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Adsorptive Stripping Voltammetric Behavior and Determination of Zolmitriptan Using Differential Pulse and Square Wave Voltammetry

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Abstract- The oxidative behaviour of zolmitriptan was studied at a glassy carbon electrode in Britton-Robinson (BR) buffer solutions using cyclic, differential pulse and square wave voltammetric techniques. The oxidation process was shown to be irreversible over the pH range (2.0-6.0) and was diffusion controlled with some adsorption character. The analytical method was developed for the determination of zolmitriptan in BR buffer solution at pH 2.0 as supporting electrolyte. The anodic peak current varied linearly with zolmitriptan concentration in the following ranges: 4.0×10^{-8} to 3.2×10^{-7} M and 4.0×10^{-10} to 3.2×10^{-9} M of zolmitriptan with limits of detection of 2.0×10^{-8} M and 2.0×10^{-10} M by differential pulse and square wave methods, respectively. Validation parameters, such as sensitivity, accuracy, precision and recovery were evaluated. The proposed method was applied to the determination of zolmitriptan in the tablet dosage form. The results were compared with those obtained by the reported methods showing higher sensitivity of our proposed method.

Keywords- Cyclic Voltammetry, Differential Pulse Voltammetry, Square Wave Voltammetry, Zolmitriptan, Tablets

1. INTRODUCTION

Migraine is a chronic, often debilitating disease that affects 12% of the general population. A working definition of migraine is benign recurring headache and/or

neurological dysfunction usually attended by pain-free interludes and often provoked by stereotyped stimuli [1,2].

Anti-migraine therapy includes, currently, potent serotonin 5-$HT_{1B/1D}$ receptor agonists, collectively known as triptan drug class. Among triptans, zolmitriptan (4S-4-({3-[2-(dimethylammino)ethyl]-1H-indol-5-yl}methyl-1,3-oxazolidin-2-one) is characterized, in humans, by a relatively high oral bioavailability (about 40%) and an in vivo plasma half-life of about 3 h. Clinical studies show that zolmitriptan half-life and bioavailability after nasal administration do not significantly differ from those obtained after oral intake of the drug [3].

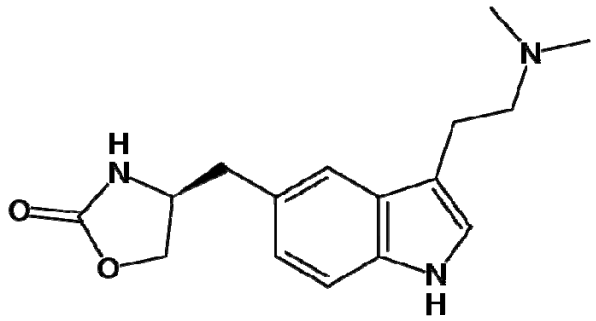

Fig. 1. The structure of zolmitriptan

Several HPLC methods for zolmitriptan determination have been reported. Quantification of zolmitriptan in human plasma using mass [4], coulometric [5], gradient ion-pair UHPLC method with UV detection [6] or fluorescence [7] was described. Chiral HPLC methods for accurate quantification of Zolmitriptan were reported [8], and stability indicating LC method for the determination and quantitative estimation of zolmitriptan [9].

Stripping voltammetry method has been shown to be an efficient electroanalytical technique for the determination of sub-nano molar levels of a wide range of drugs that have an interfacial adsorptive character onto the working electrode surface. It usually involves a simple accumulation step, and most of the excipients used do not interfere in the subsequent determination of drugs [10]. Many of the adsorptive stripping voltammetric (AdSV) approach features such as sensitivity, selectivity, simplicity and versatility attributed to the combination of an effective pre-concentration step based on adsorptive accumulation of the analyte on the electrode with advanced measurement procedures such as differential pulse voltammetry (DPV) or square wave voltammetry (SWV) [11-13].

SWV is a technique that combines the best aspects of several pulse voltammetric methods [14], which results in a fast technique that is widely applied as analytical tool for the determination of bioactive compounds [15-19].

Only one electrochemical method was used to determine zolmitriptan by using boron-doped diamond electrode [19]. Therefore, the aim of the present study is to investigate the oxidative behaviour of zolmitriptan at a glassy carbon electrode (GCE) [20,21] using cyclic, differential pulse and square wave voltammetric techniques, and to optimize the experimental conditions for determination of this compound in pharmaceutical dosage forms.

