of this product to be in accordance with the labeled claim (Table 2).

Recovery of the analyte of interest from a given matrix can be used as a measure of the accuracy of the method. In order to check the accuracy and precision of the method developed and to prove the absence of interference by excipients, recovery studies were carried out using the standard addition technique. Recovery studies were carried out after the addition of known amounts of the pure drug to various pre-analyzed formulations of DNP. The application of this procedure is explained in the Experimental section. The results obtained demonstrate the validity and accuracy of the proposed methods for the determination of DNP in film-coated tablets (Table 2). These results reveal that both methods had adequate precision and accuracy and consequently can be applied to the determination of DNP in tablets without any interference from the excipients.

Table 2: Assay results from DNP film-coated tablets (Aricept®) and mean recoveries in spiked tablets

	DPV	OSWV
Labeled claim (mg)	5.00	5.00
Amount found (mg)[a]	5.001	4.981
RSD%	1.866	0.572
Bias%	−0.02	0.38
Added (mg)	2.00	2.00
Found (mg)[a]	2.013	2.005
Recovery %	100.69	100.26
RSD % of recovery	0.823	0.812
Bias %	−0.65	−0.25

[a] Each value is the mean of 5 experiments

2.3. Determination of DNP in spiked serum samples

The optimized procedure was successfully applied to the determination of DNP in protein-free spiked human serum samples. Acetonitrile was used as a serum precipitating agent. No extraction steps other than centrifugal protein separation were required prior to assay for the drug. Fig. 4 illustrates the response of successive standard additions of DNP. Calibration equation parameters and necessary validation data are shown in Table 1. The recovery results obtained for spiked human serum samples are given in Table 3. The recovery results of DNP in serum samples were calculated from the related linear regression equations, which are given in Table 1. The LOD and LOQ values were also calculated and shown in Table 1. Repeatability and reproducibility of peak potential and current are also shown in Table 1. Typical DPV and OSWV curves of DNP examined in serum samples are shown in Figs. 4a and 4b, respectively. As can be seen in Fig. 4; no oxidation compounds and no extra peaks derived from biological material occurred in the potential range where the analytical peak appeared. Using both the procedures proposed in this paper to determine DNP in spiked serum samples, no sample pretreatment was required, other than precipitation of the serum proteins with acetonitrile and a dilution step with the selected supporting electrolyte, and no time-consuming extraction and evaporation steps are required.

Table 3: Application of the DPV and OSWV methods to the determination of DNP in spiked human serum samples

Technique	Medium	DNP added (M)	n	DNP found (M)	Average recovery (%)	RSD (%)	Bias (%)
DPV	serum	4×10^{-5}	5	4.03×10^{-5}	100.75	0.530	−0.75
OSWV	serum	4×10^{-5}	5	4.01×10^{-5}	100.25	0.442	−0.25

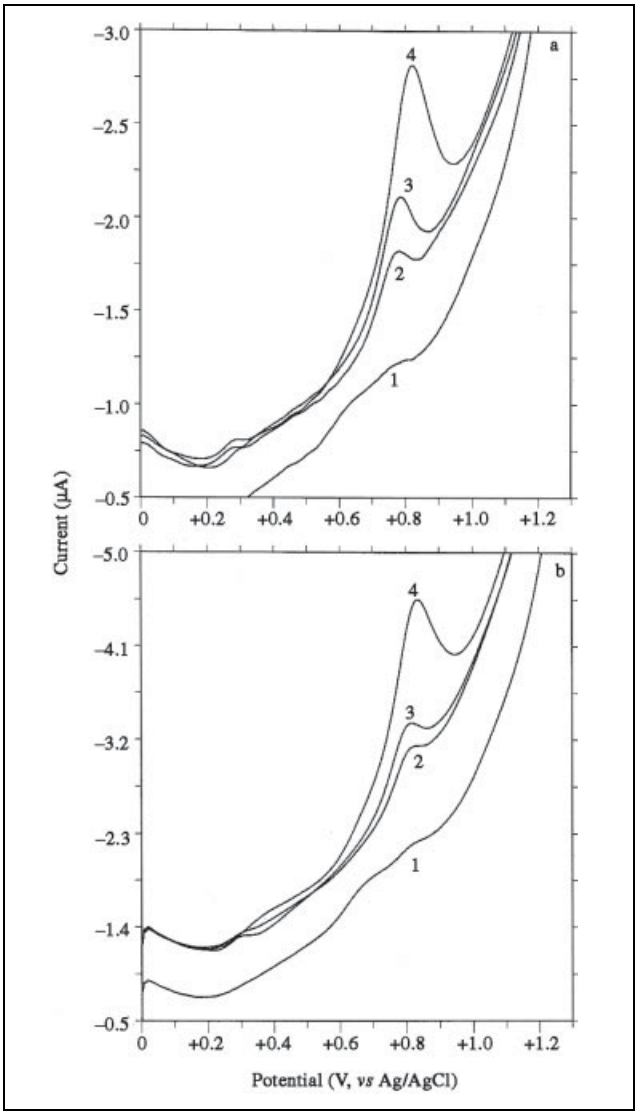


Fig. 4: Differential pulse (a) and Osteryoung square wave (b) voltammograms obtained for determination in spiked serum (1) blank; (2) 4×10^{-6} M; (3) 1×10^{-5} M; (4) 4×10^{-5} M DNP in 0.04 M Britton-Robinson buffer at pH 7.0

