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Square wave anodic stripping voltammetric determination of Mebeverin hydrochloride in tablet and urine at carbon paste electrode

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ABSTRACT

A simple and reliable square wave anodic stripping (SWAS) voltammetric method at carbon paste electrode (CPE) of Mebeverin hydrochloride (MEB) in pharmaceutical dosage forms (tablet) and in biological fluids (spiked and real urine samples) has been developed and evaluated. Different parameters such as medium, supporting electrolyte, pH, accumulation potential, scan rate and accumulation time, were tested to optimize the conditions for the determination of MEB. The adsorbed form is oxidized irreversibly under optimal conditions, viz., 0.1 M Phosphate buffer (pH~8), 0.1M KCl, a linear concentration ranges from 0.233 to 42.406 µg/mL of MEB, at accumulation times 60, 150 s, can be determined successfully. The standard addition method was used to determine the MEB in pure solutions, tablets and in biological fluids with satisfactory results. The data obtained are compared with the standard official method.

Introduction

Mebeverine hydrochloride (MEB) is chemically known as (RS)–4–(ethyl[1– (4–methoxyphenyl)propan–2–yl]amino)butyl–3,4–dimethoxybenzoate hydrochloride (Fig. 1). MEB belongs to a category of anti–spasmodics known as musculotropic drugs and is used largely in treatment of irritable bowel syndrome and gastrointestinal spasm secondary to organic disorder [1, 2]. The official procedure described in B.P.2007 [2] depends on non–aqueous potentiometric titration with 0.1 M perchloric acid for the determination of MEB in its parent form. Several methods have been reported in literature for the determination of this drug either per se or in formulations. In this concern, the following techniques have been described: Spectrophotometric methods [3–9], electrochemical methods [10–13] and Chromatographic methods [14–17].

Stripping voltammetry is a very sensitive method for the determination of many traces of organic compounds and metal ions achieving it is low level of detection by combining an accumulation process with a voltage scanning measurements [18–22]. Carbon paste electrodes are convenient and often used as working electrodes for the voltammetric measurements because of their attractive properties. From analytical point of view, these electrodes exhibit rather low background currents over a wide range of potentials when compared with other solid electrodes, and after a renewability of their surface as well as a high versatility and simplicity of modification [19, 23].

The present work is a continuation of our studies in the field of drug analysis using solid electrodes [24, 25]. Until now, no electrochemical studies dealing with MEB electrochemical oxidation behavior at CPE have been reported. The voltammetric determination of MEB by SWASV at a paraffin oil bare carbon paste electrode has not been studied yet.

Thus, the aim was to investigate the square wave anodic stripping voltammetric determination of MEB in dosage forms (tablets) and in biological fluids (spiked and real urine sample) at a paraffin oil bare carbon paste electrode (CPE).

Experimental

Apparatus

All voltammetric experiments were performed with EG&G Princeton Applied Research (PAR Princeton, NJ, USA) Model 273 A potentiostat, controlled by the Model 270/250 electrochemical software version 4.30. A three electrode cell was employed incorporating a hand–make working carbon paste electrode that prepared as previously mentioned [19], an Ag/AgCl (saturated KCl) reference electrode and a platinum wire was used as a counter electrode. Mass transport was achieved with a Teflon–coated bar at approximately 400 rpm using a magnetic stirrer (KIKA Labortechinik, Germany). All the pH measurements were made with VWR Scientific Products Model 2000.

Reagents and materials

All of the chemicals used were of analytical grade (Merck and Sigma), and all of the solutions were freshly prepared in doubly distilled water. Mebeverin hydrochloride (MEB) (Merck) stock standard aqueous solution (1×10^{-2} M) was prepared (at 25 C° 48 g MEB per 100mL doubly distilled water [1, 2]) and kept in a brown volumetric flask. MEB working standard solutions was prepared daily by serial dilution of the stock standard solution.

Pharmaceutical formulations: Mebagen and Duspatalin tablet (Memphis Co. for Pharm. & Chem. Ind. Cairo, A.R.E.) labeled to contain 10 mg MEB per tablet.