2. EXPERIMENTAL

2.1. Apparatus

The CV, DPV and SWV experiments at a stationary electrode were performed using 797VA Computrace software (1.0) from Metrohm, Switzerland, electrochemical analyzer. A three electrode cell system incorporating the glassy carbon electrode as working electrode, an Ag/AgCl (3 M KCl) reference electrode and a platinum wire auxiliary electrode were also used. Before each measurement the glassy carbon electrode was polished manually with 0.5 μm alumina powder on a smooth polishing cloth on a smooth polishing cloth. Then, it was thoroughly rinsed with methanol and double distilled water, and gently dried with a tissue paper. The data were treated with Origin (Ver. 7) software to transform the initial signal. A Mettler balance (Toledo-AB104) was used for weighing the solid materials. A cyberscan 500 digital (EUTECH Instruments, USA) pH meter with a glass combination electrode was served to carry out pH measurements. Deionized water used throughout the present study.

2.2. Reagents

The active ingredient pharmaceutical drug, zolmtriptan from amoun, and its pharmaceutical preparation No-MigrainZ Tablets 5.0 mg was used for quantitative determinations. Stock solution of 1.0×10^{-3} M of zolmitriptan was prepared by dissolving a calculated weight of the active ingredient drug in deionized water and stored in dark bottles at 4.0 °C. More dilute solutions were prepared daily just before use. Britton-Robinson (BR) buffer solutions (pH 2.0-6.0) were used as supporting electrolytes. All solutions were prepared from Analar grade reagents (Merck and Sigma) in deionized water.

2.3. General analytical procedures

Voltammetric analyses were performed in 25 ml of BR buffer. The solution was continuously stirred at 1200 rpm when accumulation was applied for a certain time and potential to the working electrode. At the end of accumulation, the stirring was stopped and a 5 sec rest period was allowed for the solution to become quiescent. The used drug was determined by using differential pulse voltammetry DPV and SWV methods. Aliquots of the drug solution were introduced into the electrolytic cell and the procedures were repeated. The voltammograms were recorded. The peak current was evaluated as the difference between

each voltammogram and the background electrolyte voltammogram. All data were obtained were carried out at room temperature.

2.4. Determination of zolmtriptan in Tablets

For tablets solution, ten tablets of "No-Migrain Z" were weighed, and the average mass per tablet was determined. A portion of a finely grounded powder equivalent to the calculated weight of the active ingredient of the pharmaceutical preparation was dissolved in deionized water to produce a 1.0×10^{-3} M solution. The solution was then filtered through a 0.45 μm Millipore filter in order to separate out the insoluble excipients and reject the first portion of the filtrate. The solution was directly analyzed, according to the general analytical procedures without the necessity for sample pretreatment or any extraction step.

2.5. Analysis of zolmtriptan in spiked urine and human plasma

Accurately measured aliquots of zolmtriptan solutions were pipetted into centrifugation tubes containing 500 μl human urine or plasma, then vortex was done for 5 min. Into each tube, 0.5 ml of methanol, 0.1 ml NaOH (0.1 M), 0.5 ml $ZnSO_4.7\ H_2O$ (5% w/v) [22], were added, then centrifuged for 8 min at 4000 rpm. The clear supernatant layer was filtered through 0.45 μm Milli-pore filter. A 0.1 ml of the supernatant liquor was transferred into the voltammetric cell then completed to 10 ml with a pH 2.0 BR buffer. Then, zolmtriptan was quantified by means of the proposed stripping voltammetric procedure.

3. RESULTS AND DISCUSSION

Fig. 2 illustrated the cyclic voltammogram of 4.0×10^{-5} M of zolmtriptan in BR buffer of pH 2.0, following 10 s accumulations at open circuit conditions. It can be seen that, in the case of GCE, the voltammogram of zolmtriptan exhibits one well-defined anodic peak, with no peak on the reverse scan, suggesting the irreversible nature of the electrode reaction.

3.1. Effect of pH

In general, it is important to investigate the effects of pH on electrochemical. Voltammetric behavior of zolmtriptan was studied at GCE in BR buffer over the pH range of 2.0-6.0. Fig. 3 illustrates shows the plot of peak current (I_p) *vs.* pH. It is obvious from the figure that the peak current reaches its maximum value at pH 2.0 and after this value the anodic current decreases as the pH value increases. Therefore, pH 2.0 was chosen as the optimum pH value for the determination of the used drug using DPV and SWV techniques.

