Asian Journal of Chemistry Vol. 21, No. 9 (2009), 7387-7397

Determination of Carbinoxamine Maleate in Pharmaceuticals by Direct and Differential Pulse Polarography

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A new, simple method for the determination of carbinoxamine maleate in pharmaceuticals, based on differential pulse polarography (DPP) and direct current polarography (DCP) in phosphate buffer pH = 1.69 are proposed. Diffusion currents (i_d) and peak currents (I_p) were measured on dropping mercury electrode (DME), static mercury dropping electrode (SMDE) and hanging mercury dropping electrode (HMDE) *vs.* Ag/AgCl. The half wave potential ($E_{1/2}$) and peak potential (Ep) for the reduction of carbinoxamine maleate were occurred over the range from -645 to -650 mV. The calibration curves $i_d = f(C)$ and $I_p = f(C)$ were linear over the ranges 12.0-238.0 μg mL^{-1} and 0.95-476.2 μg mL^{-1} with the relative standard deviations (RSD) of 2.5 and 4.3 % on DME using DCP and DPP, respectively. The proposed method was applied for the direct determination of carbinoxamine maleate in some pharmaceutical formulations (tablets, capsules, syrup and oral drops) by DPP in phosphate buffer pH =1.69 using DME, SMDE and HMDE. The obtained results showed that the difference between the expected and the found results values were less than 4 % in the worst case and the RSD was less than ± 2.0 %. Therefore, this polarographic method can be, for the first time, applied successfully for the determination of carbinoxamine maleate in pharmaceuticals.

Key Words: Differential pulse polarographic analysis, Carbinoxamine maleate, Pharmaceuticals.

INTRODUCTION

Carbinoxamine maleate, 2-[*p*-chloro-(α)-[2-dimethylamino)ethoxyl]benzyl] pyridine maleate (Fig. 1) is an antihistamine, treating allergy symptoms such as runny nose, watery/itchy eyes, rash, or hives. It works by blocking the action of histamine, which reduces the symptoms of an allergic reaction[1-5].

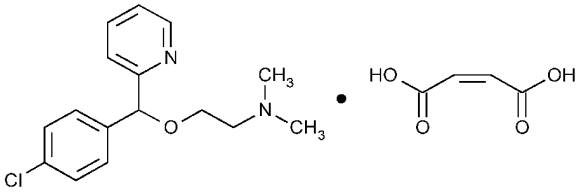

Fig. 1. Structural formula of carbinoxamine maleate

Few procedures were described for determination of carbinoxamine maleate like microemulsion electrokinetic chromatography and liquid chromatography[6,7], capillary electrophoresis[8,9], spectrophotometry in tablets containing caffeine sulphamethoxypyridazine and alginic acid[10] and by ternary complex formation with Cu(II) and eosin[11] and polarography[12,13].

The present work aims to offer simple, sensitive and selective polarographic methods for the determination of carbinoxamine maleate in both of pure form and its pharmaceutical preparations. The investigated methods can be applied to the analysis of carbinoxamine maleate in pharmaceutical industry. They are characterized by simplicity and less running costs with high accuracy and precision in comparison to the above-mentioned techniques.

EXPERIMENTAL

A Metrohm 746 VA processor was used, which includes a potentiostat with a measuring amplifier, broad banded and low noise with a piezoelectric keypad, in addition to a backlit LCD screen, which shows methods and routines. A Metrohm 747 VA stand with a multi-mode electrode (MME) comprising a dropping mercury electrode (DME), static mercury dropping electrode (SMDE) and hanging mercury dropping electrode (HMDE) as a working electrode, an auxiliary platinum electrode and a reference electrode (double junction type Ag/AgCl saturated with a 3.0 M KCl solution) completed the three-electrode cell. All measurements were done at room temperature 25 ± 2 °C, nitrogen gas was used for deoxygenation. pH-meter EUTECH model was used for the studying the pH effects.

