

A Novel Coated Graphite Electrode for Potentiometric Determination of Pyrilamine Maleate in Pharmaceutical Compounds and Biological Fluids

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Abstract- A new pyrilamine coated graphite electrode (CGE) based on pyrilamine-tetraphenylborate ion-pair (Pyra-TPB) as electroactive material has been described. The sensor exhibited a linear response with a good Nernstian slope over a relatively wide range of concentration. The membrane film of the electrode made of 3% (w/w) ion-pair, 48.5% DBP (w/w) and 48.5% PVC (w/w). The sensor displays Nernstian response of 58.4 ± 0.4 mV/decade over the concentration range of 7.7×10^{-5} to 1.0×10^{-2} mol L⁻¹ with limit of detection of 5.3×10^{-5} mol L⁻¹. The coated wire electrode has short response time ~ 10 s and it can be used in pH range of 4.0–7.0. The selectivity coefficients were determined in relation to several inorganic and organic species. The proposed sensor displayed useful analytical characteristics for the determination of pyrilamine in pharmaceutical preparation and biological fluids such as plasma and urine samples.

Keywords: Pyrilamine maleate; Potentiometry; Coated graphite electrode; Biological fluids.

1 Introduction

The development of efficient ion-selective electrodes (ISEs) has always been a big challenge for the scientists as these sensors can be involved nowadays in many fields. Ion-selective electrodes (ISEs) have found wide spread use for the direct determination of ionic species [1-11]. They were also found to be effective in the analysis of pharmaceutical formulations for their attractive properties of simple design, ease of construction, reasonable selectivity, fast response time, applicability to colored and turbid solutions and possible interfacing with automated and computerized systems.

In conventional polymeric membrane ion-selective electrodes (ISEs), the sensing membrane is interposed between two aqueous phases, the sample and the inner solution. These electrodes, however, still have certain inherent limitations.

They are mechanically complicated, and thus difficult to fabricate in small size. In a solid-contact or “coated wire” ISE, the polymer membrane is directly cast on the solid surface, with no internal reference solution being interposed. An exciting advance was made in ISEs by Cattrall and Freiser [12] when they developed coated wire ISEs. CWEs may suffer from reproducibility and long-term stability (drifting potential) problems, resulting from the poorly defined contact and mechanism of charge transfer between the membrane coating and the conducting transducer. Coated electrodes in which an electroactive species is incorporated into a thin polymeric film coated directly on a metallic or graphite conductor has been shown to be very effective for a wide variety of inorganic and organic ions [13-18].

Electrodes of this sort has unique advantages including simplicity, low cost, durability, capability of reliable response in a wide concentration range for a wide variety of both organic and inorganic ions and suitable for measurements in small volumes of sample or for the desired in vivo applications of ISEs that biomedical researchers have long awaited.

Pyrilamine {1,2-Ethanediamine N-[(4-methoxyphenyl)methyl]-N¹, N¹-dimethyl-N-2-pyridinyl-(Z)-2 butenedioate (1:1) (or) 2-[(2-Dimethyl amino) ethyl] (p-methoxybenzyl) amino pyridine maleate (1:1)} (Fig. 1) is an antihistamine with a low incidence of side effects. It is effective for use in perennial and seasonal allergic rhinitis, vasomotor rhinitis, allergic conjunctivitis due to inherent allergens and foods, mild uncomplicated allergic skin manifestations of urticaria and angioedema, angioedema, demo graphism and aneceoratum of reactions of blood or plasma. It is an antagonizing agent that competes for receptor sites with natural histamine, a biogenic amine present in most body cells and tissues. It is a common ingredient of cold and menstrual symptoms [19]. It has been found to cause liver cancer in rats when administered in large amounts [20]. It has been linked to cardio toxicity, meaning prolonged use can lead to excessive stress on the heart [21].

Several methods have been reported for the determination of pyrilamine in pharmaceutical formulations and biological fluids: high performance liquid chromatography [22-24], gas chromatography with nitrogen-phosphorous [25], ultraviolet-visible [26-29], high performance liquid chromatography/thermospray mass spectrometry and tandem mass spectrometry [30], thermospray /mass spectrometry and tandem mass spectrometry [31], gas liquid chromatography [32], partition chromatographic method [33], column liquid chromatography [34] and high-pressure liquid chromatography [35].

