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Anodic voltammetry of zolmitriptan at boron-doped diamond electrode and its analytical applications

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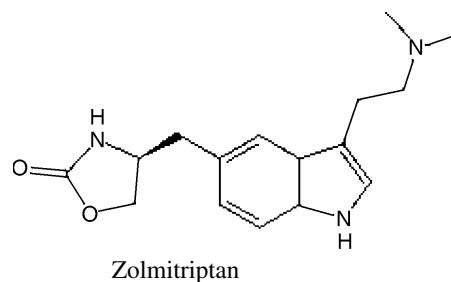
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The electrooxidative behavior and determination of zolmitriptan at a boron-doped diamond electrode were investigated using cyclic, linear sweep, differential pulse and square wave voltammetric techniques. Zolmitriptan undergoes irreversible oxidation at a peak potential of about +0.9 V (vs Ag/AgCl/3 M KCl). DPV and SWV techniques are proposed for the determination of zolmitriptan in phosphate buffer at pH 3.03, which allows quantitation over the two different ranges (8×10^{-7} – 8×10^{-6} M and 1×10^{-5} – 1×10^{-4} M) in supporting electrolyte for both methods. A linear response was obtained in phosphate buffer over two different ranges (6×10^{-7} – 8×10^{-6} M and 1×10^{-5} – 1×10^{-4} M) for spiked serum samples at pH 3.03 for both techniques. The repeatability and reproducibility of the methods for all media were determined. The standard addition method was used in serum. Precision and accuracy were also checked in all media. No electroactive interferences from the excipients and endogenous substances were found in the pharmaceutical dosage form and the biological sample, respectively.

1. Introduction

Boron-doped diamond (BDD) electrodes are becoming increasingly attractive particularly in the field of electroanalysis due to their unusual and extremely useful properties such as low and stable background current (Spataru et al. 2002; Uslu and Ozkan 2007; Compton et al. 2003), wide potential window in both aqueous and non-aqueous solvent systems (Fujishima et al. 2002) and good electroactivity towards certain organic species which deactivate the surface of other conventional electrodes (Iniesta et al. 2001; Granger et al. 1999). Recent publications have shown that several bio-molecules can be satisfactorily determined using BDD electrodes (Granger et al. 1999; Wirley et al. 2008; Zhao et al. 2009; Uslu et al. 2008; Altun et al. 2009; Dogan-Topal et al. 2007).

Zolmitriptan, [(4S)-4-({3-[2-(dimethylamino)ethyl]-1H-indol-5-yl}methyl)-1,3-oxazolidin-2-one] is a selective serotonin receptor agonist of the 1B and 1D subtypes. It is a triptan, used in the acute treatment of migraine attacks with or without aura and of cluster headaches ([http:// www.medicinenet.com](http://www.medicinenet.com); Peterlin et al. 2007). Migraine affects 18% of women and 6% of men. The significant impact of migraine results in a huge burden for the individual, health services, and society. Successful treatment of acute migraine attacks can reduce the use of healthcare resources and improve health-related quality of life (Oldman et al. 2002). The introduction of the triptans in the 1990s revolutionized the treatment of migraine, and a second-generation triptan, zolmitriptan, is highly effective in the oral treatment of acute migraine with or without aura.



Spectrophotometry (Sankar et al. 2008; Raza et al. 2007; Aydogmus and Inanli 2007) and high-performance liquid chromatography have been widely used for the quantitative determination of triptans together with UV (Rao et al. 2005; Srivasu et al. 2005; Hu et al. 2004), fluorescence (Cai et al. 2006; Yu et al. 2005), and mass spectrometry (Kilic et al. 2007; Ding et al. 2006; Chen et al. 2006; Zhang et al. 2004; Vishwanathan et al. 2000) techniques. The sensitivity achieved by all these procedures is highly satisfactory for the quantification of pharmaceutical compounds. However, in some cases, a prior step is required before quantification, involving extraction from mixtures with other compounds or from complex samples, which is not economically feasible in routine analyses.

In this context, electroanalytical techniques have proved to be excellent alternatives to determine this and other pharmaceutical compounds, since they are simple, cost little, and require relatively short analysis times, without the need for derivatization or time-consuming extraction steps. In addition to providing high precision in pharmaceutical analyses, electroanalytical