Carbinoxamine maleate standard was supplied from Kongo Chemical Company, Japan. Standard solutions were prepared daily by accurate weighing of 100 mg of carbinoxamine maleate and dissolving it in 100 mL volumetric flask using double-distilled deionized water. The resulted concentration is 1 mg mL^{-1}. Supporting electrolyte phosphate buffer (pH 1.69) was prepared by dissolving 10.40 g of $NaH_2PO_4 \cdot 2H_2O$ in 1000 mL volumetric flask by double-distilled deionized water. Appropriate volume of H_3PO_4 (90 %) was added to give the desired pH. All solutions and reagents were prepared with double-distilled deionized water and analytical grade chemicals. Ultra pure mercury from metrohm company was used throughout the experiments.

Procedure: 20 mL of supporting electrolyte (phosphate buffer pH 1.69), 1 mL of carbinoxamine maleate standard solution 1 mg mL^{-1} were added by micropipette to the measurement cell. The solution was well mixed by automatic mixer and deoxygenated with pure nitrogen gas for 5 min. The polarograms of carbinoxamine maleate was recorded by using direct current polarography (DCP) and differential pulse polarography (DPP) in the potential range from -450 to -1300 mV, scan rate 12 mV/s, step time 0.5s. The number of experiments (n = 5) according to this value the statistical calculations were done.

RESULTS AND DISCUSSION

Direct current polarography (DCP)

Effect of the pH: Effect of the pH on diffusion current (i_d) and on half wave potential ($E_{1/2}$) of carbinoxamine maleate was studied on pH range 0.41-5.00. It was found that the optimum value of pH is 1.69 for best well defined direct current polarography polarograms (Fig. 2).

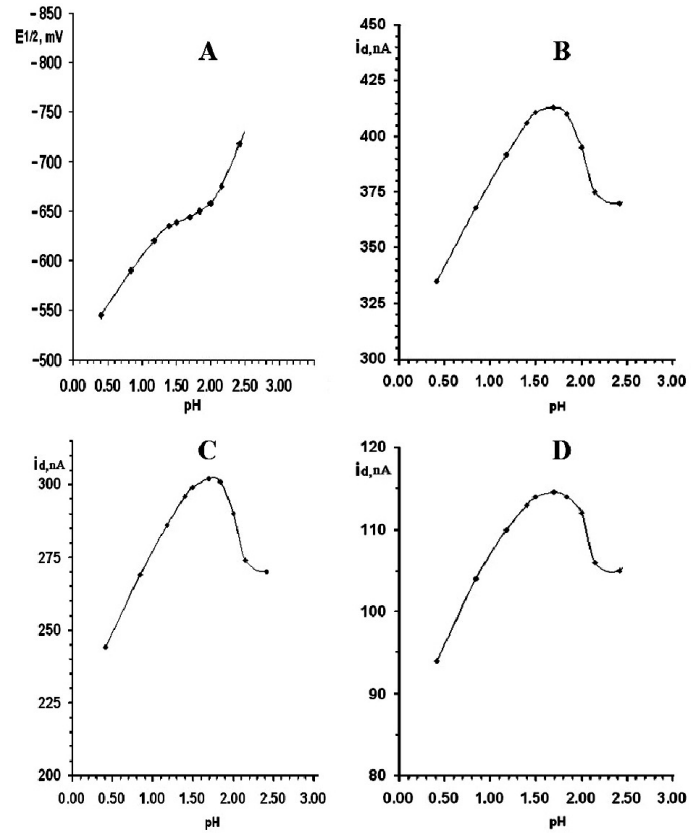

Fig. 2. Effect of pH on: (A) $E_{1/2}$ (using DME), (B) id (using DME), (C) id (using SMDE) and (D) id (using HMDE). For DCP reduction polarograms of carbinoxamine maleate 47.62 µg/mL

Effect of the electrodes DME, SMDE and HMDE: Direct current polarography polarograms were studied for standard solutions of carbinoxamine maleate on potential range from -450 to -1300 mV in phosphate buffer pH = 1.69 using DME, SMDE, HMDE electrodes. Well-defined electrochemical reduction wave for carbinoxamine maleate was noticed at the half wave potential $E_{1/2}$ range between -645 to -650 mV (Fig. 3). It was found that the diffusion factor on DME was greater than its values on SMDE and on HMDE: $K_{DME} = 1.37\ K_{SMDE} = 3.75\ K_{HMDE}$.