Stability of serum samples kept in refrigerator (+4 °C) was tested by making five consecutive analyses of the sample over a period of approximately 4 h. There were no significant changes in the peak currents and potentials between the first and last measurements.

3. Experimental

3.1. Apparatus

The cyclic, linear sweep, differential pulse and Osteryoung square-wave voltammetric experiments at a stationary electrode were performed using a BAS 100 W Electrochemical Analyser. A three-electrode cell system incorporating a glassy carbon working electrode ($\phi = 3$ mm, BAS), an Ag/AgCl (KCl 3 M, BAS) reference electrode and a platinum wire auxiliary electrode (BAS), was used. Before each measurement, the glassy carbon electrode was polished manually with alumina ($\phi = 0.01$ μm) in the presence of bi-distilled water on a smooth polishing cloth.

For analytical applications, the following parameters were employed: DP voltammetry: pulse amplitude, 50 mV; pulse width, 0.05 s; scan rate, 20 mV s^{-1}; OSW voltammetry: pulse amplitude, 25 mV; frequency, 15 Hz; scan increment, 4 mV.

pH was measured using a Model 538 pH meter (WTW, Austria) using a combined electrode (glass electrode – reference electrode) with an accuracy of ±0.05.

3.2. Reagents and solutions

DNP and its pharmaceutical formulation were kindly provided by Pfizer Pharm. Ind. (Istanbul, Turkey). A stock solution of DNP was prepared by direct dissolution in water. Stock solutions containing 10^{-3} M of DNP were prepared in water and stored in the dark under refrigeration. Four different supporting electrolytes, namely sulphuric acid (0.1 M), phosphate buffer (0.2 M; pH 2.0–12.0), Britton-Robinson buffer (0.04 M; pH 2.0–12.0) and acetate buffer (0.2 M; pH 3.52–5.72) were used. All chemicals used were of reagent grade (Merck or Sigma) and they were employed without further purification.

Standard solutions were prepared by dilution of the stock solution with the selected supporting electrolyte to give solutions containing DNP in the concentration range of 1.0×10^{-6}–1.0×10^{-4} M. The calibration curve for DPV and OSWV analysis was constructed by plotting the peak current against the DNP concentration.

The ruggedness and precision were checked on different days, both within day ($n = 5$), and between days ($n = 5$). Relative standard deviations were calculated to check the ruggedness and precision of the method (Riley and Rosanske 1996; Swartz and Krull 1997). The precision and accuracy of the analytical methods are described in a quantitative fashion by the use of relative errors (bias %).

All solutions were protected from light and were used within 24 h to avoid decomposition. Current-potential curves of sample solutions recorded 72 h after preparation did not show any appreciable change in assay values.

3.3. Tablet assay procedure

Ten tablets (each film-coated tablet contains 5.0 mg DNP) were accurately weighed and then crushed to a homogeneous fine powder by pestle and mortar. A portion equivalent to a stock solution of a concentration about 1×10^{-3} M of DNP was accurately transferred into a 50 mL calibrated flask and made up to the volume with water. The contents of the flask were sonicated for 10 min to reach complete dissolution. Appropriate solutions were prepared by taking suitable aliquots of the clear supernatant and diluting with the selected supporting electrolyte in order to obtain a final solution. DPV and OSWV were recorded as for pure DNP. The amount of DNP per tablet was calculated using the relevant linear regression equations obtained from the calibration curve of pure DNP.

3.4. Recovery experiment from tablets

Recovery of the analyte of interest from a given matrix can be used as a measure of the accuracy or the bias of the method. The same range of concentrations as employed in the linearity studies is used. To study the accuracy, precision and reproducibility of the proposed DPV and OSWV techniques and to check the interference from the excipients used in the dosage forms, recovery experiments were carried out using the standard addition method. This study was performed by adding known amounts of pure DNP to the pre-analysed tablet formulation and analysing the mixtures by the proposed techniques. After parallel analyses, the recovery results were calculated using the relevant calibration equations.

