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Differential pulse polarographic assay of tolmetin sodium capsules

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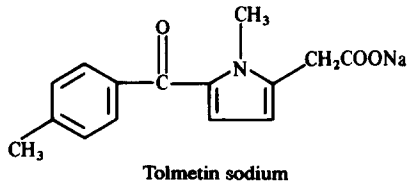
Abstract: Differential pulse polarography (DPP) is proposed as a direct method for the quantitation of tolmetin sodium in a capsule formulation (Tolectin® — 200 mg as the sodium dihydrate salt). Classical direct-current (DC) polarography has been employed to investigate the nature of the reduction occurring at the surface of the dropping mercury electrode (DME) using acetate buffer of pH 5.0 as the supporting electrolyte. The mean value of the results obtained by DPP expressed as a percentage of the stated amount, and the standard deviation, were found to be 99.87 ± 0.43. The standard addition procedure used to assess the accuracy of the proposed method gave a mean percentage recovery of the total drug of 100.15 ± 0.75%.

Keywords: *Tolmetin sodium; direct-current polarography; differential pulse polarography.*

Introduction

Tolmetin, 1-methyl-5-(4-methylbenzoyl)-1H-pyrrole-2-acetic acid is a non-steroidal anti-rheumatic drug with analgesic properties in man. Extensive clinical trials have established its efficacy in the treatment of adult and juvenile rheumatoid arthritis and in osteo-arthritis [1, 2] of both large and small joints.



Tolmetin sodium

Several procedures including thin-layer chromatography and gas–liquid chromatography [3–5], and high-performance liquid chromatography [6, 7] have been reported for the detection and quantitation of tolmetin and its metabolites in biological fluids. An indirect, lengthy colorimetric method [8] has also been published for the determination of tolmetin sodium. This procedure involves the formation of an insoluble lead salt which is separated and determined spectrophotometrically as the dithizone complex. Direct-current (DC) polarography has been used for the assay of tolmetin using methanol as solvent and Britton-Robinson buffer solution of pH 8.5, and a saturated calomel electrode as reference [9].

In this communication differential pulse polarography (DPP) is proposed as a direct and sensitive method for the assay of tolmetin sodium. The DPP, in comparison with the DC polarography method is superior with regard to simplicity, sensitivity, reproducibility and accuracy.

Experimental

Apparatus

A Metrohm polarecord assembly (unit 626) consisting of three electrodes, viz. a silver–silver chloride reference electrode, a platinum auxiliary electrode and a dropping mercury electrode (DME) was used. The polarograph stand was model E505 and the DME was a fine capillary with a drop controller supplying a steady stream of mercury droplets at a frequency of 0.5 s^{-1} and a flow of approximately 3 mg s^{-1}.

Materials and reagents

Tolmetin sodium. Authentic tolmetin sodium dihydrate (Lot No. 87 P2427) and purity of 100.1% was kindly donated by Cilag AG (8201 Schaffhausen, Switzerland). Tol-

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metin capsules (Tolectin® — 200 mg) were kindly supplied by Cilag Scientific Office (Riyadh, Saudi Arabia).

Acetate buffers, pH 4.6 and 5.0, borate buffer pH 9.0 and phosphate buffer pH 7.4 were made according to ref. 10.

Standard tolmetin sodium solution. This was prepared by dissolving 100 mg in, and diluting to, 100 ml with acetate buffer pH 5.0 to produce 1 mg ml^{-1} solution.

Gelatin solution (maximum suppressor). Prepared fresh daily as 0.1% w/v solution in the acetate buffer pH 5.0.

Procedure

Twenty capsules were accurately weighed, emptied carefully and the mass of the collected powder was determined. The empty shells were weighed and the net fill weight per capsule was calculated. A quantity of the mixed powder equivalent to about 100 mg of tolmetin sodium was accurately weighed into a 100-ml volumetric flask. 60 ml of acetate buffer pH 5.0 was added and the mixture was shaken for 10 min. The extract was diluted with the same buffer to 100 ml and filtered. The first few millilitres of the filtrate were discarded. Accurately measured volumes (0.50–4.0 ml) of the sample solution were transferred quantitatively to eight 100-ml volumetric flasks. 2 ml of gelatin solution was added to each flask and the solution was diluted to 100 ml with the acetate buffer, pH 5.0.

Twenty-five millilitres of each solution were transferred to the polarographic vessel and deaerated for 5 min with a stream of oxygen-free nitrogen. The differential pulse polarograms were recorded under the set of experimental conditions in Table 1 and the peak current, i_p, was measured from the base-line of each polarogram. The concentrations of tolmetin in the samples were calculated using the standard graph or its regression equation. The standard curve was obtained by using a series of volumes of the standard tolmetin solution (0.5, 1.0, 1.5, . . . 4.5 and 5.0 ml) treated as described for the sample solution.

Results and Discussion

Polarography of organic compounds is influenced by pH since hydrogen ions are involved in the electrode reaction. Acetate buffer (pH 4.6), phosphate buffer (pH 7.4) and borate buffer (pH 9.0) were each investigated for use as the electrolyte for the development of the DC polarogram of tolmetin sodium at room temperature. Ill-defined waves were obtained for phosphate and borate buffers; however, the acetate buffer yielded a comparatively discernible wave [Fig. 1(a)].

Variation of pH of the acetate buffer from 2.45 to 5.5 containing 80 μg ml^{-1} tolmetin sodium solution indicated that the maximum polarographic current was obtained at pH 5.0. Consequently, acetate buffer of pH 5.0 was chosen as the electrolyte for the quantitative measurements.