This work describes construction and investigation of performance characteristics of novel ISEs based on coated wire electrodes for the determination of pyrilamine maleat in bulk powder, pharmaceutical formulations and biological fluids.

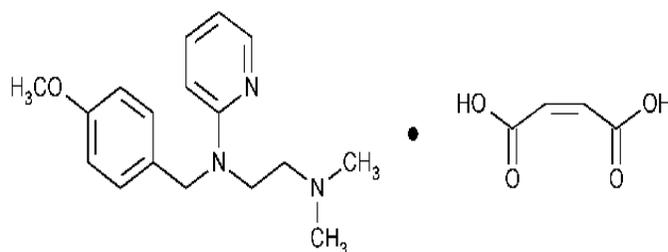


Fig. 1. Chemical structure of pyrilamine maleate.

2 Experimental

2.1 Reagents and materials

All chemicals were of analytical grade. Double distilled water was used throughout all experiments. Pure-grade pyrilamine maleate ($M_w = 401.46 \text{ g mol}^{-1}$) was supplied by Egyptian International Center for Import, Cairo, Egypt. Sodium tetraphenylborate (NaTPB), poly (vinyl chloride) of high molecular weight (PVC), tetrahydrofuran (THF) and dibutyl phthalate (DBP) were purchased from Merck (Germany). The metal salts were provided by BDH company (UK) as nitrates or chlorides. Stock solutions of the metal salts were prepared in bidistilled water and standardized when-ever necessary. In the analysis of biological fluids, human urine and plasma were used; plasma was obtained from Regional Blood Transfusion Services, Beni-Suef, Egypt.

2.2 Apparatus

Laboratory potential measurements were performed using 702 titroprocessor equipped with a 665 dosimat (Switzerland) made by Metrohm. Silver-silver chloride double-junction reference electrode (Metrohm 6.0222.100) in conjugation with different drug ion-selective electrode was used. A mLW W20 circulator thermostat was used to control the temperature of the test solutions.

2.3 Preparation of the ion-pair

The ion-pair compound, Pyra-TPB was prepared by slow addition of 100 mL of 1.0×10^{-2} mol L⁻¹ sodium tetraphenylborate solution to 100 mL of 1.0×10^{-2} mol L⁻¹ pyrilamine maleate under stirring for 15 min. The resulting precipitate was filtered off through a Whatman filter paper No. 42, washed with cold distilled water several times and dried at room temperature. The composition of the ion-pair was confirmed by elemental analysis to be 1:1 (Pyra:TPB).

2.4 Conductometric measurements

Conductometric titrations were followed with a Jenway conductivity meter. 50 mL of 1.0×10^{-2} mol L⁻¹ pyrilamine maleate solution was transferred to the 100 mL cell and the solution titrated against a 1.0×10^{-2} mol L⁻¹ NaTPB solution using a microburette. The conductance of the solution was measured after thorough stirring of each addition (2 min, intervals). Conductance values were corrected by multiplying by the dilution coefficient and plotted versus molar ratio. The titration plot showed a break which corresponds to the stoichiometry of the ion-pair.

2.5 Preparation of the coated wire sensors

CWEs were constructed using silver, copper and aluminum metal wires (1 mm diameter) and graphite rod (4 mm diameter) following the procedures described in details elsewhere [36]. The polished and cleaned electrodes were dipped in the coating solution and allowed to dry in air. The process was repeated several times till a layer of the proper thickness was formed covering the terminal of the rod. The prepared electrode was preconditioned by soaking for 30 min in 1.0×10^{-3} mol L⁻¹ pyrilamine maleate. When not in use, the electrode was stored in air.

2.6 Construction of calibration curves

The conditioned electrodes were immersed in conjunction with the double-junction Ag/AgCl reference electrode in solutions of pyrilamine maleate in the range of 1.0×10^{-6} – 1.0×10^{-2} mol L⁻¹. They were allowed to equilibrate whilst stirring and recording the e.m.f. readings within ± 1 mV. The mV-concentration profiles were plotted. The regression equations for the linear part of the curves were computed and used for subsequent determination of unknown concentrations of pyrilamine maleate.