General analytical procedure

The preconcentration step was performed by immersing the carbon paste electrode in a stirred 15 mL sample solution for a given period of time at potential range from + 0.20 to + 1.4 V. The stirring was then stopped and after a delay period of 10 s to settle the solution and decrease the background current, cyclic or square wave voltammogram was recorded in the positive potential direction. A renewed carbon paste surface was used for each measurement.

For determination of MEB in biological fluids (spiked and real urine samples), 1 mL aliquot of urine (blank or containing drug) was transferred to a 250 mL separating funnel containing

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5 mL of diethyl ether (Merck). The mixture was thoroughly shaken for 15 min, then, the organic layer was transferred to a glass tube, and the solvent was evaporated in water bath to dryness. The residue was reconstituted in doubly distilled water. Then, 20 µL urine sample (containing 6.73 ng/mL of the drug in case of spiked urine and unknown a mount of excreted drug in real urine samples), was added to 15 mL voltammetric cell and mixed thoroughly with 0.1 M phosphate buffer pH~8.0 containing 0.1 M KCl. The solution was stirred at 400 rpm at open circuit conditions and the square wave voltammogram was recorded. Also, in case of dosage forms, 10 tablets of the drug were weighed into a small dish, powdered and mixed well. A portion equivalent 0.1294 g was weighed and dissolved in 100mL of doubly distilled water, shaken well and filtered using filter paper. An aliquot of the filtrate was then transferred into a calibrated flask and it was completed to volume with the same solvent. 20 µL of each solution was then added to the measurement cell. In all measurements, the square wave voltammogram was recorded in positive potential direction. Table 1 contains the optimum operational parameters selected for the determination of MEB by SWASV using CPE.

Table 1: The optimum operational parameters selected for the determination of MEB by SWASV at CPE

Parameter	Selected value
Accumulation potential	+ 0.2 V
Final potential	+ 1.5 V
Frequency	100 Hz
Scan increment	2 mV
Accumulation time	Various
pH	8.0
Buffer type	0.1 M Phosphate buffer
Supporting electrolyte	0.1 M KCl

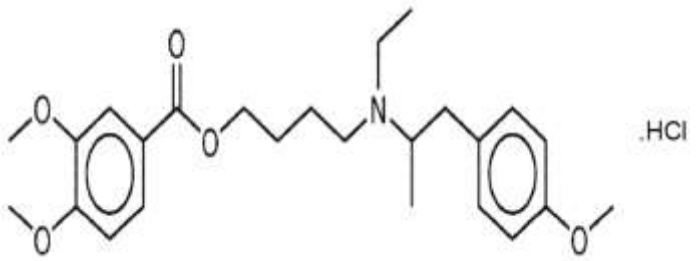

Fig 1. Mebeverin Hydrochloride (MEB)

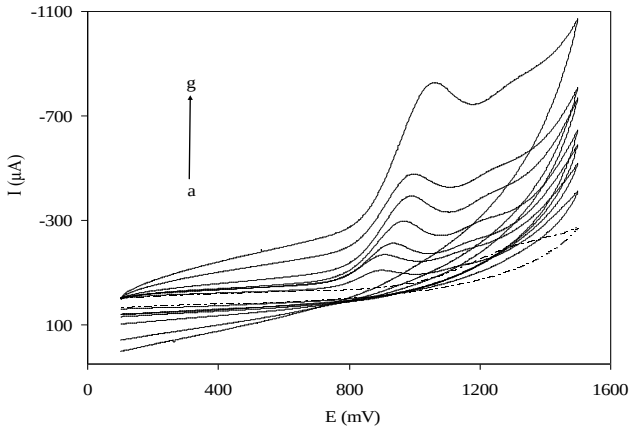

Fig 2. Effect of scan rate on 9.3 µg/mL MEB; residual (dashed line), at different scan rate from 30, 60, 70, 150, 200, 250, 650 mV/sec. (from a to g, respectively).