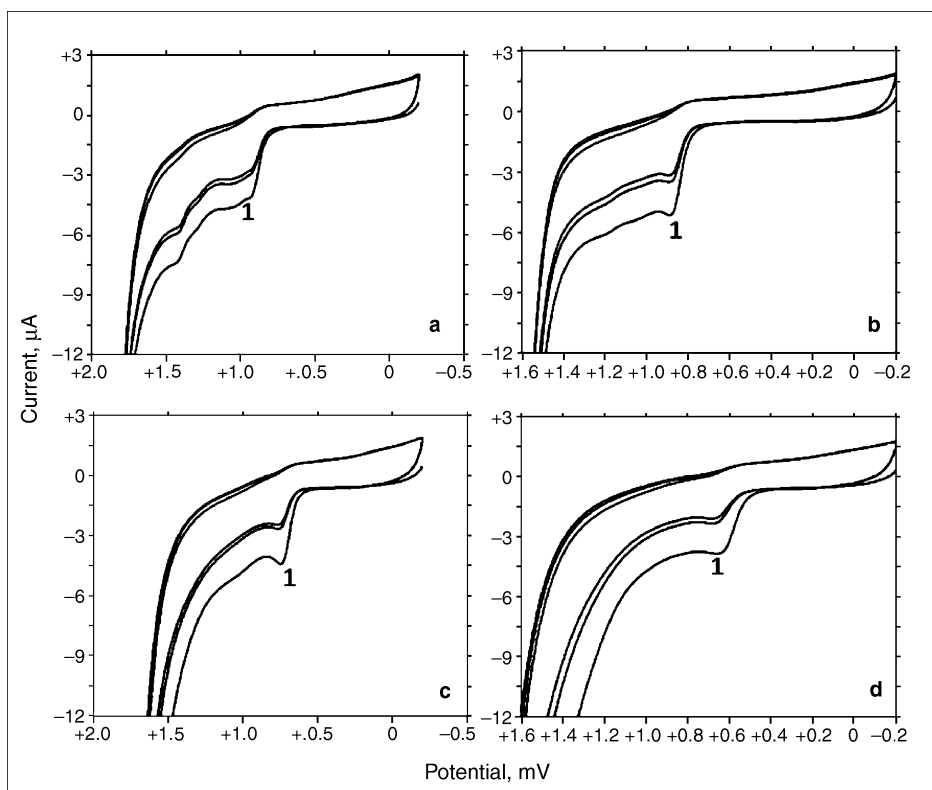


Fig. 1: Repetitive cyclic voltammograms of 8×10^{-5} M zolmitriptan in 0.1 M sulphuric acid (a); acetate buffer at pH 4.7 (b); Britton-Robinson buffer at pH 6.98 (c); Britton-Robinson buffer at pH 9.01 (d)

techniques yield information about the kinetics and charge transfer mechanisms involved in a given reaction. This information is useful for evaluating the redox properties of these compounds and to supply information about their metabolism and their redox and pharmaceutical properties in the human organism, since the reaction in humans is very similar to the redox process that occurs when electroanalytical techniques are employed (Wang 1998). Among the electroanalytical techniques currently available for use with BDD electrodes and various electrode surfaces, differential pulse (DP) and square-wave (SW) voltammetry have proved to be extremely sensitive methods for the detection of pharmaceutical formulations.

No report has been published on the voltammetric determination of zolmitriptan in pharmaceutical formulations and no monograph on zolmitriptan has yet been included in the official pharmacopoeias.

This study therefore investigated the electrochemical behavior of zolmitriptan and developed an analytical procedure to quantify this compound in commercial formulations and serum samples, employing BDD electrodes.

2. Investigations, results and discussion

2.1. Electrochemical behavior of zolmitriptan at BDD electrode

Zolmitriptan appears to be an electroactive drug, but there are no reports about the electrooxidation of zolmitriptan in the scientific literature. Therefore, the electrochemical behavior of zolmitriptan on a BDD electrode was studied by cyclic voltammetry (CV), DPV and SWV. Various supporting electrolytes for zolmitriptan were investigated using DPV and SWV: phosphate buffer, acetate buffer and sulphuric acid. Zolmitriptan was electrochemically oxidized in a broad pH range (0.33–11.0) using a BDD electrode (Fig. 1). The best results were obtained

with phosphate buffer at pH 3.03; peak and two wave potentials, 0.89 V, 1.23 V and 1.33 V vs Ag/AgCl (3.0 mol L^{-1} KCl), respectively were obtained for zolmitriptan. On repetitive cyclic voltammograms the second and successive scans show a substantially smaller peak indicating the passivation of the electrode surface by oxidation product (Fig. 2). Voltammograms obtained for zolmitriptan at a BDD electrode presented irreversible chemical behavior.

A linear plot of peak current vs square root of the scan rate was obtained, with a 0.9954 correlation coefficient, indicating that the electrode process is controlled by mass transport. The