2.7 Selectivity coefficient determination

The separate solution method and the matched potential method (MPM) [37-39] are employed to determine the selectivity coefficients, $\log K_{\text{Pyra}, J}^{\text{pot}, z^+}$, of the potentiometric sensor towards different species. In the separate solution method, the potential of a cell comprising a working electrode and a reference electrode is measured in two separate solutions, where E_1 is the potential measured in 1.0×10^{-3} mol L⁻¹ pyrilamine maleate, E_2 the potential measured in 1.0×10^{-3} mol L⁻¹ of the interfering compound, z_1 and z_2 are the charges of pyrilamine and interfering species, respectively and S is slope of the electrode calibration plot. The selectivity coefficients were determined by the separate solution method using the rearranged Nicolsky equation:

$$\log K_{\text{PyraJ}^{z+}}^{\text{pot}} = ((E_1 - E_2)/S) + (1 + (z_1/z_2)) \log a$$

In the matched potential method, the selectivity coefficient was determined by measuring the change in potential upon increasing the primary ion activity from an initial value of a_A to \hat{a}_A and a_B represents the activity of interfering ion added to the reference solution of primary ion of activity a_A which also brings the same potential change. It is given by expression:

$$K_{A,B}^{MPM} = (\hat{a}_A - a_A) / a_B$$

In the present studies a_A and \hat{a}_A were kept at 1.0×10^{-4} and 1.2×10^{-4} mol L⁻¹ pyrilamine maleate and a_B was experimentally determined.

2.8 Potentiometric determination of pyrilamine maleate

The standard addition method was applied [40], in which small increments of the standard solution 1.0×10^{-2} mol L⁻¹ of pyrilamine maleate were added to 50 mL aliquot samples of various concentrations from pure drug or pharmaceutical preparations. The change in millivolt reading was recorded for each increment and used to calculate the concentration of pyrilamine maleate sample solution using the following equation:

$$C_x = C_s V_s (V_x + V_s)^{-1} (10^{n(\Delta E/S)} - V_x (V_x + V_s)^{-1})$$

Where: C_x and V_x are the concentration and the volume of the unknown, respectively, C_s and V_s the concentration and the volume of the standard solution, respectively, S the slope of the calibration graph and ΔE is the change in mV due to the addition of the standard solution.

2.9 Potentiometric titration of pyrilamine maleate

An aliquots of 1.0×10^{-2} mol L⁻¹ drug solution (pure or caplet) were transferred into 50 mL volumetric flasks and made up to the mark with bidistilled water. Different concentrations of pyrilamine maleate were prepared, then titrated potentiometrically with a standard solution of 1.0×10^{-2} mol L⁻¹ NaTPB. The volume of the titrant at equivalence point was obtained using the conventional S-shaped curves. The differential graphs of the titration curves have also been constructed to obtain well defined and accurate end points using the computer program Origin lab.

2.10 Determination of pyrilamine maleate in pharmaceutical preparations

An accurate weight of pyrilamine caplets ground and finely powdered in a small Petri dish and dissolved in bidistilled water up to 30 mL by stirring for 1 h. The solution was filtrated in a 50 mL measuring flask. The residue was washed three times with bidistilled water; the volume was completed to the mark by water. The potentials of drug solutions were directly measured using CGE electrode.

2.11 Determination of pyrilamine maleate in biological fluids

Different amounts of pyrilamine maleate, and 5 mL of plasma or urine of a healthy person were transferred to 50 mL measuring flask and completed to the mark using bidistilled water. The contents of the measuring flask were transferred to a 100 mL beaker, and subjected to potentiometric determination of pyrilamine maleate by standard addition method.

Results and discussion

Pyrilaminium cation was found to form 1:1 water insoluble ion-pair with tetraphenylborate anion as indicated by elemental analysis [calculated %C=81.37, %H=7.11 and %N=6.95, and found %C=81.53, % H=7.12 and %N=7.05] and ascertained using conductometric titration (Fig. 2). The prepared ion-pair was identified and examined in CGE sensor responsive for Pyra cation.