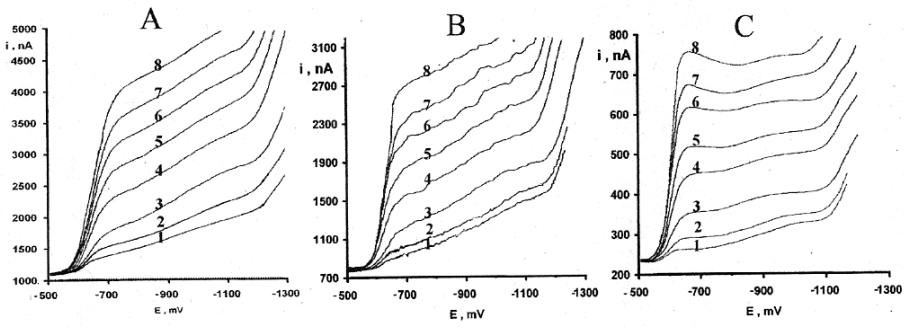

Fig. 3. DCP polarograms in phosphate buffer pH = 1.69 for concentrations of carbinoxamine maleate: (1) 12; (2) 24; (3) 48; (4) 96; (5) 132; (6) 165; (7) 200; (8) 238 μg/mL using DME (A), SMDE (B) and HMDE (C)

Calibration curves: Calibration curves for the determination of carbinoxamine maleate by DCP on DME, SMDE and HMDE electrodes were studied. The heights of current wave id were proportional to the concentrations of carbinoxamine maleate over the ranges 12.0-238.0 μg mL^{-1} (Fig. 4), with a relative standard deviations over the ranges 1.9-2.5, 3.6-4.1 and 2.0-2.3 % using DME, SMDE and HMDE, respectively (Table-1).

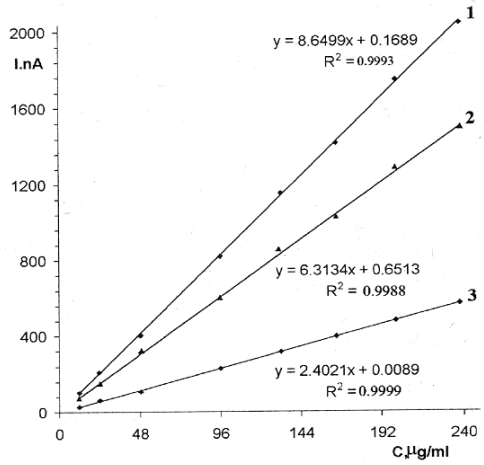

Fig. 4. Calibration curves for the determination of carbinoxamine maleate by DCP on DME (1), SMDE (2) and HMDE (3) electrodes

Differential pulse polarography (DPP)

Effect of the pH: Effect of pH on current peak (Ip) and potential peak (Ep) of carbinoxamine maleate was studied in the pH range 0.41-5.00. It was found that the optimum value of pH is 1.69 for best well defined DPP polarograms (Fig. 5).

