COMPARATIVE ELECTROCHEMICAL STUDY OF SOME PHENOTHIAZINES WITH CARBON PASTE, SOLID CARBON PASTE AND GLASS-LIKE CARBON ELECTRODES

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Received November 18, 1999
Accepted April 28, 2000

Presented at International Conference on Modern Electroanalytical Methods, Seč, September 19–23, 1999.

In order to obtain modified electrodes with phenothiazines and to develop electrochemical methods for their determination in pharmaceutical formulations, promazine maleate, promethazine maleate and levomepromazine, were studied by linear sweep voltammetry using different types of working electrodes: carbon paste, solid carbon paste and glass-like carbon electrodes. A comparative electrochemical study of the above mentioned phenothiazines was performed in aqueous-alcoholic solutions, investigating the influence of pH, ionic strength and concentration on the current–potential curves. Linear sweep voltammetry in potential range from –0.1 to +1.3 V revealed that the oxidation potential and the current, strongly depend on the type of electrode and pH, the best results being obtained in acid buffer (pH 1.0). The current intensity depending linearly on the concentration in the range of $2.5\cdot10^{-5}$–$5\cdot10^{-4}$ M promazine maleate, $2.5\cdot10^{-5}$–$2.5\cdot10^{-4}$ M promethazine maleate and $6.2\cdot10^{-5}$–$1.2\cdot10^{-3}$ M levomepromazine permits the development of electroanalytical methods to determine these phenothiazines in pharmaceuticals. The electrochemical determination yielded results comparable with spectrophotometric methods. Linear sweep voltammetry of carbon paste electrodes modified by incorporation of phenothiazines opens the possibility to use them as mediators in the design of some enzyme selective electrodes.

Key words: Phenothiazines; Linear sweep voltammetry; Promazine maleate; Promethazine maleate; Levomepromazine; Electrochemical determination; Neuroleptics; Antihistaminics.

Phenothiazines were introduced in modern pharmacotherapy with the discovery of their psychotropic properties (neuroleptic and/or antidepressant), and the examination of their pharmacological profile found many other effects such as antihistaminic, antiparkinsonian, anticholinergic, anti-inflammatory, antibacterial and antimycotic[1].

An important physico-chemical property of phenothiazines is their redox behavior. The oxidized species can be generated either in oxidative or reductive way, the electron transfer being realized by chemical, photochemical, electrochemical or biochemical processes, which were the subject of a great number of papers. In most electrochemical investigations using controlled potential electrolysis[2], cyclic voltammetry[1] and voltamperometry in acetonitrile, were performed at different pH values[3,4,18].

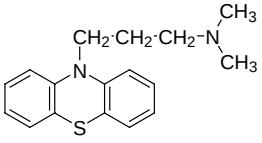
Studying the kinetics and mechanism of oxidation of some phenothiazines, Gasco and Carlotti[5] established some relations among their structure, pharmacodynamic action and redox features. Thus, phenothiazines with three carbon atoms in the side chain, increase the oxidation rate of biogenic amines (noradrenaline, dopamine, 5-hydroxytryptamine), catalyzed by ceruloplasmine, whereas imipramine inhibits this oxidation. Phenothiazines with two carbon atoms in the side chain show no effect[6]. Løvsted[7] related this behavior to the formation of cation radicals, favored by ceruloplasmine and to further oxidation by means of cation radicals. The study of free radical formation from some phenothiazines, dimetacrine and imipramine by oxidation with Ce(IV) suggested that different reactions of neuroleptic phenothiazines, antihistaminics and antidepressants with biogenic amines in the presence of ceruloplasmine could be related to different reduction potentials. The relationship between stable cation radical formation and psychotropic activity of phenothiazines is well documented, the unusual behavior of quisultidine without antihistaminic and anticholinergic activity being related to the difficulty in oxidation and the reactivity of the resulting radical[19].

The results obtained by P. W. Crawford *et al.*[8] from cyclic voltammetric study of eight phenazines and phenazine-*N*-oxides and eleven quinoxalines and quinoxaline-*N*-oxides revealed some relationships between their reduction potential and reported antimicrobial activity.

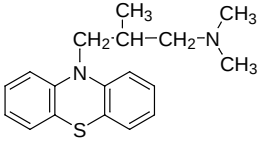
The electrochemical behavior of various phenothiazines was studied in different solvents as acetonitrile[18], methanol[20] or water using different working electrodes, like platinum[18–20], gold[20] and carbon paste[21].

In a recent paper[9] an electrode with immobilized horseradish peroxidase was used for amperometric determination of phenothiazine in drug formulations. In fact, a great number of papers dealing with biosensors, enzyme or NADH-modified electrodes[10–15] mention the use of phenothiazine derivatives (Meldola Blue or Toluidine Blue O) as mediators, due to their redox properties.