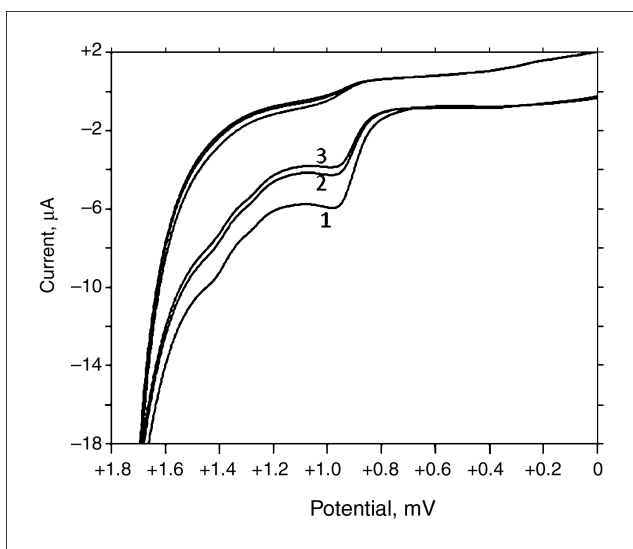


Fig. 2: Repetitive cyclic voltammograms of 8×10^{-5} M zolmitriptan in phosphate buffer at pH 3.03. Scan rate 100 mV s^{-1} . Numbers indicate number of scan

equation is given below in phosphate buffer at pH 3.03:

$$I_p (\mu A) = 0.2647 v^{1/2} (mVs^{-1}) + 0.272 (r : 0.9954, n : 9) \quad (1)$$

A plot of logarithm of peak current versus logarithm of scan rate gave a straight line with a slope of 0.48, very close to the theoretical value of 0.5 for an ideal reaction for the diffusion-controlled electrode (Kissenger and Heineman 1996). The equation obtained is:

$$\log i_p (\mu A) = 0.4784 \log v (mVs^{-1}) - 0.493 (r : 0.9985, n : 9) \quad (2)$$

A tafel plot was obtained in phosphate buffer at pH 3.03 with a scan rate of $5 mVs^{-1}$, beginning from a steady-state potential, and from the slope of the linear part αn was found to be 0.34. The number of electrons participating in the electrode reaction process can be calculated to be 1, assuming α is 0.34. Assuming α_n (the number of the electrons transferred in the rate determining step) = n , the value of α (the charge transfer coefficient) is 0.34. The exchange current density (I_0) is $2.34 \times 10^{-11} A/cm^2$ for this system. These values together with the absence of a cathodic wave in cyclic voltammetry (Fig. 2) indicated the irreversibility of the oxidation reaction of zolmitriptan. The peak potential shifted to more positive potentials (about 51 mV) in the anodic direction when the scan rate increased from $5-1000 mVs^{-1}$. Fig. 3a presents the peak potential vs pH plot for zolmitriptan. Peak potential varies linearly with pH below pH 9.0, while above this pH potential is independent, with a break at pH 9.0, which can be associated with the pKa of zolmitriptan of about 9.64 ([http:// www.drugfuture.com/chemdata/zolmitriptan.html](http://www.drugfuture.com/chemdata/zolmitriptan.html)). The relationship between E_p and pH at BDD electrode derived using linear regression analysis can be expressed by the equation:

$$E_p(mV) = 1057.83 - 54.108 pH (r : 0.9880, \text{ between pH } 2.00 - 9.00) \quad (3)$$

The slope of $\sim 54.108 mV$ per pH unit, being close to the expected $59 mV$ per pH unit, indicates that 1 proton and 1 electron are involved in the oxidation of zolmitriptan (Beltagi et al. 2002).

A comparative study on 5-hydroxy indole, indole-3-acetic acid and etodolac was performed by cyclic voltammetry as a function of pH, in order to identify the oxidation process of zolmitriptan, taking into account that the CV of these substances closely matches the voltammogram of zolmitriptan. This molecule is extensively metabolized *in vivo*, mainly through oxidative processes. We assume that the oxidation occurs first on the nitrogen atom in the indole ring of the molecule, which is electroactive in both acidic and basic media, leading finally to hydroxylation of the benzene ring (Suzen et al. 2003; Bozkaya et al. 2006; Goyal et al. 1998; Yilmaz et al. 2001).

When the logarithm of the current at a potential of about $+0.88 V$ obtained in pH 3.03 phosphate buffer was plotted against the logarithm of zolmitriptan concentration in the two ranges ($8 \times 10^{-7} - 8 \times 10^{-6} M$ (Part I) and $1 \times 10^{-5} - 1 \times 10^{-4} M$ (Part II)), linear relationships were obtained.

$$\log i(\mu A) = 0.06 \log C (M) + 0.49 \text{ Part I } (r : 0.9913, n : 6) \quad (4)$$