TABLE-1
EVALUATION OF ACCURACY AND PRECISION OF THE PROPOSED METHODS FOR DETERMINATION OF CARBINOXAMINE MALEATE ON DME, SMDE AND HMDE BY DCP

Electrodes sorts	Taken conc. (mg/L)	Found conc. (mg/L)	Limits of confidence (mg/L)	RSD (%)
DME	12.0	11.9	11.9±0.37	2.5
	24.0	24.0	24.0±0.72	2.4
	48.0	48.1	48.1±1.37	2.3
	96.0	95.8	95.8±2.70	2.3
	132.0	132.0	132.0±3.60	2.2
	165.0	165.0	165.0±4.30	2.1
	200.0	200.3	200.3±5.00	2.0
	238.0	237.8	237.8±5.60	1.9
SMDE	12.0	11.8	11.8±0.610	4.1
	24.0	24.1	24.1±1.220	4.1
	48.0	48.5	48.5±2.40	4.0
	96.0	95.6	95.6±4.60	3.9
	132.0	130.7	130.7±6.20	3.8
	165.0	165.0	165.0±7.80	3.8
	200.0	200.1	200.1±9.20	3.7
	238.0	238.4	238.4±10.7	3.6
HMDE	12.0	11.9	11.9±0.35	2.3
	24.0	24.0	24.0±0.68	2.3
	48.0	48.1	48.1±1.24	2.2
	96.0	95.8	95.8±2.50	2.1
	132.0	132.0	132.0±3.50	2.1
	165.0	165.0	165.0±4.10	2.0
	200.0	200.3	200.3±5.20	2.1
	238.0	237.8	237.8±6.80	2.3

Effect of time step (t.Step): Effect of time step on Ip and Ep for the reduction of carbinoxamine maleate using DME was studied. Fig. 6 shows the DPP polarograms with many time steps. The Ip = f(t.step) was proportional to time steps over the range 0.2-0.5 s. Whereas the peak potential Ep didn't show any response by the changing of time step. Time step = 0.5 s was chosen as an optimum value.

Effect of pulse amplitude: Effect of pulse amplitude on DPP polarograms using DME for carbinoxamine maleate in phosphate buffer pH = 1.69 was studied. The peak current Ip increased proportional as a function to the increasing of pulse amplitude up to the value 50 mV. Therefore the value of pulse amplitude E = 50 mV was chosen as an optimum value Fig. 7.

Effect of the electrodes DME, SMDE and HMDE: DPP polarograms was studied for standard solutions of carbinoxamine maleate on the potential range from -550 to -750 mV in phosphate buffer pH = 1.69 by using DME, SMDE, HMDE electrodes. Well-defined electrochemical reduction wave for carbinoxamine maleate