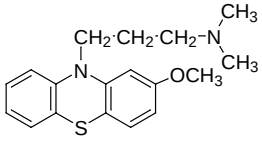
The above mentioned reasons initiated the linear sweep voltammetric study of three phenothiazines currently used in therapy, promazine maleate, promethazine maleate and levomepromazine.



promazine
(neuroleptic)



promethazine
(antihistaminic)



levomepromazine
(neuroleptic)

Furthermore, we developed electrochemical methods for quantitative determination of phenothiazines in drug formulations and body fluids and eventually, their incorporation in modified carbon paste electrodes.

EXPERIMENTAL

Apparatus

A Bruker E 100 potentiostat and XY Hewlett–Packard 7035 B recorder were used for linear sweep voltammetric studies performed in a polarographic cell, containing working electrodes – carbon paste electrode (CPE), solid carbon paste electrode (SCPE) or glass-like carbon electrode (GCE), Ag/AgCl as a reference and a platinum wire as an auxiliary electrode.

Sample volumes were measured with 10, 100 and 500 μl Hamilton syringes and with adjustable digital pipettes (Biohyt - OY, Finland).

The pH of solutions was determined with a Chemcadet 5986-62 pH-meter (Cole Palmer) using a combined glass electrode. All experiments were carried out at room temperature (22 ± 1 °C).

Reagents

Promazine maleate and promethazine maleate, both from Sicomed S.A. (Bucharest, Romania) and levomepromazine from Terapia S.A. (Cluj-Napoca, Romania) were of pharmaceutical grade (Romanian Pharmacopoeia 10th ed.).

All other chemicals were of analytical grade (Merck or Reactivul S.A. Bucharest) and were used as received, without further purification.

Stock solution of 10^{-2} M promazine maleate and 10^{-2} M promethazine maleate were prepared daily in 1 : 1 (v/v) mixture of ethanol and double distilled water. A $5 \cdot 10^{-3}$ M levomepromazine solution was prepared in the same way in ethanol. All stock solutions were kept in the dark to avoid oxidation.

Three 0.1 M buffer solutions were used. The pH 1.0 solution contained 0.1 M HCl, the pH 6.0 buffer contained a mixture of 2.25% disodium hydrogenphosphate and 0.77% citric acid and the pH 9.0 buffer 11 ml of 0.1 M NaOH and 89 ml of 0.1 M glycine.

Commercial drug formulations Romergan, vials (50 mg/2 ml), were from Sicomed S.A. (Bucharest, Romania), Romergan, coated tablets (30 mg) and Levomepromazin, tablets (25 mg) and vials (25 mg/1 ml) were from Terapia S.A. (Cluj-Napoca, Romania).

Electrode Preparation

Carbon paste (CP) was prepared by mixing thoroughly in a mortar liquid paraffin and graphite (1 : 2).

The solid carbon paste (SCP) was prepared by thoroughly mixing in a mortar with a pestle, solid paraffin and graphite particles (1 : 2 ratio). The paste homogenization was realized after the melting of solid paraffin, maintaining the mortar at 46–48 °C.

The modified carbon pastes were prepared as follows: graphite (63%) and phenothiazine (5%) were mixed and homogenized with a glas spatula using 50 µl of diethylether. After the evaporation of ether, liquid paraffin and 50 µl of ether were added, thoroughly mixed and stored at room temperature for 24 h. The pastes were stored in a cold, dark place when not in use.

The carbon paste, solid carbon paste and the phenothiazine modified carbon pastes (MCPE) working electrodes were prepared by packing the pastes into the Teflon body of the electrode (1 mm i.d.). Before measurements, the electrode was smoothed on a clean paper card.

Linear Sweep Voltammetry (LSV)

Linear sweep voltammetric measurements were performed in three different buffer solutions at pH 1.0, 6.0 and 9.0 using a conventional three-electrode cell comprising the working electrode (carbon paste, solid carbon paste or glass-like carbon with an active area of 1 mm in diameter), an Ag/AgCl (3 M NaCl) reference electrode and platinum wire as an auxiliary electrode.

A potential range from –0.1 to +1.1 or +1.3 V, at 50 mV s^{-1} scan rate and 500 nA V^{-1} or 1 µA V^{-1} sensitivities were used. The pH study and the electrode type influence as well as calibration curves were made in the concentration range $2.5\cdot10^{-5}$–$5\cdot10^{-4}$ M promazine maleate in a 50% aqueous-alcoholic solution, $2.5\cdot10^{-5}$–$2.5\cdot10^{-4}$ M promethazine maleate solution in the same solvent and $6.2\cdot10^{-5}$–$1.2\cdot10^{-3}$ M levomepromazine solution in absolute ethanol. The solutions were stirred with a magnetic bar at approximately 300 rpm before each measurement and replicates. The measurement was performed by adding increasing volumes of phenothiazine stock solutions.

The modified carbon paste with phenothiazines were studied by recording three successive runs with the freshly smoothed electrode surface.