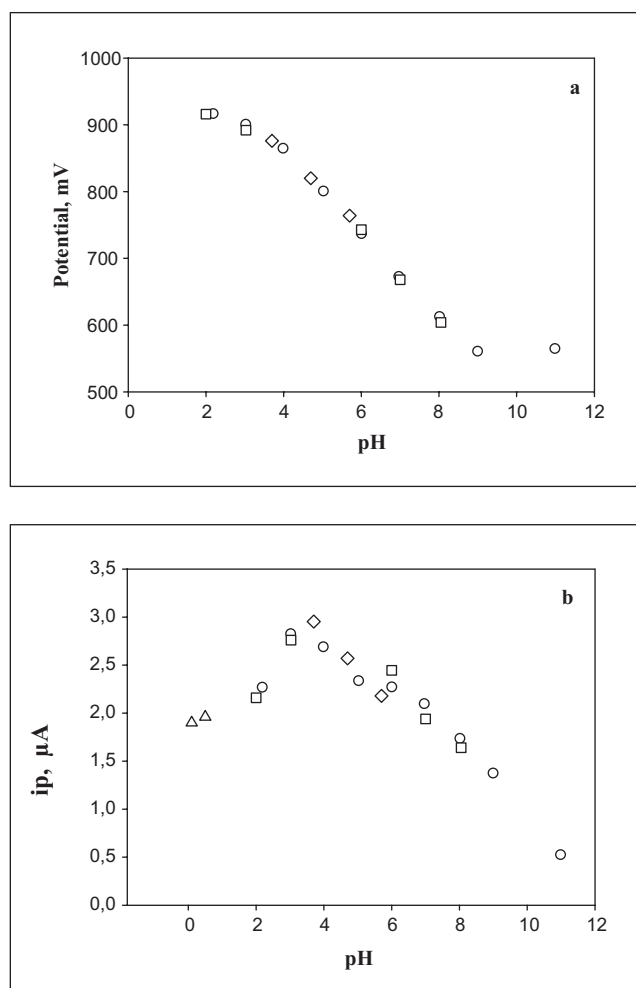


Fig. 3: Effect of pH on zolmitriptan anodic peak potential (a) and peak current (b); Zolmitriptan concentration $8 \times 10^{-5} M$. (o) Britton-Robinson buffer (□) Phosphate buffer (Δ) Sulphuric acid (◇) Acetate buffer

$$\log i(\mu A) = 0.31 \log C (M) + 1.88 \text{ Part II } (r : 0.9940, n : 6) \quad (5)$$

The slopes of these equations give the order of the reaction. These kinetic parameters and the reaction order showed that there was a mechanism related to the surface events, and the reaction seems to be of first order.

2.2. Analytical applications

2.2.1. Validation of the analytical procedure

Two techniques, based on DPV and SW methods, were developed for the quantitative determination of zolmitriptan. The peak potential versus pH plots were similar to those obtained by CV, DPV and SW voltammetric techniques. The experimental results showed that the shapes of the curve and maximum peak current were better in phosphate buffer at 3.03 for analytical applications (Fig. 3b).

Two linear calibration graphs were obtained over different concentration ranges between $1 \times 10^{-6} - 8 \times 10^{-6} M$ (Part I) and $1 \times 10^{-5} - 1 \times 10^{-4} M$ (Part II) for DPV and SWV. Characteristics of these graphs (Part I) are reported in Table 1. Validation of the optimized procedure for the quantitative assay of zolmitriptan was examined by evaluating the limit of

Table 1: Regression data of calibration lines (for Part I) for quantitative determination of zolmitriptan by DPV and SWV in standard solution and human serum

	DPV		SWV	
	Standard solution	Serum	Standard solution	Serum
Measured potential (V)	0.875	0.876	0.905	0.901
Linearity range (M)	$8 \times 10^{-7} - 8 \times 10^{-6}$	$6 \times 10^{-7} - 8 \times 10^{-6}$	$8 \times 10^{-7} - 8 \times 10^{-6}$	$6 \times 10^{-7} - 8 \times 10^{-6}$
Slope ($\mu\text{A M}^{-1}$)	3.64×10^4	2.04×10^4	3.59×10^4	3.06×10^4
Intercept (μA)	0.110	0.077	0.120	0.055
Correlation coefficient	0.999	0.997	0.994	0.995
SE of slope	5.63×10^2	4.85×10^2	1.64×10^2	1.34×10^3
SE of intercept	2.77×10^{-3}	2.02×10^{-3}	8.06×10^{-2}	5.61×10^{-3}
LOD (M)	7.30×10^{-8}	2.94×10^{-7}	2.63×10^{-7}	3.41×10^{-9}
LOQ (M)	2.44×10^{-7}	9.80×10^{-7}	8.78×10^{-7}	1.14×10^{-8}
Repeatability of peak current (RSD%)	0.79	0.93	0.23	1.53
Repeatability of peak potential (RSD%)	0.18	0.24	0.20	0.23
Reproducibility of peak current (RSD%)	0.31	1.55	0.14	1.96
Reproducibility of peak potential (RSD%)	0.32	0.40	0.36	0.40

detection (LOD), limit of quantification (LOQ), repeatability, reproducibility, accuracy, precision and recovery.

LOD and LOQ were calculated on the peak current using the following equation (Riley and Roosanske 1996; Swartz and Krull 1997):

LOD: 3.3 s/m; LOQ: 10 s/m

Where s is the standard deviation of the peak current (three runs) and m is the slope of the calibration curve. The LOD and LOQ values are also shown in Table 1.