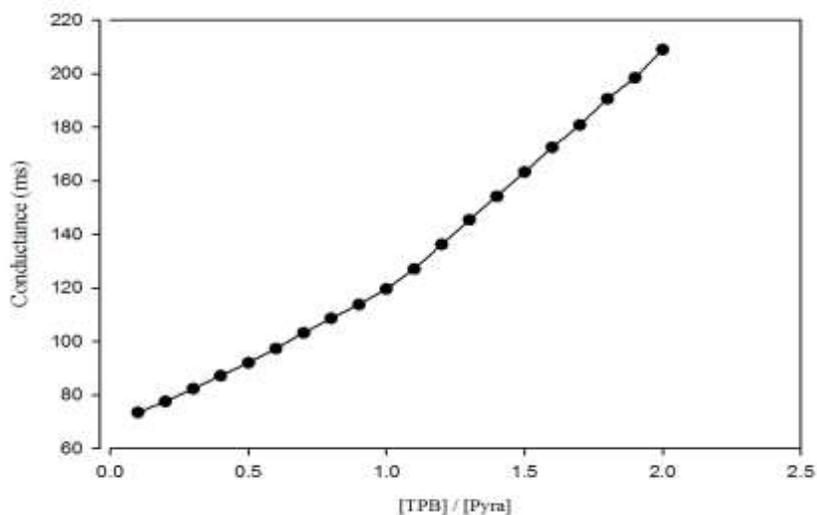


Fig. 2. Conductometric titration curve of $1.0 \times 10^{-2} \text{ mol L}^{-1}$ pyrilamine maleate against $1.0 \times 10^{-2} \text{ mol L}^{-1}$ of NaTPB.

3.1 Effect of sensor bed

To investigate the effect of the bed nature on the efficiency of coated wire electrodes, the optimized coating mixture was used in the preparation of electrodes with different conductive beds, namely silver, copper, graphite and aluminum. After conditioning, each electrode was examined in the concentration range 1.0×10^{-6} to $1.0 \times 10^{-2} \text{ mol L}^{-1}$ of pyrilamine solution. The dynamic range of concentration and the limit of detection for the electrodes were evaluated according to the IUPAC recommendations [41]. Examining the results compiled in Table 1, one can notice that all wires give inferior response towards pyrilamine as compared to that of graphite rod-coated electrode (CGE). Coated graphite electrode (Fig. 3) has a slope of $58.4 \pm 0.4 \text{ mV/decade}$ over the concentration range of 7.7×10^{-5} - $1.0 \times 10^{-2} \text{ mol L}^{-1}$ and a detection limit of $5.3 \times 10^{-5} \text{ mol L}^{-1}$. This is attributed to high conductivity of graphite rod. Therefore, graphite rod was used as the inner solid contact for the electrodes in this study.

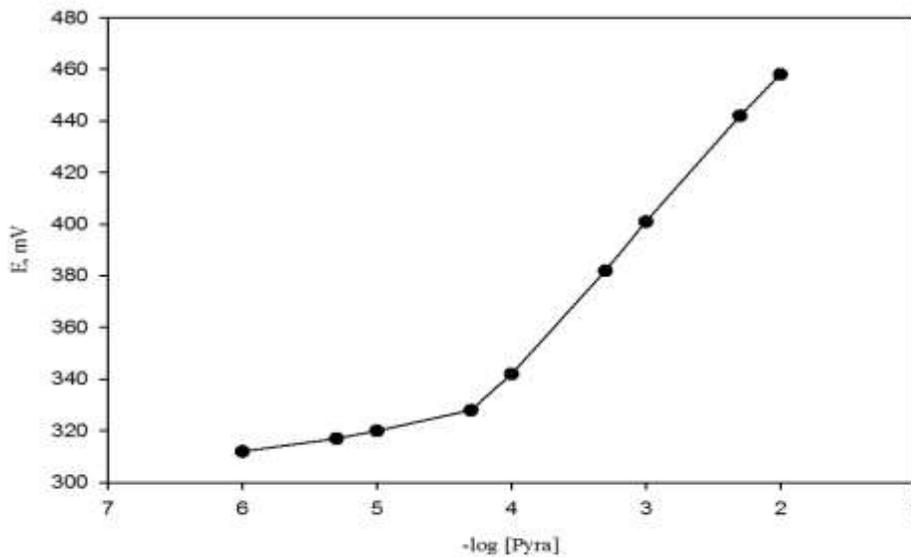


Fig. 3. Calibration curve of CGE electrode

Table 1. Optimization of membrane compositions and their potentiometric response for coated wire pyrilamine selective electrodes

Composition of membrane% (w/w; mg)				Slope mV/de cade	Linear concentration range (mol L^{-1})	LOD (mol L^{-1})	LOQ (mol L^{-1})	RSD %
Pyra-TPB	PVC	DBP	Electrode bed					
3	48.5	48.5	Graphite	58.4	$7.7 \times 10^{-5} - 1.0 \times 10^{-2}$	5.3×10^{-5}	1.8×10^{-4}	0.49
3	48.5	48.5	Silver	57.5	$4.5 \times 10^{-5} - 1.0 \times 10^{-2}$	2.0×10^{-5}	6.7×10^{-5}	0.61
3	48.5	48.5	Copper	56.0	$9.8 \times 10^{-5} - 1.0 \times 10^{-3}$	6.0×10^{-5}	2.0×10^{-4}	0.63
3	48.5	48.5	Aluminium	42.5	$9.6 \times 10^{-5} - 1.0 \times 10^{-3}$	1.1×10^{-5}	3.7×10^{-5}	0.84

LOD: limit of detection.