Result and discussion

Cyclic voltammetry

The cyclic voltammogram of the oxidation of MEB at paraffin oil bare carbon paste electrode in phosphate buffer (pH~8.0) containing 0.1 M KCl was studied. In the forward scan, one well–defined anodic peak owing to the oxidation of amino group was observed and no peak was noticed in the reverse direction. The peak current decrease with succeeding potential scans suggesting an adsorbed species formation on the electrode surface. This indicates that the oxidation of MEB is irreversible. The effect of scan rate, *v*, on the peak current and peak potential was evaluated and showing in Fig. 2. The peak potential was shifted to more positive values on increasing scan rate, which confirms the irreversible nature of the oxidation process.

Effect of accumulation potential

The effect of accumulation potential on the peak current was also investigated in potential range from – 0.2 to + 0.8 V at 60 s preconcentration time for 9.3 µg/mL MEB solution (pH~8.0) as showed in Fig. 3. Experiments proved that the peak current of MEB increases with positive shifting of starting potential in the range from – 0.2 to + 0.2 V and then decrease with positive shifting from + 0.2 to + 0.8 V. The Peak current has its maximum value at initial potential + 0.2 V, which was used in the subsequent examinations of other decencies.

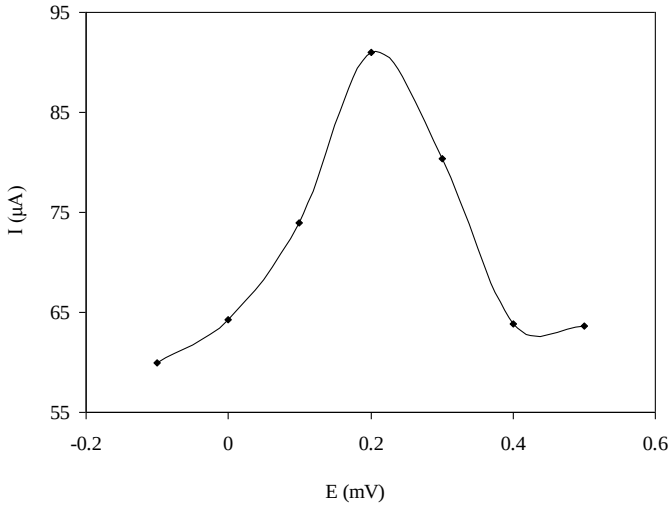

Fig 3. Effect of initial potential on 9.3 µg/mL MEB in 0.1 M phosphate buffer containing 0.1 M KCl.

Effect of buffer type, pH, supporting electrolyte and ionic strength

The effect of type of buffer used as electrolyte (sodium borate–HCl buffer, phosphate buffer, Britton–Robinson and sodium borate–boric acid buffer) on the analytical signal was investigated. Both the peak height and peak shape were taken into consideration when choosing type of buffer. A study of the influence of the ionic strength of the medium on the definition of the voltammetric peak revealed that minimal background current, the best curve and the highest peak were obtained in 0.1 M phosphate buffer.

The effect of pH on the oxidation of MEB at CPEs was studied over the pH range 2.5–11.2 at the concentration 9.3 µg/mL MEB by square wave voltammetry as shown in Fig. 4. A small current was observed at pH~3.5, which increased gradually up to pH~8 and then decreased at higher pH. Thus, pH~8 was used in all measurements. Approximately, there no change occurs in the potential of anodic peak of MEB with increasing values of the pH.

The influence of type of supporting electrolyte (KCl, $NaNO_3$, $NaClO_4$) was studied. The best choice that has ability to give the best shape and highest current was

KCl. The addition of 0.1M KCl to the voltammetric cell contain phosphate buffer (pH~8) containing 9.3 µg/mL MEB at

60 s accumulation time cause large excess in peak current when compared with the similar peak current in absence of KCl.

The influence of ionic strength on the efficiency of accumulation of 9.3 µg/mL MEB was studied for a 60 s preconcentration time. Changing the KCl concentration in range from 0.05 to 0.4 M in the chosen buffer type varied the ionic strength. The result showed that increasing ionic strengths were found to be of great significance on the degree of accumulation. The effect of concentration of KCl was very important. However, the best accumulation is attained in presence of 0.1 M KCl.