Five experiments on 1×10^{-5} M zolmitriptan were repeated using both techniques to test the repeatability and reproducibility of peak current and peak potentials. The results are also shown in Table 1. Repetition of sample analysis after 48 h did not show any significant change in the results of the analyses.

2.2.2. Assay of zolmitriptan in tablets

The results with standard solutions and the validation parameters obtained encourage the use of the proposed method as described for the assay of zolmitriptan in tablet dosage forms. With no sample extraction or filtration step, but simply by dissolution and adequately diluting the analyte present in the solution of Zomig Rapimelt® tablets, DPV and SWV methods can be used for the direct determination of zolmitriptan using the relevant calibration straight lines. The results show that the proposed methods were successfully applied to the assay of zolmitriptan in its tablet dosage form (Table 2). The accuracy of the method was evaluated by recovery experiments after adding known amounts

Table 2: Application of proposed voltammetric methods to analysis of commercial tablets

	DPV	SWV
Labeled claim (mg)	2.500	2.500
Amount found (mg) ^a	2.494	2.488
RSD (%)	0.35	0.49
Bias (%)	0.013	0.024
Added (mg)	0.625	0.625
Found (mg) ^a	0.6254	0.6248
Recovery (%)	100.064	99.968
RSD % of recovery	0.583	0.032
Bias (%)	-0.064	-0.62

^a Each value is the mean of five experiments

of pure drug to various pre-analyzed formulations of zolmitriptan and applying the procedure specified in the experimental section.

Recovery studies were carried out after the addition of known amounts of the pure drug to various pre-analyzed formulations of zolmitriptan. According to the results, excipients present in the tablet do not interfere with the analysis (Table 2). There is no official method for zolmitriptan in any pharmacopoeias. The results demonstrate the validity of the proposed method for the determination of zolmitriptan in tablets. These results show that the proposed DPV and SWV methods have adequate precision and accuracy and consequently can be applied to the determination of zolmitriptan pharmaceuticals without any interference from the excipients.

2.2.3. Determination of zolmitriptan in spiked serum samples

Fig. 4 illustrates DP and SW voltammograms obtained from serum spiked at different concentrations of zolmitriptan using the optimized conditions.

The peak current was linearly related to zolmitriptan concentration over the two different ranges $6 \times 10^{-7} - 8 \times 10^{-6}$ M (Part I) and $1 \times 10^{-5} - 8 \times 10^{-5}$ M (Part II) according to the equations:

For DPV

$$I_p(\mu\text{A}) = 2.04 \times 10^4 C (\text{M}) + 0.077$$

Part I (r : 0.9970, n : 7) (6)

$$I_p(\mu\text{A}) = 7.05 \times 10^3 C (\text{M}) + 0.41$$

Part II (r : 0.9900, n : 5) (7)

$$\text{For SWV } I_p(\mu\text{A}) = 3.06 \times 10^4 C (\text{M}) + 0.055$$

Part I (r : 0.9952, n : 7) (8)

$$I_p(\mu\text{A}) = 0.17 C (\text{M}) + 0.45 \text{ Part II (r : 0.9976, n : 5)} \quad (9)$$

The estimated detection limits for both methods are also shown in Table 1 for Part I. The amount of zolmitriptan in serum was

Table 3: Determination of zolmitriptan in human serum samples for DPV and SWV methods

Techniques	Zolmitriptan added (M)	Zolmitriptan found ^a (M)	Average recovery (%)	Bias (%)
DPV	4.00×10^{-6}	$4.03 \times 10^{-6} \pm 0.32$	100.75	-0.75
SWV	4.00×10^{-6}	$4.01 \times 10^{-6} \pm 0.27$	100.25	-0.25

^a Average value \pm SD of five experiments

calculated from the relevant linear regression (Part I) equation for both techniques. The precision and accuracy for zolmitriptan in serum were assessed from five replicates at 6×10^{-6} M. Good recoveries of zolmitriptan were achieved from serum (Table 3). As can be seen in Fig. 4, in the potential range where the analytical peak appeared there were no reduction compounds and no extra noise peaks were found from biological materials. Stability of serum samples kept in a refrigerator (+4 °C) was tested by making five consecutive analyses of the sample over a period of approximately 8 h. No significant changes were observed in the peaks were currents and potentials between the first and last measurements.

3. Experimental

3.1. Apparatus

Voltammetric experiments were performed using a BAS 100 W (Bioanalytical System, USA) electrochemical analyzer together with a one-compartment glass electrochemical cell equipped with a three-electrode system consisting of a BDD (Windsor Scientific Ltd.; ϕ :3 mm, diameter) working electrode, a platinum wire counterelectrode and an Ag/AgCl saturated KCl reference electrode. Before each experiment the BDD electrode was polished manually with an aqueous slurry of alumina powder (ϕ :0.01 μ m) on a damp smooth polishing cloth (BAS velvet polishing pad). All measurements were made at room temperature.

The pH measurements were made using a model 538, WTW pH-meter (Austria) with a combined electrode (glass-reference electrode) with an accuracy of ± 0.05 pH.