3.5. Analysis of DNP from spiked human serum samples

Serum samples, obtained from healthy individuals (after obtaining their written consent), were stored frozen until assay. After gentle thawing, an aliquot volume of sample was spiked with DNP dissolved in water to achieve a final concentration of 1.0×10^{-3} M and treated with 1.0 mL of acetonitrile as a serum denaturating and precipitating agent, and then the volume was completed to 2.5 mL with the same serum sample. The tubes were vortexed for 10 min and then centrifuged for 10 min at 5000 × g to remove protein residues. The supernatant was taken carefully. The concentration of DNP in the human serum samples was varied in the range of 1×10^{-6}–1×10^{-4} M for both techniques. These solutions were analysed in the voltammetric cell containing Britton-Robinson buffer at pH 7.0. The amount of DNP in the spiked serum samples for the recovery studies was calculated from the relevant linear regression equation.

References

Adrisano V, Bartolini M, Gotti R, Cavrini V, Felix G (2001) Determination of inhibitors' potency (IC_{50}) by a direct high-performance liquid chromatographic method on an immobilized acetylcholinesterase column. J Chromatogr B: Biomed Sci Appl 753: 375–383.

Bermejo E, Zapardiel A, Perez-Lopez JA, Chicharro M, Sanchez A, Hernandez L (2000) Electrochemical study of mefexamide at glassy-carbon electrodes and its determination in urine by differential pulse voltammetry. J Electroanal Chem 481: 52–61.

Demircigil BT, Özkan SA, Çoruh Ö, Yımaz S (2002) Electrochemical behaviour of formoterol fumarate and its determination in capsules for inhalation and human serum using differential pulse and square wave voltammetry. Electroanalysis 14: 122–127.

Farger G, Gartner I (2002) Quantitative determination of donepezil, haloperidol and olanzapine by HPLC. Pharmacopsychiatry 35: X–XI.

Grimshow J (Ed.) (2000) Electrochemical reactions and mechanisms in organic chemistry, 1st Ed., Elsevier Sci. Pub., Amsterdam, p. 201.

Kissenger PT, Heineman WR (1996) Laboratory techniques in electroanalytical chemistry, 2nd Ed. Marcel Dekker, New York.

Laviron E, Roullier L, Degrand C (1980) A multiplayer model for the study of space distributed redox modified electrodes: Part II. Theory and application of linear potential sweep voltammetry for a simple reaction. J Electroanal Chem 112: 11–23.

Lu YH, Wen HM, Wei W, Chi YM, Zhang ZX (2004) Determination of donepezil hydrochloride (E2020) in plasma by liquid chromatography-mass spectrometry and its application to pharmacokinetic studies in healthy, young Chinese subjects. J Chromatogr Sci 42: 234–237.

Matsui K, Oda, Y, Nakata H, Yoshimura T (1999) Simultaneous determination of donepezil (Aricept®) enantiomers in human plasma by liquid chromatography-electrospray tandem mass spectrometry. J Chromatogr B: Biomed Sci Appl 729: 147–155.

Pappa H, Farru R, Vilanova O, Palacios M, Pizzorno MT (2002) A new HPLC method to determine donepezil hydrochloride in tablets. J Pharm Biomed Anal 27: 177–182.

Physicans Desk Reference (PDR 2003 Electronic Version) Medical Economics Company Inc., Montvale, NJ.

Riley CM, Rosanske TW (1996) Development and validation of analytical methods, Elsevier Science Ltd., New York.

Swartz ME, Krull IS (1997) Analytical method development and validation, Marcel Dekker, New York.

Smyth MR, Vos JG (1992) Analytical voltammetry, Volume XXVII, Svehla G (Ed.) Elsevier, Amsterdam.

Uslu B, Özkan SA (2002) Electroanalytical characteristics of nefazodone hydrochloride and their analytical application from pharmaceuticals and human serum. Anal Chim Acta 462: 49–57.

Uslu B, Özkan SA (2004) Anodic voltammetry of abacavir and its determination in pharmaceuticals and biological fluids. Electrochim Acta 49: 4321–4329.

Uslu B, Dogan B, Özkan SA (2005) Electrochemical studies of ganciclovir at glassy carbon electrodes and its direct determination in serum and pharmaceutics by square wave and differential pulse voltammetry. Anal Chim Acta 537: 307–313.

Wang J (1996) Electroanalytical techniques in clinical chemistry and laboratory medicine, VCH, New York.

Wang J (2000) Analytical electrochemistry, 2nd Ed., Wiley-VCH Publishers, Canada.

Yasui-Furukori N, Furuya R, Takahata T, Tateishi T (2002) Determination of donepezil, an acetylcholinesterase inhibitor, in human plasma by high-performance liquid chromatography with ultraviolet absorbance detection. J Chromatogr B: Anal Technol Biomed Life Sci 768: 261–265.