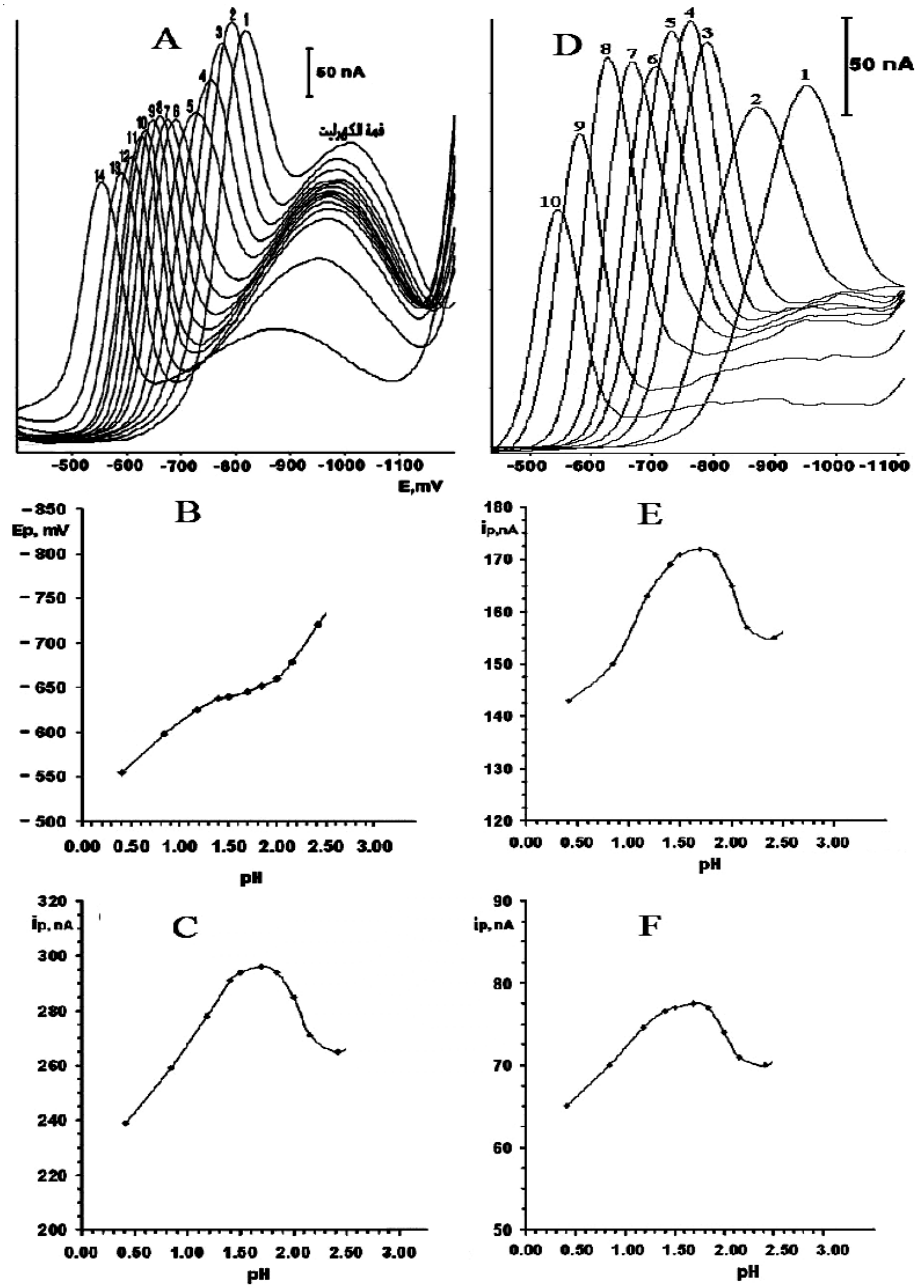

Fig. 5. Effect of pH on: (A) polarograms (1-14) represent pH = 3.33, 3.08, 2.85, 2.61, 2.42, 2.15, 2.00, 1.84, 1.69, 1.50, 1.40, 1.18, 0.84 and 0.41 (using DME), (B)$E_{1/2}$ (using DME), (C) Ip (using DME), (D) polarograms (1-10) represent pH = 3.74, 3.00, 2.75, 2.48, 2.22, 2.15, 1.94, 1.47, 0.94 and 0.45 (using SMDE), (E) Ip (using SMDE) and F- Ip (using HMDE) (for DPP of carbinoxamine maleate 47.62 µg/mL in phosphate buffer

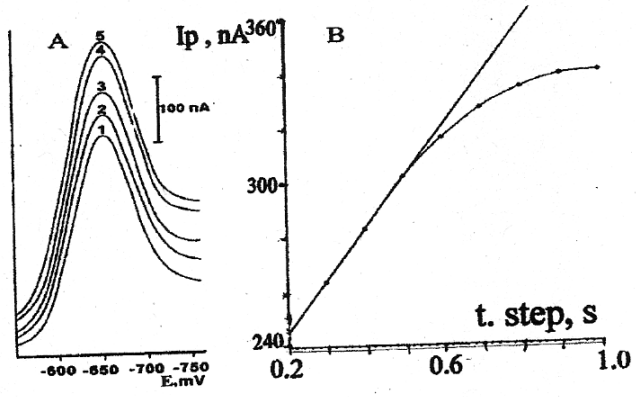

Fig. 6. Effect of time step for DPP of carbinoxamine maleate 47.62 µg/mL using DME on: (A) polarograms 1-5 represent t.step: 0.3, 0.4, 0.5, 0.6, 0.7 s respectively. (B) Ip