LOQ: limit of quantitation.

RSD: relative standard deviation (four determinations).

3.2 Life time

The life time of the electrode was determined by soaking the electrode (CGE) in $1.0 \times 10^{-3} \text{ mol L}^{-1}$ pyrilamine maleate solution for different intervals till the electrode lost the Nernstian behaviour. This behavior can be attributed to the decomposition of the ion-pair and loss of other components in the membrane phase that were in contact with aqueous test solution containing pyrilamine cation. The response of the electrode has been measured by recording the calibration graph at 25°C at different intervals. The results showed that the life time measured in this way was found to be 8 days. It was established that continuous soaking had a negative impact on the response of the sensor due, probably, to the leaching of the active ingredients (ion-exchanger and plasticizer) to the bathing solution [42]. The life span of the coated wire electrodes, in general, are less than those of the corresponding liquid contact electrodes. This may be attributed to the poor mechanical adhesion of the PVC-based sensitive layer to the conductive bed [43].

3.3 Response time, reversibility and reproducibility

Dynamic response time is an important factor, for the evaluation of any sensor. To measure the dynamic response time of the proposed electrode, the concentration of the test solution was successively changed from 1.0×10^{-5} to $1.0 \times 10^{-2} \text{ mol L}^{-1}$. The resulting data show that the time needed to reach a constant potential within $\pm 1 \text{ mV}$ of the final equilibrium value after successive immersion of a series of pyrilamine maleate solution, each having a 10-fold difference in concentration is 10 s for CGE electrode as shown in Fig. 4. To evaluate the reversibility of the electrode, the practical potential response of the electrode was recorded by changing solutions with different pyrilamine maleate concentrations from 1.0×10^{-2} to $1.0 \times 10^{-5} \text{ mol L}^{-1}$. The measurements were performed from the highest concentration to the lowest. The potentiometric response of the electrode was reversible and had no memory effect (Fig. 4).

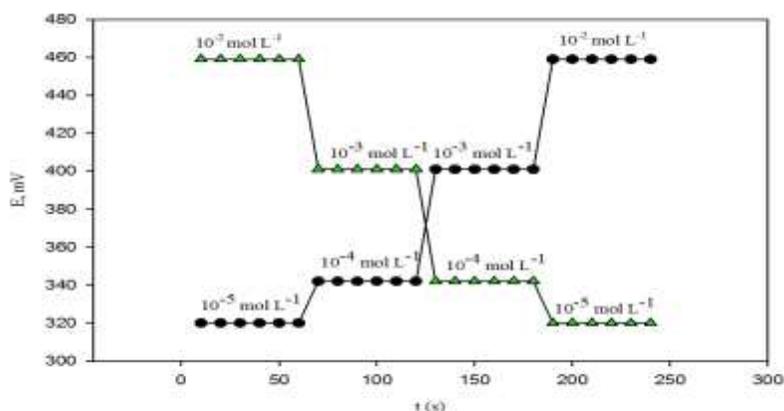


Fig. 4. Potential-time plot for the response of CGE sensor.

3.4 The effect of pH on the response of the electrode

Since pK_a of pyrilamine is 8.9, therefore at $\text{pH } 7.9$ pyrilamine is nearly completely ionized, i.e. pyrilamine will be in the cationic form. The concentration distribution diagram for pyrilamine maleate species is constructed using SPECIES program [44] (Fig. 5).

The influence of pH on the response of the CGE was examined for the 1.0×10^{-3} and $1.0 \times 10^{-4} \text{ mol L}^{-1}$ pyrilamine solutions. The pH was adjusted by adding small volumes of $(0.1-1.0) \text{ mol L}^{-1}$ HCl or NaOH to the test solutions and the variation in potential was

followed. It can be seen from Fig. 6 that the variation in potential due to pH change is considered acceptable in the pH range 4.0–7.0. However, there is an observed drift at pH values lower than 4.0 which may be due to H^+ interference. On the other hand, the potential decreases gradually at pH values higher than 7.0. The decrease may be attributed to the formation of the free drug base in the test solution.