Effect of accumulation time and reproducibility

The dependence of the peak current on accumulation time was studied for four levels of concentration named as: 0.28, 2.80, 28.0 µg/mL MEB. The stripping signal increased linearly with increase accumulation time up to 600 s (Fig. 5). Repeating three experiments on 2.8 µg/mL MEB at 60 s accumulation time checked the reproducibility of the adsorption process. The relative standard deviation was computed to be 4%.

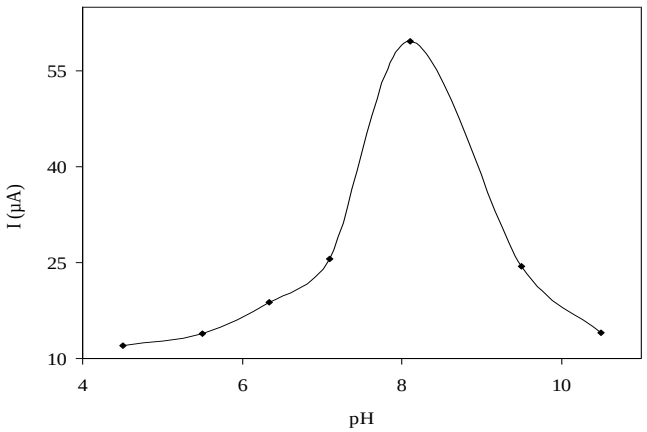

Fig 4. Effect of pH on 9.3 µg/mL MEB in 0.1 M phosphate buffer containing 0.1 M KCl

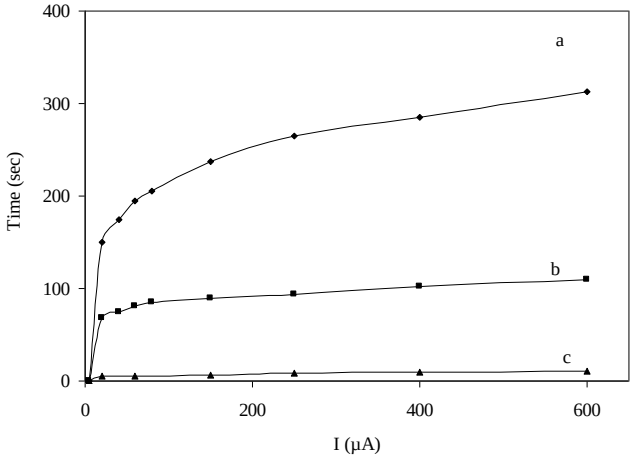

Fig 5. Effect of time on different concentrations of MEB: (a) 28.0 µg/mL, (b) 2.8 µg/mL and (c) 0.28 µg/mL in phosphate buffer (pH~8) containing 0.1 M KCl.

Effect of concentration and detection limit

The square wave anodic stripping peak for MEB yields a well–defined concentration dependence using SWASV method. The calibration plots over the MEB concentration range, following different preconcentration times were investigated. However, a well defined peak was observed over the concentration range 0.23–42.42 µg/mL MEB at 60 and 150 with the stirring at + 0.8 V. The results show positive deviation from linearity at concentrations higher than 4.20 µg/mL at 60 s and 23.86 µg/mL at 120 s. The detection limits estimated [19, 23, 26] as $3\sigma/b$, where b is the slope and σ = standard deviation (S.D.) of the intercept and the quantitative limits also calculated as $10\sigma/b$.

The results obtained from the proposed method shown that MEB can be detected from 8.3×10^{-7} M (0.38 µg/mL), with standard deviation 0.22 %, correlation coefficient r = 0.9921 (n = 5) at accumulation time 60 s. The proposed method was very sensitive than the reported methods. The repeatability of the peak current at new surfaces as measured by relative standard deviation (R.S.D.) was 2.5 % and at the same electrode after consecutive accumulation and cleaning step (the paste was cleaned by washing with doubly distilled water) was 3.0 % (n = 3).