The experimental conditions for DPV were: pulse amplitude, 50 mV; pulse width, 50 ms; scan rate, 20 mVs⁻¹.

The experimental conditions for SWV were: pulse amplitude, 50 mV; frequency, 15 Hz; potential step, 4 mV.

3.2. Chemicals and standards

Zolmitriptan was kindly supplied by AstraZeneca (İstanbul, Turkey). The other chemicals were reagent grade (Merck or Sigma).

A 1×10^{-3} M stock solution of zolmitriptan was prepared in bidistilled water and kept in the dark in a refrigerator. Working standards of zolmitriptan were freshly prepared just before the assay, by adding appropriate amounts of stock solution with the selected supporting electrolytes. Sulphuric acid (0.1 and 0.5 M), phosphate buffer (0.2 M, pH 2.00–8.05), acetate buffer (0.2 M, pH 3.70–5.70), and Britton-Robinson buffer (0.04 M, pH 2.20–12.01) were used as supporting electrolytes.

All solutions were kept in the dark and were used within 24 h to avoid decomposition. However voltammograms of the sample solutions recorded one week after preparation did not show any appreciable change in assay values.

3.3. Pharmaceutical dosage form assay procedure

Six Zomig Rapimelt® tablets (each tablet containing 2.5 mg zolmitriptan) was thoroughly ground to a fine powder in a mortar and the amount of sample corresponding to a stock solution of $ca 1 \times 10^{-3}$ M was accurately weighed, transferred to a 100 mL calibrated flask and dissolved in bidistilled water. The mixture was sonicated for 30 min until complete dissolution. Appropriate solutions were prepared by taking suitable volumes of the clear supernatant liquor and diluting with pH 3.03 phosphate buffer. Recovery studies were performed to study the accuracy of the proposed method and to check for possible interferences from common excipients. For these experiments, known amounts of the pure drug were added to the previously analyzed rapid melt tablet formulation of zolmitriptan. Each measurement was repeated five times. These data gave an average zolmitriptan content of $2.484 \pm 8.6 \times 10^{-3}$ mg for DPV and $2.488 \pm 1.2 \times 10^{-2}$ mg for SWV, in close agreement with the 25 mg/tablet quoted by the manufacturer. The nominal content of the drug was calculated from the corresponding regression equation.

3.4. Analysis of serum

Drug-free human blood, obtained from healthy volunteers (after obtaining their written consent) was centrifuged (5000 rpm) for 30 min at room temperature, and separated serum samples were stored frozen until assay. An aliquot of serum sample was fortified with zolmitriptan dissolved in bidistilled water to achieve a final concentration of 1×10^{-3} M. Acetonitrile removes serum proteins effectively and the appropriate ratio of volumes to eliminate the protein was 1 to 1.5. After vortexing for 30 s, the mixture was then centrifuged for 10 min at 5000 rpm in order to eliminate serum protein residues, and the supernatant was taken carefully.

Appropriate volumes of this supernatant were transferred into a volumetric flask and diluted up to the volume with pH 3.03 phosphate buffer.

Quantifications were performed by means of the calibration curve method from the related calibration equation. In conclusion, the electrochemical