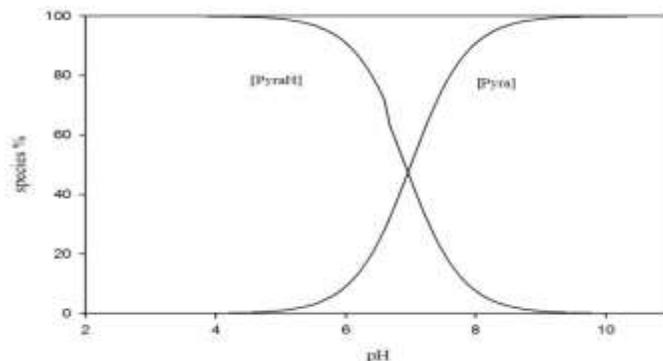


Fig. 5. Representative concentration distribution diagram for pyrilamine maleate species.

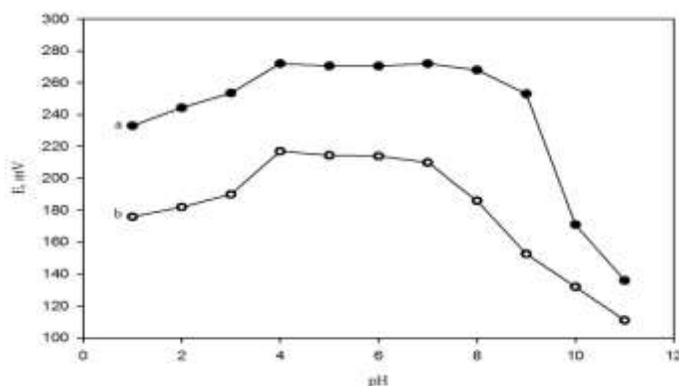


Fig. 6. Effect of pH of the test solutions on the potential response of CGE electrode: (a) 1.0×10^{-3} , (b) 1.0×10^{-4} mol L⁻¹ Pyra solution.

3.5 Selectivity of the electrode

The influence of some inorganic cations, sugars and amino acids on the pyrilamine electrode was investigated graphically by plotting the potential response of the electrode for different interferents against their varying concentration. As shown from the calibration curves (Fig. 7), except for pyrilamine cation there is no significant response of the electrode for all interferents tested. The selectivity coefficients (Table 2) were determined by the separate solution and matched potential methods. The results reflect a very high selectivity of the investigated electrode for the pyrilamine cation. The inorganic cations do not interfere owing to the differences in ionic size and consequently their mobilities and permeabilities as compared with pyrilaminium ion. The selectivity sequence significantly differs from the so called Hofmeister selectivity sequence [45] (i.e. selectivity solely based on lipophilicity of cation). In case of non-ionic species, the high selectivity is mainly attributed to the difference in polarity and to the lipophilic nature of their molecules relative to pyrilaminium ion. The mechanism of selectivity is mainly based on the stereospecificity and electrostatic environment, and is dependent on how much matching is present between the location of the lipophilic sites in the two competing

species in the bathing solution side and those present in the receptor of the ion-exchanger [46]. In the case of sugars and amino acids, the high selectivity is mainly attributed to the difference in polarity and lipophilic character of their molecules relative to pyrilamine maleate.

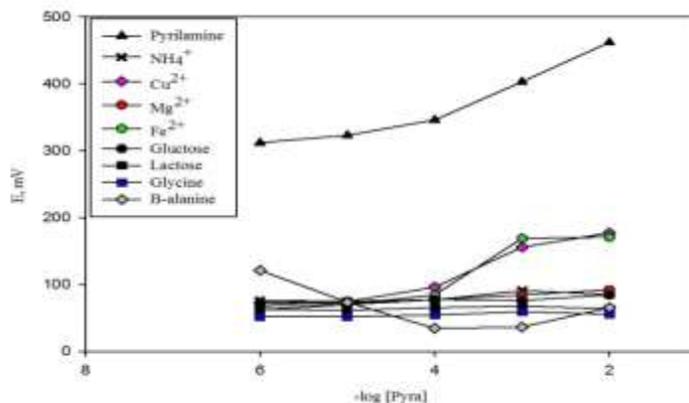


Fig. 7. Calibration graphs of some inorganic cations, sugars and amino acids using CGE electrode.