Effect of interferences

To test the efficiency and selectivity of the proposed analytical method to pharmaceutical formulations, a systematic study of sample solutions containing a fixed amount of MEB (4.6 µg/mL) spiked with excess amount of some common excipients and additives that are used in pharmaceutical preparations **(**10 000:1**)** (e.g. glucose, sucrose, lactose and fructose) under the optimum experimental conditions was made to know the effect of such excipients and additives on the efficiency and selectivity of the proposed analytical method to pharmaceutical formulations. Experimentals showed that there was no serious interference occurred from the classical additives tested. Therefore, the proposed method can be used as a selective method. The influence of ascorbic acid, which is a potentially interfering compound present in biological samples, was investigated. It was found that an equimolar concentration or even at higher molar excess (10 000:1) of ascorbic acid had no effect on the peak response of MEB. Also interference of some metal ions was tested under the same conditions, It was observed that 10 000–fold excess of Al(III), Ca(II), Sr(II), Cd(II), Ni(II), Co(II), Mg(II), and Cu(II) metal ions had no effects on MEB determination.

Analytical applications

The proposed method was successfully applied to determine MEB in pharmaceutical preparations, spiked and real urine samples.

Pharmaceutical preparations

The square wave voltammogram of the used tablet sample was recorded after preconcentration time for 60 and 150 s, in 0.1 M phosphate buffer (pH ~ 8.0) containing 0.1 M KCl solution. The content of the tablet in the cell was determined by standard addition method [27]. One peak was observed on addition of pure drug to the sample at + 0.8 V. On increasing the MEB concentration, the peak current was increased linearly from 0.35 to 4.2 µg/mL at 60 s and from 0.35 to 23.86 µg/mL at 150 s which fitted the equation Y = 16.71 X + 7.49 with correlation coefficient of 0.9921 and Y = 8.85 X + 20.01 with correlation coefficient 0.9976, respectively. The obtained values were compared statistically by Student's t–test for accuracy and f–test for precision with the official method [1,2] at the 95 % confidence level with five degrees of freedom, was calculated. The result showed that the t– and f–test values were less than the critical value, indicating that there was no significant difference between the proposed and the official methods. Because the proposed method was more reproducible with high recoveries than the official method, it can be recommended for the routine analysis in the majority of drug quality control laboratories.

Spiked urine samples

The proposed method was applied to the determination of MEB in spiked urine samples from healthy volunteers using

standard addition method. The square wave response to definite concentration of MEB in urine samples, after 60 s accumulation time of MEB was recorded. The electrode response was linearly related to the MEB concentration within the range 0.35–4.2 μg/mL of MEB, with correlation coefficients of 0.9987; standard deviation for slope and intercept of the calibration curve were 0.95 and 2.12 %, respectively. The detection limit was 0.11 μg/mL at 60 s accumulation time (S.D. = 0.56 % and r = 0.9998 (n = 5)). The repeatability of total analytical process was determined from multiple measurements at each of the urine samples (n = 5). An average deviation of 3.5 % was obtained.

Real urine samples

The proposed method was also applied to the determination of MEB in human urine samples from healthy volunteers who received a single oral dose of 10 mg of Mebagen and Duspatalin tablet. The samples of individuals were collected for up to 24 h after administration of dosage form and urinary volumes were recorded as well. MEB was well separated from organic components and excipients did not interfered [19]. The result obtained shown that a small amount of an administered dose are excreted in the urine. The results showed a high correlation coefficient (r≥0.9990). Also, the obtained result from the proposed method for voltammetric assay of MEB in real urine samples were compared with those obtained by official method [1, 2], in which about 60% of an oral dose is excreted in the human urine in the first 24 h.

Accuracy and repeatability

Applying the proposed method for the analysis of dosage forms and urine validated the accuracy of the suggested procedure. The analysis of MEB in spiked and real urine samples exhibited the correlation coefficient of 0.9935, the standard deviation of both slopes of ≤ 0.35 % and the intercept of ≤ 0.65 %, indicating adequate precision and accuracy of the proposed method.