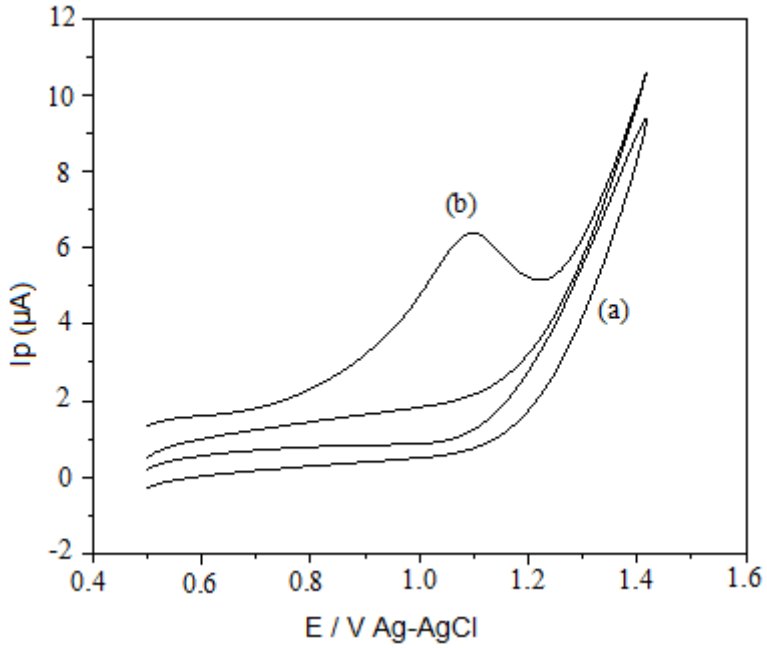

Fig. 2. Cyclic voltammogram of 4.0×10^{-5} M zolmtriptan at GCE (a) in BR buffer of pH 2.0 (b) the blank, scan rate 100 mV s^{-1}

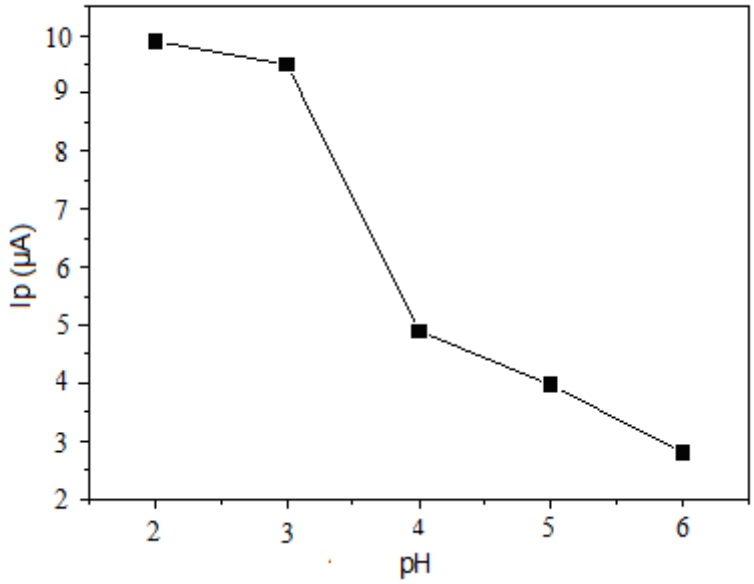

Fig. 3. Effect of pH on peak current of 4.0×10^{-5} M zolmtriptan solution in BR buffer at GCE, and Scan rate 100 mV s^{-1}

3.2. The effect of scan rate

The influence of the scan rate on the anodic peak current (I_p) of zolmtriptan was studied within the range 10-250 mV s^{-1}. There is a linear increase in the anodic peak current with the scan rate. The plot of log Ip against log ν displayed linear correlation with slope values of

0.58. This behavior indicated that the oxidation process of zolmtriptan was diffusion controlled with some adsorption character [23].