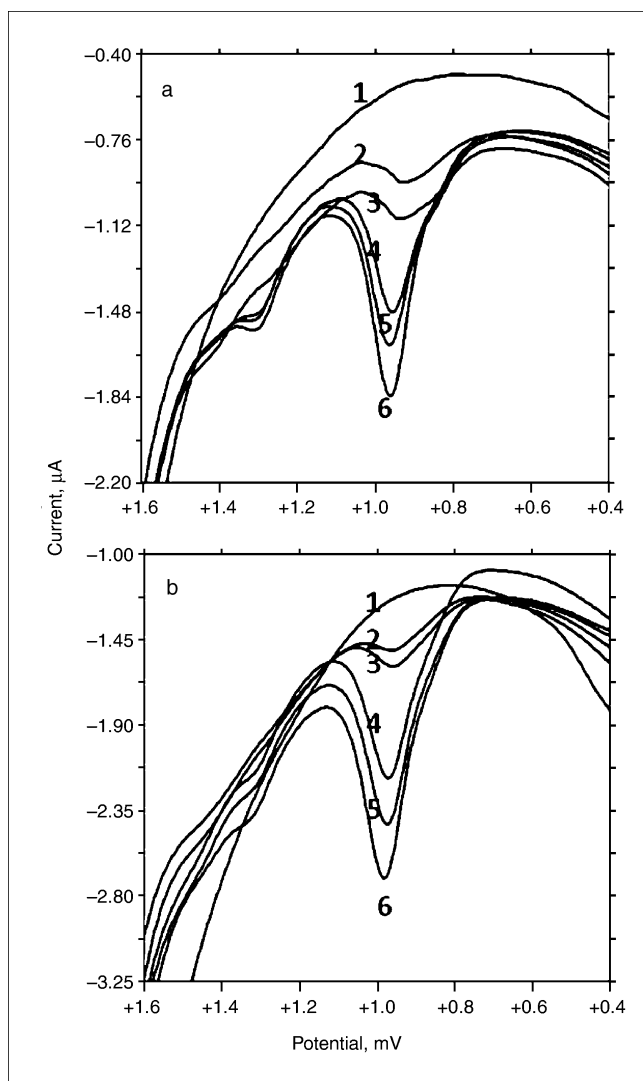


Fig. 4: Differential pulse (a) and square wave (b) voltammograms obtained for determination in spiked serum 1) blank; 2) 2×10^{-6} M; 3) 4×10^{-6} M; 4) 2×10^{-5} M; 5) 4×10^{-5} M; 6) 6×10^{-5} M zolmitriptan extract in phosphate buffer at pH 3.03

behavior of zolmitriptan on a BDD electrode was established and studied for the first time. Zolmitriptan undergoes irreversible oxidation at positive potentials. The BDD electrode was shown to be perfectly suitable for analysis of zolmitriptan using the DPV and SWV techniques. The advantage of the BDD electrode is that it is highly stable and sensitive.

This work shows that zolmitriptan concentrations in human serum and pharmaceutical dosage forms can be determined voltammetrically on the basis of the oxidation of their indole moiety over the BDD electrode. This behavior provides a useful tool for detection and quantification of drugs at low levels in biological samples.

This paper is not intended to be a study of the pharmacodynamic properties of zolmitriptan, since only healthy and non-drug using volunteers were used for sample collection and results may be of no significance. It showed the possibility of monitoring this drug compound, making the method likely to be useful for pharmacokinetic and pharmacodynamic purposes.