Conclusion

The SWASV method with carbon paste electrode for the quantitative determination of MEB was found to be simple and highly sensitive. A detection limit of 8.3×10^{-7} M (0.38 μg/mL) at 60 s accumulation time with the standard deviation 0.51% was obtained in pure solutions. The method can be used successfully to assay the drug in dosage form as well as in spiked and real urine samples.

References:

1. J. E. F. Reynolds, Martindale, The Extra Pharmacopoeia, 29th ed., The Pharmaceutical Press, London, 1989.
2. British Pharmacopoeia, Vol. I, Her Majesty's Stationery Office, London, 2007.
3. A. M. El–Didamony, Spectrochim. Acta, 69 (2008) 770.
4. S. A. Shama, A. S. Amin, Spectrochim. Acta, 60 (2004) 1769.
5. K. Sreedhar, C. S. P. Sastry, M. N. Reddy, D. G. Sankar, Mikrochim. Acta, 126 (1997) 131.
6. M. N. Reddy, K. V. S. Rao, D. G. Sankar, K. Sridhar, Indian Drugs, 33 (1996) 604.
7. E. M. Hassan, A. A. Gazy, M. M. Bedair, Drug Dev. Ind. Pharm., 21 (1995) 633.
8. M. Walash, M. Sharaf El–Din, N. El–Enany, M. Eid, Sh. Shalan, J. Fluoresc., 20 (2010) 1275.
9. G. H. Ragab, M. S. Elmasry, A. A. Aboul Kheir, Anal. Chem.: An Indian J., 3 (2007) 140.
10. H. Ibrahim, Y. M. Issa, H. M. Abu–Shawish, J. Pharm. Biomed. Anal., 44 (2007) 8.
11. H. Ibrahim, Y. M. Issa, H. M. Abu–Shawish, J. Pharm. Biomed. Anal., 36 (2005) 1053.
12. C. Perrin, Y. Vander–Heyden, M. Maftouh, D. L. Massart, Electrophoresis, 22 (2001) 3203.
13. M. S. Elazazy, M. S. Elmasry, W. S. Hassan, Int. J. Electrochem. Sci., 7 (2012) 9781.
14. M. S. Elmasry, I. S. Blagbrough, M. G. Rowan, H. M. Saleh, A. A. Kheir, P. J. Rogers, J. Pharm. Biomed. Anal., 54 (2011) 646.
15. M. I. Walash, M. M. Kh. Sharaf El–din, N. M. El–enany, M. I. Eid, S. M. Shalan, Chem. Cent. J., 6 (2012) 13.
16. O. Al–Deeb, B. M. Al–Hadiya, N. H. Foda, Chromatographia, 44 (1997) 427.
17. M. A. Radwan, H. H. Abdine, H. Y. Aboul–Enein, Biomed. Chromatogr., 20 (2006) 211.
18. O. A. Farghaly, Microchem. J. 75 (2003) 119.
19. O. A. Farghaly, Talanta 63 (2004) 497.
20. O. A. Farghaly, J. Pharm. Biomed. Anal. 23 (2000) 783.
21. A. M. M. Ali, O. A. Farghaly, M. A. Ghandour, Anal. Chim. Acta 412 (2000) 99.
22. O. A. Farghaly, H. M. Abd El–Wadood, M. A. Ghandour, J. Pharm. Biomed. Anal. 21 (1999) 233.
23. O.A. Farghaly, N. A. Mohamed, Talanta 62 (2004) 531.
24. O. A. Farghaly, M. A. Taher, A. H. Naggar, A.Y. El–Sayed, J. Pharm. Biomed. Anal., 38 (2005) 14.
25. A. H. Naggar, M. ElKaoutit, I. Naranjo–Rodrigueza, A. Y. El–Sayed, J. L. Hidalgo–Hidalgo de Cisneros, Talanta 89 (2012) 448.
26. O. A. Farghaly, M. A. Ghandour, Environ. Res. 97 (2005) 229.
27. O. A. Farghaly, M. A. Ghandour, Talanta 49 (1999) 31.