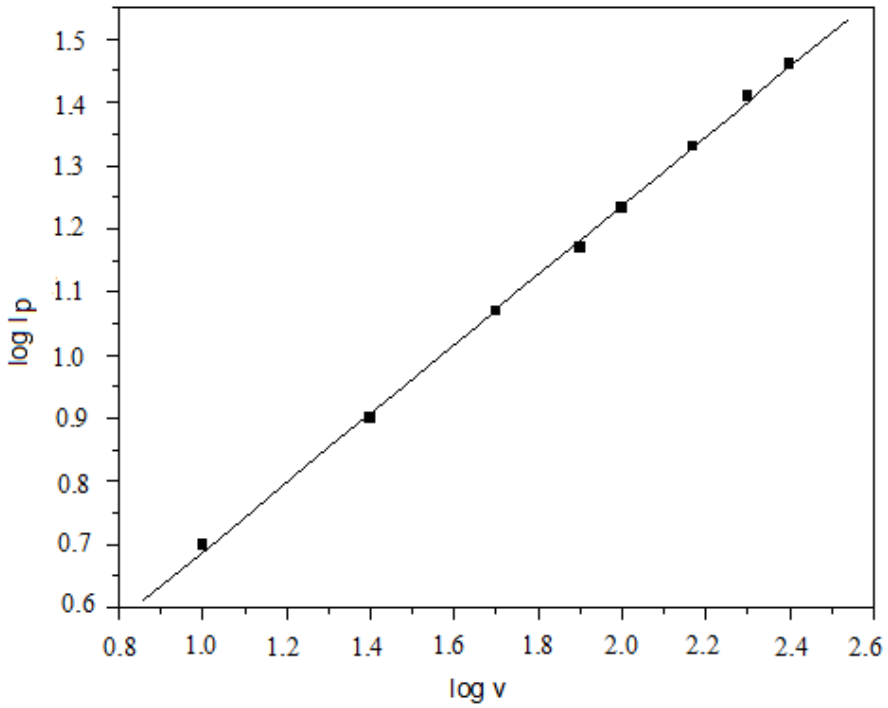

Fig. 4. Anodic peak current response of 4.0×10^{-5} M zolmtriptan as a function of log scan rate (υ) in BR buffer of pH 2.0 at GCE

3.3. Effect of accumulation potential

Also, the dependence of peak current on accumulation potential (acc. pot) was evaluated over the range 0.0 to 2.0 V for 4.0×10^{-5} M zolmtriptan in pH 2.0. It is obvious from the figure that the peak current reaches its maximum value at 0.0 V (open circuit) and the anodic current decreases as the value of accumulation potential increases. Therefore, The results obtained show that the I_p shows the maximum value at accumulation potential 0.0 V, as shown in Fig. 5.

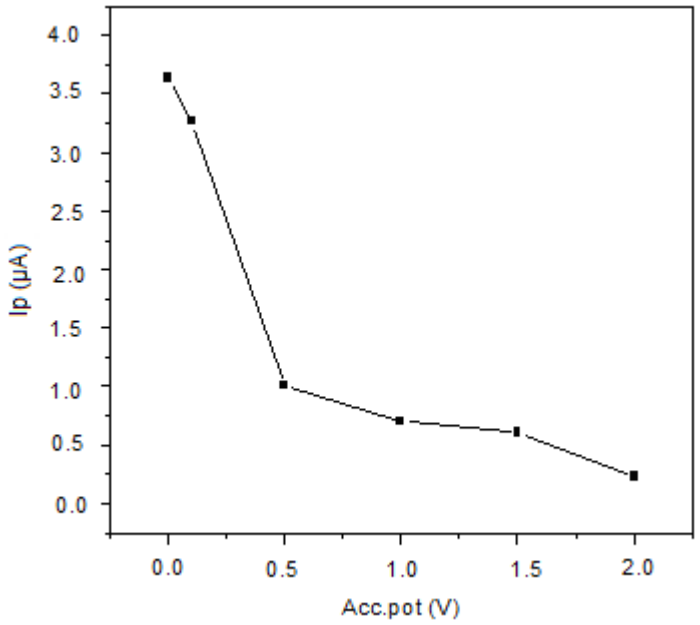

Fig. 5. Effect of accumulation potential on the peak current of 4.0×10^{-5} M zolmtriptan in BR buffer of pH 2.0 at GCE

3.4. Effect of accumulation time

The effect of accumulation time (acc. time) on the I_p was studied. The anodic peak current increases as the accumulation time increases and reach its maximum value at accumulation time 10 second and after this value the anodic current decreases. Accumulation time 10 second is chosen as the optimum accumulation time.

3.5. Effect of pulse amplitude and frequency

In addition, the impact of varying the excitation wave pulse amplitude on the voltammetric current intensity was also evaluated. The effect of this operating variable was studied over the range of 10-100 mV (Fig. 7) and the current was increased by increasing of pulse amplitude. It was observed that the best shape of peak was obtained at 50 mV pulse amplitude. After 50 mV, the shape of the peak was not so good. So, 50 mV pulse amplitude was the ideal choice for this operational parameter. Moreover, varying the value of square wave frequency also plays an important role for the measured signal of SW-AdSV approach. Varying this parameter over the range of 10-100 Hz resulted in a substantial enhancement of the voltammetric peak current particularly at range of 10-60 Hz as can be seen from Fig. 8, then the peak of current was approximately constant till 90 Hz and then gradually decreased. Accordingly, for work 60 Hz SW frequency value was adopted.