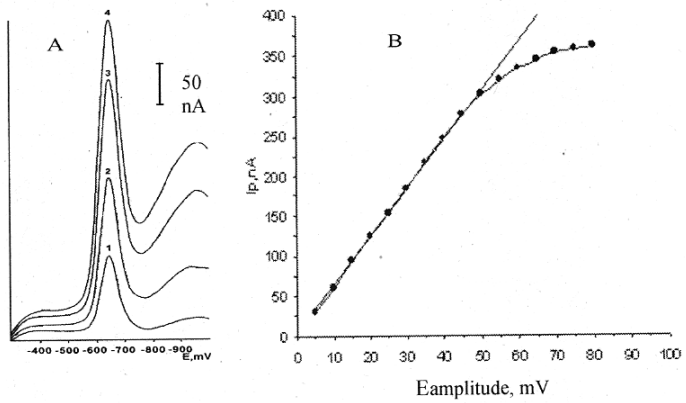

Fig. 7. Effect of pulse amplitude for DPP of carbinoxamine maleate 47.62 µg/mL using DME on: (A) Polarograms 1-4 represent pulse amplitude: 15, 25, 40, 50 mV, respectively, (B) Ip

was noticed at Ep range between -645 to -650 mV (Fig. 8). It was found that the diffusion factor on DME was greater than their values on SMDE and on HMDE: $K_{DME} = 1.72\ K_{SMDE} = 3.845\ K_{HMDE}$.

Calibration curves: Calibration curves for determination of carbinoxamine maleate by DPP on DME, SMDE and HMDE electrodes were studied. The heights of current peaks I_p was proportional to the concentration of carbinoxamine maleate over the range 0.95-476.2 µg mL^{-1} (Fig. 9), with a relative standard deviations over the ranges 4.3-1.3 and 9.2-1.4% for the concentrations from 0.95 µg mL^{-1} to 476.2 µg mL^{-1} using DME and SMDE, respectively and over the range 5.1-1.5 % for the concentration from 3.81-476.19 µg mL^{-1} using HMDE (Table-2).

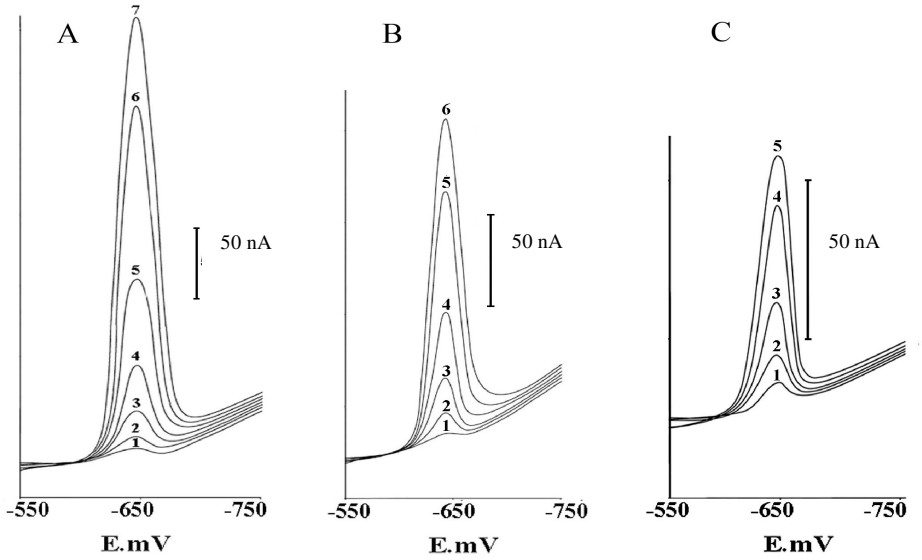

Fig. 8. DPP polarograms in phosphate buffer pH = 1.69 for different concentrations of carbinoxamine maleate: (A) 1: 0.95; 2: 1.90; 3: 4.76; 4: 9.52; 5: 19.05; 6: 38.10; 7: 47.62 µg/mL (using DME); (B) 1: 1.90; 2: 4.76; 3: 9.52; 4: 19.05; 5: 38.10; 6: 47.62 µg/mL (Using SMDE); (C) 1: 4.76; 2: 9.52; 3: 19.05; 4: 38.10; 5: 47.62 µg/mL (using HMDE)