Table 2. Selectivity coefficient values of the CGE electrode.

Interferent	$K_{P \text{ in } J}^{\text{pot}}$	
	SSM	MPM
K^+	8.5×10^{-3}	----
NH_4^+	8.8×10^{-4}	----
Li^+	9.6×10^{-3}	----
Fe^{2+}	5.7×10^{-4}	----
Ca^{2+}	1.5×10^{-6}	----
Mg^{2+}	6.7×10^{-4}	----
Mn^{2+}	8.9×10^{-7}	----
Cu^{2+}	2.9×10^{-3}	----
Co^{2+}	4.3×10^{-4}	----
Vitamine C	----	----
Glucose	----	8.2×10^{-3}
Fructose	----	1.1×10^{-2}
Lactose	----	1.4×10^{-3}
Maltose	----	8.6×10^{-3}
Urea	----	7.5×10^{-3}
Glycine	----	8.6×10^{-3}
β -alanine	----	7.8×10^{-3}

3.6 Analytical applications

The proposed electrode was found to work well under laboratory conditions. It can be seen that the amount of pyrilamine can be accurately determined using the proposed electrode. To assess the applicability of the proposed electrode, pyrilamine maleate was determined in pure solution, pharmaceutical preparations, spiked urine and plasma samples, by applying the standard addition method. The obtained average recovery and relative standard deviation values are summarized in Tables 3 and 4, which reflect the high accuracy and precision of the electrode. The optimized pyrilamine maleate selective electrode was successfully applied as indicator

electrode in the potentiometric titration of pyrilamine maleate solution with NaTPB solution (Table 3). The well-defined potential jumps of the titration curves (Fig. 8) correspond to formation of a Pyra-TPB ion-pair of 1:1 stoichiometry indicating the high sensitivity of the electrode. Obviously, the two methods, standard addition and potentiometric titration, can be applied to the determination of pyrilamine maleate in bulk powder and in pharmaceutical formulations or in biological fluids without interference by the excipients expected to be present in tablets or the constituents of body fluids.

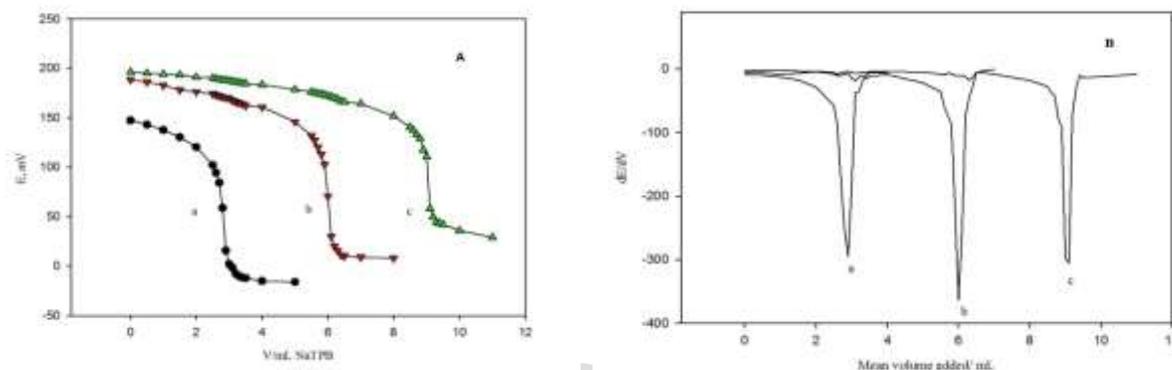


Fig. 8. Potentiometric titration curves (A) and its first derivative (B) of (a) 3, (b) 6 and (c) 9 mL of $1.0 \times 10^{-2} \text{ mol L}^{-1}$ pyrilamine maleate using CGE electrode and $1.0 \times 10^{-2} \text{ mol L}^{-1}$ NaTPB as titrant.

3.7 Statistical analysis and validity of the proposed method

The linearity, limit of detection, precision, accuracy, and ruggedness/robustness were the parameters which were used for the method validation. As mentioned before, the measuring range of the pyrilamine electrode is between 7.7×10^{-5} and $1.0 \times 10^{-2} \text{ mol L}^{-1}$ pyrilamine maleate.