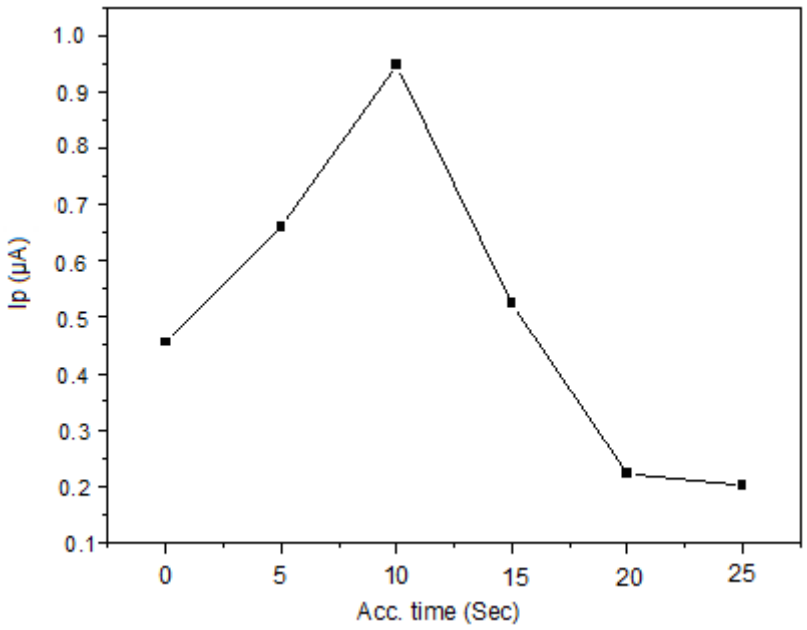

Fig. 6. Effect of accumulation time on the peak current of 4.0×10^{-5} M zolmtriptan in BR buffer of pH 2.0 at GCE

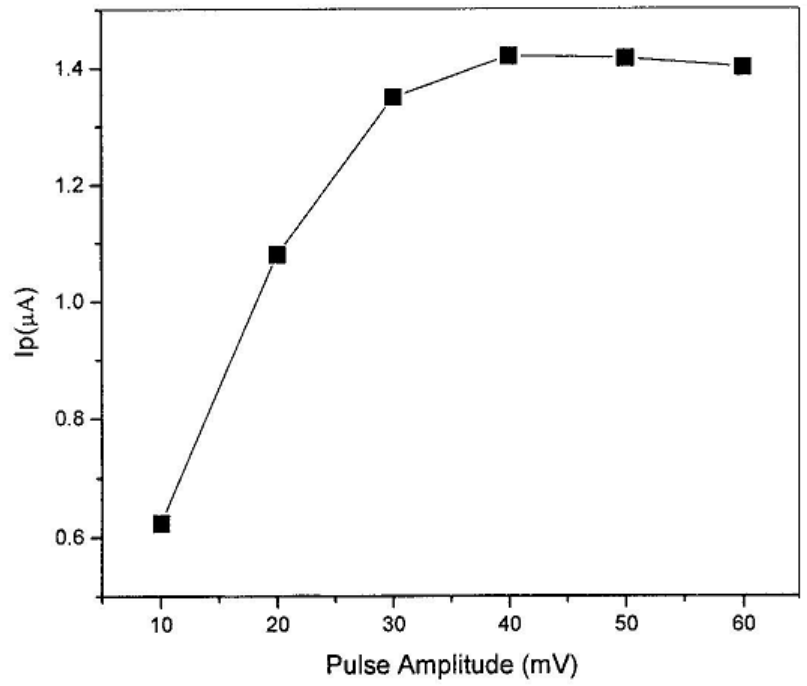

Fig. 7. Effect of pulse amplitude on the peak current of 4.0×10^{-5} M zolmtriptan in BR buffer of pH 2.0 at GCE

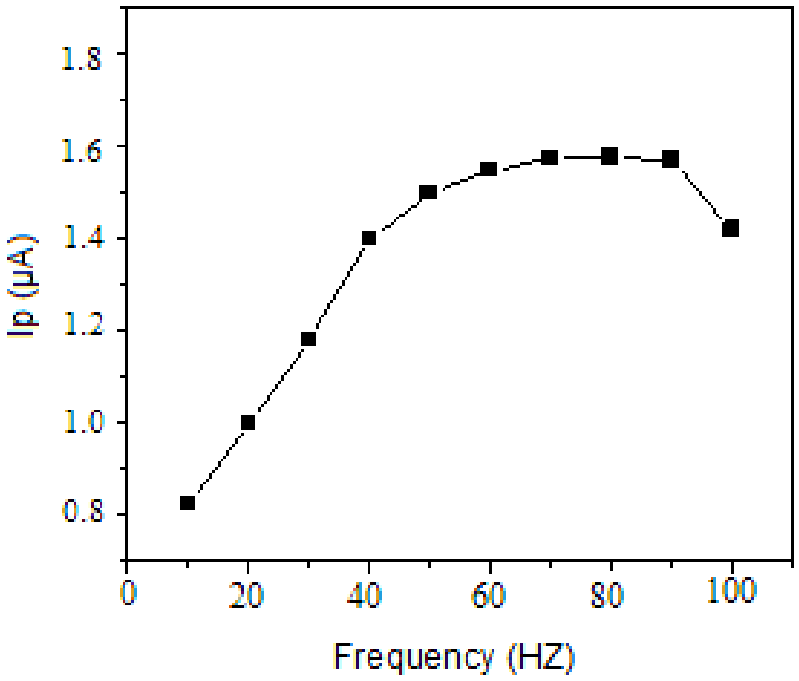

Fig. 8. Effect of frequency on the peak current of 4.0×10^{-5} M zolmtriptan in BR buffer of pH 2.0 at GCE