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References

- Altun Y, Dogan-Topal B, Uslu B, Ozkan SA (2009) Anodic behavior of sertindole and its voltammetric determination in pharmaceuticals and human serum using glassy carbon and boron-doped diamond electrodes. *Electrochim Acta* 54: 1893–1903.
- Aydogmus Z, Inanlı I (2007) Extractive spectrophotometric methods for determination of zolmitriptan in tablets. *J. AOAC Int* 90: 1237–1241.
- Beltagi AM, Ghoneim MM, Radi A (2002) Electrochemical reduction of meloxicam at mercury electrode and its determination in tablets. *J Pharm Biomed Anal* 27: 795–801.
- Bozkaya P, Dogan B, Suzen S, Nebioglu D, Ozkan SA (2006) Determination and investigation of electrochemical behavior of 2-phenylindole derivatives: discussion on possible mechanistic pathways. *Canadian J Anal Sci Spectrosc* 51: 125–139.
- Cai J, Jiang XG, Chen J, Xiang ZG, Jin L (2006) Study on determination of zolmitriptan in rat plasma by HPLC. *Chinese Pharm J* 412: 1171–1174.
- Chen X, Liu D, Luan Y, Jin F, Zhong D (2006) Determination of zolmitriptan in human plasma by liquid chromatography-tandem mass spectrometry method: Application to a pharmacokinetic study. *J Chromatogr B Anal Tech Biomed Life Sci* 832: 30–35.
- Compton RG, Foord JS, Marken F (2003) Electroanalysis at diamond-like and doped-diamond electrodes. *Electroanalysis* 15: 1349–1363.
- Ding JS, Zhu RH, Zhu YG, Li HD (2006) Determination of zolmitriptan in human plasma by HPLC-MS and study on bioequivalence of domestic and import zolmitriptan tablets. *Chinese Pharm J* 41: 1488–1490.
- Dogan-Topal B, Uslu B, Ozkan SA (2007) Investigation of electrochemical behavior of lipid lowering agent atorvastatin calcium in aqueous media and its determination from pharmaceutical dosage forms and biological fluids using boron-doped diamond and glassy carbon electrodes. *Combinat Chem High Throughput Screen* 10: 571–582.
- Fujishima A, Tereahima C, Honda K, Sarado BV, Rao TN (2002) Recent progress in electroanalytical applications of diamond electrodes. *New Diamond Frontier Carbon Technol* 12: 73–81.
- Goyal RN, Kumar N, Singhal NK (1998) Oxidation chemistry and biochemistry of indole and effect of its oxidation product in albino mice. *Bioelectrochem Bioenerg* 45: 47–53.
- Granger MC, Xu JS, Strojek JW, Swain GM (1999) Polycrystalline diamond electrodes: Basic properties and applications as amperometric detectors in flow injection analysis and liquid chromatography. *Anal Chim Acta* 397: 145–161. <http://en.wikipedia.org/wiki/zolmitriptan> <http://www.drugfuture.com/chemdata/zolmitriptan.html> <http://www.medicinet.com/zolmitriptan/article.htm>.
- Hu YZ, Yao TW, Wang XJ (2004) HPLC determination of zolmitriptan and its related substances. *J Zhejiang Univ Med Sci* 33: 37–40.
- Iniesta J, Michaud PA, Panizza M, Cerisola C, Aldaz A, Cominiellis C (2001) Electrochemical oxidation of phenol at boron-doped diamond electrode. *Electrochim Acta* 46: 3573–3578.
- Kılıç B, Özden T, Toptan S, Özilhan S (2007) Simultaneous LC-MS-MS determination of zolmitriptan and its active metabolite N-desmethylzolmitriptan in human plasma. *Chromatographia* 66: 129–133.
- Kissinger PT, Heineman WR (1996) Laboratory techniques in electroanalytical chemistry, second ed., Marcel Dekker, New York.
- Oldman AD, Smith LA, Mc Quay HJ, Moore RA (2002) Pharmacological treatments for acute migraine: Quantitative systematic review. *Pain* 97: 247–257.
- Peterlin, BL, Rapoport AM (2007) Clinical pharmacology of the serotonin receptor agonist, zolmitriptan. *Expert Opin Drug Metabol Toxicol* 3: 898–911.
- Rao BM, Srivasu MK, Sridhar G, Kumar PR, Chandrasekhar KB, Islam A (2005) A stability indicating LC method for zolmitriptan. *J Pharm Biomed Anal* 39: 503–509.
- Raza A, Ansari TM, Niazi SB (2007) A novel spectrophotometric method for the determination of zolmitriptan in pharmaceutical formulation. *J Chinese Chem Soc* 54: 1413–1417.
- Riley CM, Roosanske TW (1996) Development and validation of analytical methods. Elsevier Science Ltd., New York.
- Sankar DG, Nagesh-Babu A, Rajeswari A, Krishna MV, Devi KV (2008) Spectrophotometric determination of zolmitriptan in pharmaceutical dosage forms. *Asian J Chem* 20: 4960–4962.
- Spataru N, Sarada BV, Tryk DA, Fujishima A (2002) Anodic voltammetry of xanthine, thyphylline, theobromine and caffeine at conductive diamond electrodes and its analytical application. *Electroanalysis* 14: 721–728.
- Srivasu MK, Rao BM, Sridhar G, Chandrasekhar KB, Kumar PR (2005) A validated chiral LC method for the enantiomeric separation of zolmitriptan key intermediate, ZTR-5. *J Pharm Biomed Anal* 39: 796–800.
- Suzen S, Demircigil BT, Buyukbingol E, Ozkan SA (2003) Electrochemical evaluation and determination of 5-(3'-indolyl)-2-thiohydantoin derivatives by voltammetric studies: possible relevance to *in vitro* metabolism. *New J Chem* 27: 1007–1011.
- Swartz ME, Krull IS (1997) Analytical development and validation. Marcel Dekker, New York.
- Uslu B, Dogan-Topal B, Ozkan SA (2008) Electroanalytical investigation and determination of pefloxacin in pharmaceuticals and serum at boron-doped diamond and glassy carbon electrodes. *Talanta* 74: 1191–1200.
- Uslu B, Ozkan SA (2007) Solid electrodes in electroanalytical chemistry: present applications and prospects for high-throughput screening of drug compounds. *Combinator Chem High Throughput Screen* 10: 495–513.
- Vishwanathan K, Bartlett MG, Stewart JT (2000) Determination of antimigraine compounds rizatriptan, zolmitriptan, naratriptan and sumatriptan in human serum by liquid chromatography/electrospray tandem mass spectrometry. *Rapid Commun Mass Spectr* 14: 168–172.
- Wang J (1998) Electroanalytical techniques in clinical chemistry and laboratory medicine, VCH, New York.
- Wirley F, Ribeiro P, Cardosa AS, Portela RR, Lima JES, Machado SAS, Neto PL, Souza D, Correia AN (2008) Electroanalytical determination of promethazine hydrochloride in pharmaceutical formulations on highly boron-doped diamond electrodes using square wave adsorptive voltammetry. *Electroanalysis* 20: 2031–2039.
- Yılmaz S, Uslu B, Özkan SA (2001) Anodic oxidation of etodolac and its square wave and differential pulse voltammetric determination in pharmaceuticals and human serum. *Talanta* 54: 351–360.
- Yu L, Yao T, Ni S, Zeng S (2005) Determination of zolmitriptan enantiomers in rat liver microsomes by chiral high performance liquid chromatography with fluorescence detection. *Biomed Chromatogr* 19: 191–195.
- Zhang Z, Xu F, Tian Y, Li W, Mao G (2004) Quantification of zolmitriptan in plasma by high-performance liquid chromatography-electrospray ionization mass spectrometry. *J Chromatogr B Anal Tech Biomed Life Sci* 813: 227–233.
- Zhao X, Hou Y, Liu H, Qiang Z, Qu J (2009) Electro-oxidation of diclofenac at boron doped diamond: Kinetics and mechanism. *Electrochim Acta* 54: 4172–4179.