The effect of corrected mercury height (h, cm) on the polarographic current (i, nA) was studied. The linear regression equation describing the relationship between i and $h^{1/2}$ was calculated to be $i = 55.93 + 127.96\ h^{1/2}$, $n = 8$, and the Pearson correlation coefficient, $r = 0.9996$. At the 99% level of confidence and 7 degrees of freedom (d.f.) the calculated r-value is 0.798 [1]. It may therefore be stated that the relationship between i and $h^{1/2}$ is linear, suggesting that the recorded current is probably diffusion-controlled [12].

The logarithmic plot of the polarographic wave, obtained under the experimental conditions adopted for the DC-mode, (Fig. 2) was evaluated by linear regression; the r-value was

Table 1
Experimental conditions for DC and DPP modes

Parameter	DC	DPP
Modulation amplitude	—	50 mV
Initial range	−0.75 V	−0.80 V
Final range	−1.35 V	−1.35 V
t (drop/s)	0.5	0.5
Sensitivity	20 nA mm^{-1}	2.5 nA mm^{-1}
Sweep rate	−5 mV s^{-1}	−5 mV s^{-1}
Chart speed	100 mV cm^{-1}	100 mV cm^{-1}
Damp	2	2

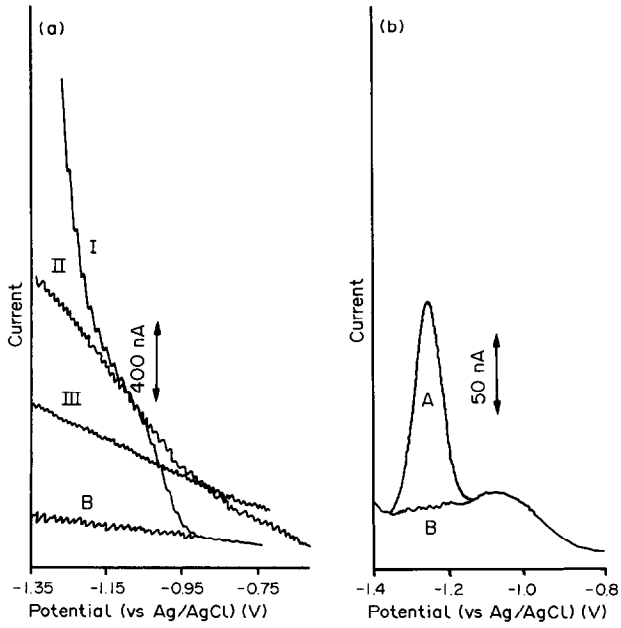

Figure 1
(a) DC polarograms of tolmetin sodium 80 μg ml^{-1} in acetate buffer, pH = 5.0 (I), borate buffer, pH = 9.0 (II), phosphate buffer, pH = 7.4 (III) and B = blank. (b) Typical differential pulse polarogram of (A) tolmetin sodium, 25 μ8g ml^{-1}, in acetate buffer pH = 5.0, and (B) blank solution.

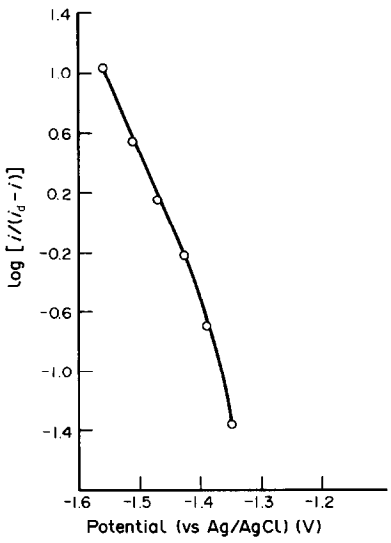

Figure 2
Relationship of log ($i/i_d - i$) to applied voltage.

found to be 0.991. Since the calculated *r*-value at 99% level of confidence and 5 d.f. [11] is 0.874, the electrode reaction may be reversible [13].

DPP is more sensitive and accurate than DC polarography [14] and, unlike the peak current (i_p) of the differential pulse polarogram [Fig. 1(b)], the estimation of the polarographic current of a DC-polarogram is rather arbitrary. The peak current in DPP measured from the base-line is linearly related to concentration (C) over the range 5–50 μg ml^{-1} ($i_p = 11.16 + 10.56C$, where C is in μg ml^{-1} and i_p is in nanoamperes; $r = 0.998$).

The mean percentage and standard deviation of the results obtained for eight determinations of tolmetin capsules (Tolectin®) was found to be 99.87 ± 0.43. The mean percentage recovery and standard deviation of the total drug when the standard addition method was used (Table 2) was 100.15 ± 0.75, indicating satisfactory accuracy.

In conclusion, the DPP method is recommended for the determination of tolmetin sodium due to its satisfactory sensitivity, reproducibility and accuracy.

Table 2
Results of assay of tolmetin sodium capsules (Tolectin®) by the proposed differential pulse polarographic method

Assay of sample			Added recovery		
Claimed weight of drug in sample taken (mg)	Weight found (mg)	% Found	Claimed weight of drug in sample taken (mg)	Authentic drug added	% Total mass recovered
100.8	100.6	99.87	50.2	50.0	100.0
100.2	99.7	99.50	40.2	59.5	101.9
99.5	99.4	99.87	30.2	71.3	100
100.1	99.8	99.70	20.4	80.7	100
100.5	99.8	99.30	10.8	91.6	99.8
99.8	99.9	100.10	60.3	39.2	99.5
101.0	100.9	99.87	72.5	38.1	100.3
98.5	99.2	100.75	81.8	19.2	99.7
Mean ± SD RSD = 0.57	99.87 ± 0.43				100.15 ± 0.75

SD = standard deviation.
RSD = relative standard deviation.

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