3.6. Determination of zolmtriptan

The determination of zolmtriptan at GCE was performed by DPV and SWV and the results are shown in Fig. 9 and 10. The I_p increased with increasing zolmtriptan concentration at GCE and there is a linear relation between the peak current and drug concentration in the range of 4.0×10^{-8} to 3.2×10^{-7} M with limit of detection (LOD) 2.0×10^{-8} M and limit of quantification (LOQ) 6.6 x 10^{-8} M in case of DPV. The linear range of 4.0×10^{-10} to 3.2×10^{-9} M, with LOD and LOQ 2.0×10^{-10} M and 6.6×10^{-10} M, respectively in case of SWV.

The percentage recoveries were found in the following ranges: 99.5-100.9% and 100.3-101.6% for DPV and SWV, respectively [24]. The relative standard deviations (RSD) were found in the following ranges: 0.71-1.36% and 0.38-0.84% in case of DPV and SWV, respectively. The results were given in Table 1.

This obtained sensitivity was significantly preferable than those reported for other analytical techniques used for determination of zolmtriptan such as gradient ion-pair UHPLC method with UV detection (LOD: 1.98×10^{-7} M) [6], a stability indicating LC method (linear range: 8.70×10^{-5} - 5.22×10^{-4} M) [9] and the electrochemical methods (linear ranges: 8.0×10^{-7} - 5.22×10^{-6} M and 1.0×10^{-5} - 1.0×10^{-4} M) [19].

Table 1. Analytical parameters of the calibration curve of zolmitriptan

Parameters	**DPV**	**SWV**
Calibration equations i_p/ μA	0..28+0.701 C (10^{-7} M)	0.309+4.39 C (10^{-9} M)
Concentration range/ M	4.0×10^{-8} -3.2×10^{-7}	4.0×10^{-10} -3.2×10^{-9}
RSD*,%	0.71-1.36	0.38-0.84
Correlation coeff., r^2	0.9950	0.9980
LOD, M	2.0×10^{-8}	2.0×10^{-10}
LOQ, M	6.6×10^{-10}	6.6×10^{-8}
Recovery, %	99.5-100.9	100.3-101.6

* Five different concentration of zolmitriptan; number of replicates (n)=5

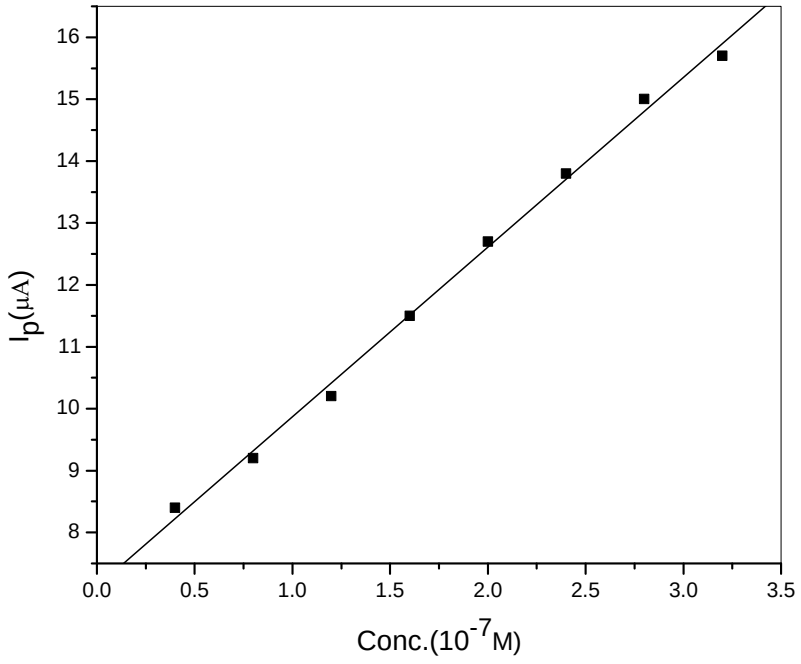

Fig. 9. Calibration curve of zolmtriptan at GCE, by DPV, pulse amplitude 50 mV, and scan rate 10 mV s^{-1}