3.7.1. Ruggedness

For ruggedness of the method, a comparison was performed between the intra- and inter-day assay results for pyrilamine obtained by two M. Sc. students. The RSD values for the intra- and inter-day assays of pyrilamine in the cited formulations performed in the same laboratory by the two analysts did not exceed 1.42% which indicates that the method is capable of producing results with high precision.

3.7.2. Robustness

The robustness was examined while the parameter values (pH of the medium and the laboratory temperature) were being deliberately slightly changed. Pylamine recovery percentages were good under most conditions, not showing any significant change when the critical parameters were modified.

The results obtained from the standard addition method of the drug were compared with those obtained from the potentiometric titration method by applying F- and t-tests [47]. The results (Table 3) show that the calculated F- and t-values did not exceed the theoretical values, reflecting the accuracy and precision of the applied method.

4. Conclusion

The proposed pyrilamine coated wire electrode based on Pyra-TPB as electroactive material might be a useful analytical tool and interesting alternative for the determination of pyrilamine ions in pure, pharmaceutical formulations and biological fluids. The sensor shows favorable performance characteristics with short response times (~ 10 s), low limit of detection $5.3 \times 10^{-5} \text{ mol L}^{-1}$ over the concentration range from 7.7×10^{-5} to $1.0 \times 10^{-2} \text{ mol L}^{-1}$.

This study was compared with the other reported methods. The results of this study showed wider linear range, 7.7×10^{-5} - $1.0 \times 10^{-2} \text{ mol L}^{-1}$ than the other methods. It is characterized by reasonable selectivity, low cost and fast response. The data are given in Table 5, thus proving that it is a good pyrilamine-ion selective electrode for the pure, pharmaceutical preparations and biological fluids with high accuracy and precision.

Table 3. Determination of pyrilamine maleate in pure solutions and pharmaceutical preparations applying the standard addition and the potentiometric titration methods.

Sample	Standard addition			Potentiometric titration		
	Taken (mg)	Recovery (%)	RSD (%)	Taken (mg)	Recovery (%)	RSD (%)
Pure solution	1.00	101.61	0.96	12.04	98.44	1.37
	1.61	101.01	0.97	24.09	99.22	0.68
	2.01	99.29	1.42	36.13	100.00	1.00
	4.02	98.65	0.35			
Mean ± SD		100.14±1.39			99.22±0.79	
F-ratio		3.09 (19.20) [a]				
t-ratio		1.01 (2.571) [b]				
Midol [®] complete	1.00	97.58	0.77	12.04	99.22	0.01
	1.61	99.55	0.78	24.09	99.44	0.97
	2.01	100.41	0.95	36.13	100.74	0.64
	4.02	99.83	0.69			
Mean ± SD		99.34±1.24			99.80±0.82	
F-ratio		1.01 (9.55) [a]				
t-ratio		0.56 (2.571) [b]				

SD: standard deviation.

F-ratio: Tabulated F-value at 95% confidence level.

t-ratio: Tabulated t-value at 95% confidence level and five degrees of freedom.

Table 4. Determination of pyrilamine maleate in spiked plasma and urine samples applying the standard addition method.

Electrode	Taken (mg)	Spiked plasma		Spiked urine	
		Recovery (%)	RSD (%)	Recovery (%)	RSD (%)
CGE	1.00	101.29	1.43	97.49	0.55
	1.61	97.70	1.23	99.87	0.41
	2.01	100.69	1.24	100.41	0.95
	4.02	100.00	1.83	99.00	1.09

Table 5. Comparison between the suggested and some of the other published methods for determination of pyrilamine maleate.

Reagent/method	Linear range mol L ⁻¹	LOD mol L ⁻¹	r ²	RSD %	Ref
Column liquid chromatography	$3.5 \times 10^{-4} - 2.5 \times 10^{-6}$	2.5×10^{-7}	0.9990	173.7	[34]
Uv-visible spectrometry	$2.5 \times 10^{-3} - 6.9 \times 10^{-3}$	7.0×10^{-6}	0.9999	1.626	[26]
High performance liquid chromatography	$1.5 \times 10^{-3} - 1.3 \times 10^{-4}$	7.5×10^{-6}	0.9990	1.45	[23]
CGE	$7.7 \times 10^{-3} - 1.0 \times 10^{-2}$	5.3×10^{-3}	0.9999	0.49	[P.S]

Ion Selective Electrode

r²: Correlation coefficient.

P.S: Present study.

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