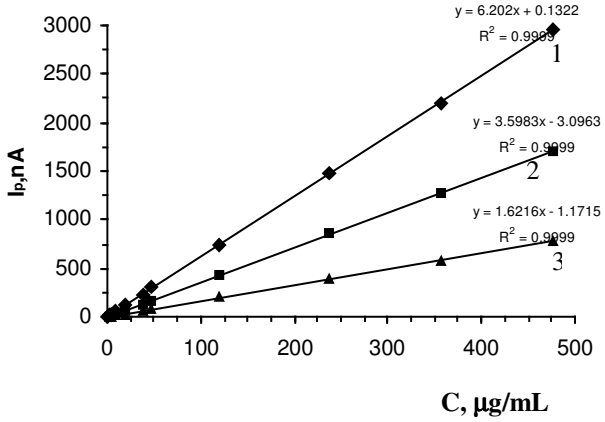

Fig. 9. Calibration curves for the determination of carbinoxamine maleate by DPP on DME (1), SMDE (2) and HMDE (3) electrodes

Applications: Many applications for the determination of carbinoxamine maleate in pharmaceutical preparations (tablets, capsules, syrup, oral drops) were proceeded by differential pulse polarography at pH = 1.69 phosphate buffer and dropping mercury electrode.

TABLE-2
EVALUATION OF ACCURACY AND PRECISION OF THE PROPOSED METHODS FOR DETERMINATION OF CARBINOXAMINE MALEATE ON DME, SMDE AND HMDE BY DPP

Electrode sorts	Taken conc. (mg/L)	Found conc. (mg/L)	Limits of confidence (mg/L)	RSD (%)
DME	0.95	0.960	0.96 ± 0.051	4.3
	1.90	1.910	1.91 ± 0.070	3.0
	3.81	3.810	3.81 ± 0.110	2.3
	4.76	4.730	4.73 ± 0.110	1.9
	9.52	9.510	9.51 ± 0.200	1.6
	19.05	19.10	19.1 ± 0.380	1.6
	38.10	37.90	37.9 ± 0.730	1.6
	47.62	47.90	47.9 ± 0.930	1.5
	119.04	119.10	119.1 ± 2.000	1.4
	238.09	239.00	239.0 ± 4.100	1.4
	357.14	356.50	356.5 ± 6.000	1.3
	476.19	477.90	477.9 ± 7.700	1.3
SMDE	0.95	0.87	0.87 ± 0.100	9.2
	1.90	1.89	1.89 ± 0.100	4.2
	3.81	3.82	3.82 ± 0.150	3.1
	4.76	4.74	4.74 ± 0.160	2.7
	9.52	9.52	9.52 ± 0.220	1.9
	19.05	19.10	19.1 ± 0.430	1.8
	38.10	37.80	37.8 ± 0.920	1.7
	47.62	47.50	47.5 ± 0.980	1.7
	119.04	120.20	120.2 ± 2.400	1.6
	238.09	238.20	238.2 ± 4.700	1.6
	357.14	355.80	355.8 ± 6.500	1.4
	476.19	477.40	477.4 ± 8.400	1.4
HMDE	0.95	-	-	-
	1.90	1.79	1.79 ± 0.080	9.5
	3.81	3.76	3.76 ± 0.240	5.1
	4.76	4.78	4.78 ± 0.220	3.8
	9.52	9.60	9.60 ± 0.290	2.4
	19.05	19.20	19.2 ± 0.550	2.3
	38.10	37.90	37.9 ± 1.000	2.2
	47.62	47.30	47.3 ± 1.200	2.1
	119.04	119.60	119.6 ± 2.900	1.9
	238.09	237.90	237.9 ± 5.000	1.7
	357.14	357.80	357.8 ± 7.180	1.6
	476.19	476.30	476.3 ± 8.800	1.5