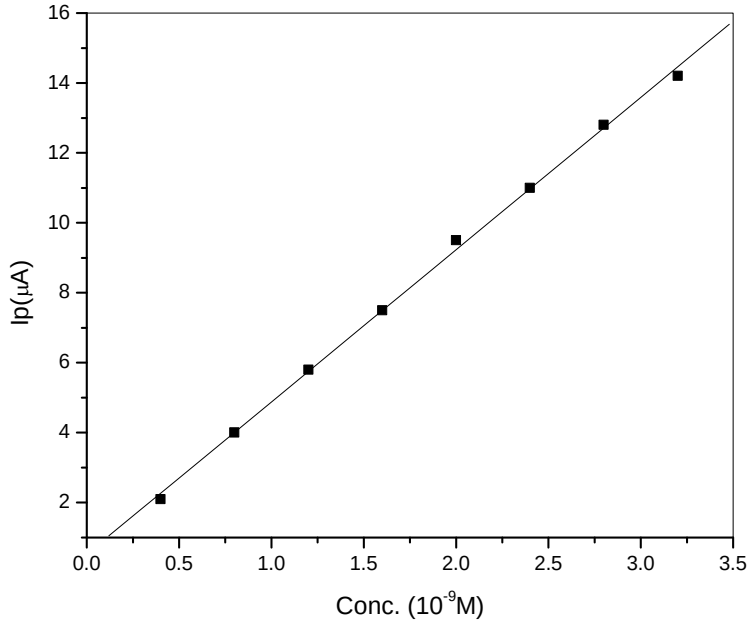

Fig. 10. Calibration curve of zolmtriptan at GCE, by SWV, pulse amplitude 50 mV, frequency 50 and scan rate 10 mV s^{-1}

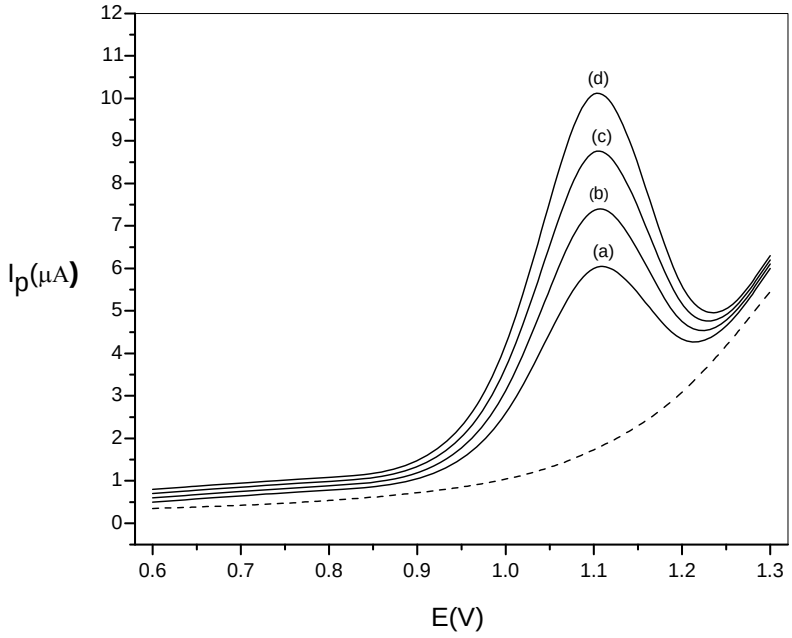

Fig. 11. Square wave voltamogram of zolmtriptan pulse amplitude 50 mV, frequency 50 Hz, and scan rate 10 mV s^{-1} with concentrations (a) 0.8 (b) 1.2 (c) 1.6 (d) 2×10^{-9} M

Table 2. Determination of zolmitriptan in tablets

Parameters	DPV	SWV
Linearity range (M)	4.0×10^{-8} -3.2×10^{-7}	4.0×10^{-10} -3.2×10^{-9}
RSD*,%	0.88-1.5	0.77-1.12
Recovery, %	99.1-101.4	99.3-100.5

***** Five different concentration of zolmitriptan; number of replicates (n)=5

4. ANALYTICAL APPLICATIONS

4.1. Determination of zolmtriptan in tablets

The developed DPV and SWV methods were used to determine zolmtriptan in commercial pharmaceutical dosage form (No-MigrainZ). The determination of zolmtriptan in tablets method was carried out without any sample extraction prior to analysis. The content of zolmtriptan in tablet was found to be 99.1-101.4% and 99.3-100.5% of the label claim by investigated DPV and SWV method, respectively. The results were given in Table 2.

4.2. Determination of zolmtriptan in spiked urine and plasma samples

The applicability of the procedure for the analysis of zolmtriptan in biological samples was also evaluated by estimating its recovery from spiked urine and plasma samples. As can be extracted from Table 3, this SW-AdSV method allowed the determination of zolmtriptan in spiked urine and plasma samples with mean recoveries of 99.33% ± 0.80 and 99.85% ±1.0, respectively.

Table 3. Analytical results for zolmitriptan recoveries from biological Fluids

Parameters	Spiked urine	Spiked plasma
Linearity range (M)	4.0×10^{-10} - 3.2×10^{-9}	4.0×10^{-10} - 3.2×10^{-9}
Mean recovery, %	99.85	99.33
Mean RSD*, %	±1.0	±0.8

***** Five different concentration of zolmitriptan; number of replicates (n)=5

5. CONCLUSION

The proposed adsorptive stripping voltammetric procedures can be successfully applied for determination of zolmtriptan in pharmaceutical formulation and biological fluids. The method allows a fast and reproducible determination of this compound with no interference from ingredients present. The present method is found to be practically rapid, convenient, accurate, low cost and precise. As applied to spiked urine and plasma samples, these methods have the advantage that no prior extraction procedure is required prior to the analysis. The developed methods are more sensitive than already reported analytical methods showing the detection limits of 2.0×10^{-8} M and 2.0×10^{-10} M for DPV and SWV methods, respectively. The method could possibly be adopted for the quality control laboratories.

REFERENCES

[1] F. D. Sheftell, M. Feleppa, S. J. Tepper, M. Volcy, A. M. Rapoport, and M. E. Bigal, Headache 44 (2004) 661.

[2] D. K. Arulmozhi, A. Veeranjaneyulu, and S. L. Bodhankar, Vasc. Pharmacol. 43 (2005) 176.

[3] P. J. Goadsby, and R. Yates, Headache 46 (2006) 138.

[4] Z. Zhang, F. Xu, J. Y. Tian, W. Li, and G. Mao, J. Chromatogr. B 813 (2004) 227.

[5] E. M. Clement, and M. Franklin, J. Chromatogr. B 766 (2002) 339.

[6] M. Dousa, P. Gibala, S. Radl, O. Klecan, Z. Mandelova, J. Brichac, and T. Pekarek, J. Pharm. Biomed. Anal. 58 (2012) 1.

[7] J. Chen, X. G. Jiang, W. M. Jiang, N. Mei, X. L. Gao, and Q. Z. Zhang, J. Pharm. Biomed. Anal. 35 (2004) 639.

[8] M. K. Srinivasu, B. M. Rao, G. Sridhar, P. R. Kumar, K. B. Chandrasekhar, and A. Islam, J. Pharm. Biomed. Anal. 37 (2005) 453.

[9] B. M. Rao, M. K. Srinivasu, G. Sridhar, P. R. Kumarb, K. B. Chandrasekhar, and A. Islam, J. Pharm. Biomed. Anal. 39 (2005) 503.

[10] J. Wang, Analytical Electrochemistry, 2nd ed. Wiley-VCH, New York (2002).

[11] J. Wang, Stripping Analysis: Principles, Instrumentation and applications. VCH Publishers Inc., Florida (1985) 1.

[12] K. H. Brainina, and E. Neyman, Electroanalytical Stripping Methods. John Wiley and Sons, New York (1993) 71.

[13] R. Kalvoda, and J. Zuka, Adsorptive Stripping Voltammetry in Analytical Chemistry II, Ellis Horwood, New York (1996).

[14] J. A. Bard, and L. R. Faulkner, Electrochemical methods (2nd ed.). New York: Wiley, (2001).

[15] V. Adam, R. Mikelova, J. Hubalek, P. Hanustaik, M. Beklova, P. Hodek, A. Horna, L. Trnkova, M. Stiborova, L. Zeman, and R. Kizek, Sensors7 (2007) 2402.
[16] J. G. Teixeira, C. B. Dias, and D. M. Teixeira, Electroanal. 21 (2009) 2345.
[17] R. Jain, A. Dwivedi, R. Mishra, and J. Hazard. Mater. 169 (2009) 667.
[18] H. K. Maleh, A. A. Ensafi, and A. R. Allafchian, J. Solid State Electrochem. 14 (2010) 9.
[19] B. Uslu, and D. Canbaz, Pharmazie, 65 (2010) 245.
[20] A. K. Attia, Sens. Electroanal. 5 (2010) 209.
[21] A. K. Attia, R. A. Saber, Anal. Bioanal. Electrochem. 3 (2011) 291.
[22] A. H. Al-Ghamdi, A. F. Al-Ghmdi, M. A. Al-Omar, Anal. Lett. 41 (2008) 90.
[23] D. K. Gosser, Cyclic Voltammetry Simulation and Analysis of Reaction Mechanism, VCH, New York (1994).
[24] J. C. Miller and J. N. Miller, Statistics for Analytical Chemistry, Ellis Horwood Series, Prentice Hall, New York (1993).