Procedure: Twenty tablets or content of 30 capsules were weighed and well ground to a fine powder. The amount corresponding to the weight of 10 tablets or content of 20 capsules (which contain 40 mg of carbinoxamine maleate) were weighed and dissolved in 50 mL volumetric flask with double-distilled deionized water. The flask was sonicated for 15 min and filtered. 1 mL of the resulted solution was transferred to 25 mL volumetric flask and diluted to mark with phosphate buffer pH 1.69 (each 1 mL contains 32 mg of carbinoxamine maleate).

Direct transferring 1 mL of syrup or the oral drops to 25 mL volumetric flask and diluted to mark with phosphate buffer pH 1.69.

The sample solutions obtained above, were applied to the differential pulse polarography determination of carbinoxamine maleate. The results of quantitative analysis for carbinoxamine maleate were calculated by the standard addition methods (Table-3).

TABLE-3
RESULTS OF DPP DETERMINATION OF CARBINOXAMINE MALEATE IN SOME PHARMACEUTICAL FORMULATIONS

Commercial name	Contents	$\bar{x}$	RSD (%)	Recovery (%)
SEDO-GRIP Tablet (Future, Syria)	Carbinoxamine maleate (4 mg/tablet) and pseudoephedrine HCl (60 mg/tablet)	4.14 mg/tablet	1.7	103.5
RHINOMODE Capsule (MPI, Syria)	Carbinoxamine maleate (2 mg/capsule) and phenylephrine HCl (10 mg/capsule)	2.01 mg/capsule	1.9	100.5
SEDO-GRIP Syrup (Future, Syria)	Carbinoxamine maleate (4 mg/5 mL of syrup) and pseudoephedrine HCl (60 mg/ 5 mL of syrup)	4.16 mg/5 mL	1.7	104.0
FULAMINE Syrup (Future, Syria)	Carbinoxamine maleate (4 mg/5 mL of syrup), pseudoephedrine HCl (60 mg/5 mL of syrup) and dextromethrophan HBr (12.5 mg/5 mL of syrup)	4.09 mg/5 mL	1.6	102.2
CEMO Syrup (MPI, Syria)	Carbinoxamine maleate (2 mg/5 mL of syrup), ephedrine HCl (4 mg/5 mL of syrup) and ammonium chloride (100 mg/5 mL of syrup)	2.03 mg/5 mL	2.0	101.5
SEDO-GRIP Oral drops (Future, Syria)	Carbinoxamine maleate (2 mg/1 mL of oral drop) and pseudoephedrine HCl (25 mg/ 1 mL of oral drop)	2.03 mg/1 mL	1.5	101.5
FULAMINE Oral drops (Future, Syria)	Carbinoxamine maleate (2 mg/1 mL of oral drop), pseudoephedrine HCl (25 mg/1 mL of oral drop) and dextromethrophan HBr (3.5 mg/1 mL of oral drop)	2.06 mg/1 mL	1.6	103.0

Conclusion

The recent direct current polarography and differential pulse polarography methods were applied for the determination of carbinoxamine maleate over the ranges 12.0-238.0 μg mL^{-1} and 0.95-476.2 μg mL^{-1} with RSD of 2.5 and 4.3 % on DME, respectively.

Differential pulse polarography determination of carbinoxamine maleate in some pharmaceutical formulations (tablets, capsules, syrup and oral drops) was studied. The obtained results showed that the difference between the expected and the results found values by this method were less than 4 % in the worst case with the RSD is less than ± 2.0 %. Therefore, this polarographic method successfully applied for the determination of carbinoxamine maleate in pharmaceuticals.

ACKNOWLEDGEMENT

The authors would like to thank Prof. Abdul Wahab Allaf for technical assistance.

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(*Received*: 18 May 2009; *Accepted*: 24 August 2009) AJC-7779