Drug Formulation Treatment

Twenty tablets were weighed and powdered. The needed quantity of powder to obtain 10^{-2} M phenothiazine solution was weighed in calibrated 25 ml flask, shaked with aqueous-alcoholic 1 : 1 mixture for 30 min and then filled up to the mark with the same solvent. In the case of levomepromazine, the solvent was absolute ethanol. Before use the suspensions were filtered using a dry quantitative filter paper. The required vial amount to obtain 10^{-2} M solution was diluted to 25 ml in calibrated flask with the above mentioned solvents. All calibrated flasks were covered by aluminium foil during experiments.

RESULTS AND DISCUSSION

Influence of pH

Carbon Paste Electrodes

In the pH 1.0 buffer, $1.25 \cdot 10^{-4}$ M promazine maleate shows two well defined oxidation peaks at +0.55 ± 0.02 and +1.12 ± 0.02 V, respectively (Fig. 1a), due to the phenothiazine oxidation with S-oxide formation. The increase of the pH value shifts the oxidation peaks and increases the corresponding current. Thus, at pH 6.0 (Fig. 1d) the first peak appears at +0.56 ± 0.01 V and the current increases, due to one-electron oxidation, which corresponds to the formation of a coloured monocation radical. The second

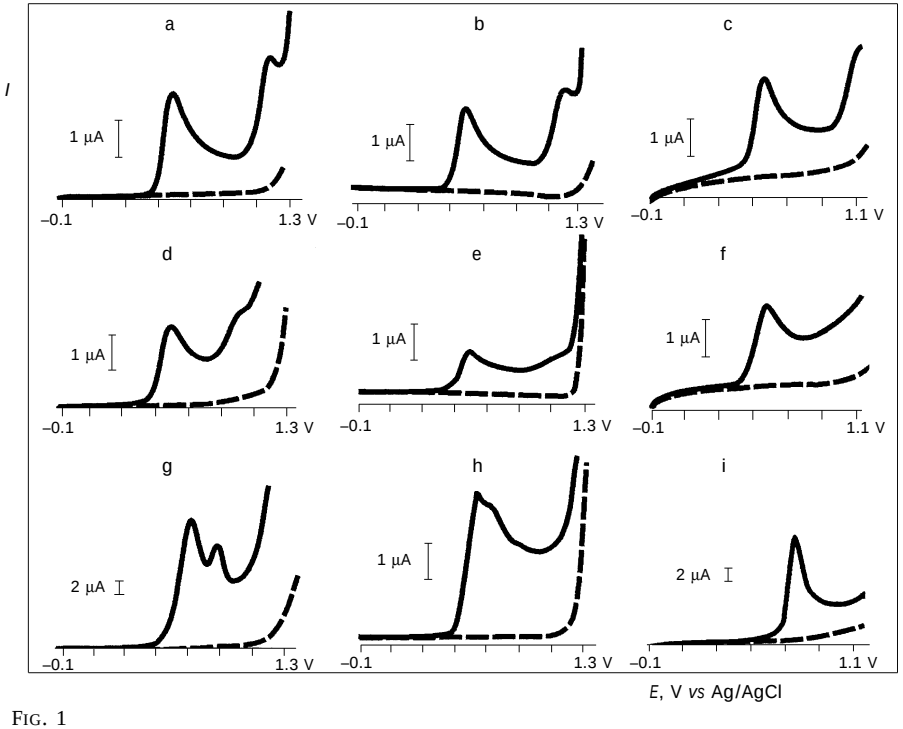


FIG. 1

Linear sweep voltammograms of $1.25 \cdot 10^{-4}$ M (d, f–i) and $2.5 \cdot 10^{-4}$ M (a–c, e) promazine maleate in aqueous-alcoholic solution (1 : 1) at three pH values: 1.0 (a, b, c), 6.0 (d, e, f) and 9.0 (g, h, i) using carbon paste (a, d, g), solid carbon paste (b, e, h) and glass-like carbon electrodes at 50 mV s^{-1} scan rate (- - - - baseline). Horizontal axes represent potentials *vs* Ag/AgCl reference and vertical axes currents

peak appears between +0.95 and +1.0 V as a shoulder and it was attributed to the formation of dication diradical or sulfoxide in acidic media as a result of second one-electron oxidation step. This behavior is much more pronounced in alkaline medium (pH 9.0), where the two peaks are well defined, and overlapping, the first at +0.65 ± 0.01 V and the second at +0.84 ± 0.01 V (Fig. 1g), probably due to the irreversible hydrolysis of sulfoxide, which is oxidized to a sulfoxide diradical[18,20–22]. The peak current is ten times higher than at pH 1.0 and 6.0, but the reproducibility is very poor, either because of significant unstability of the first oxidation product (dication radical or sulfoxide) or due to fast corrosion of the electrode surface in alkaline medium.

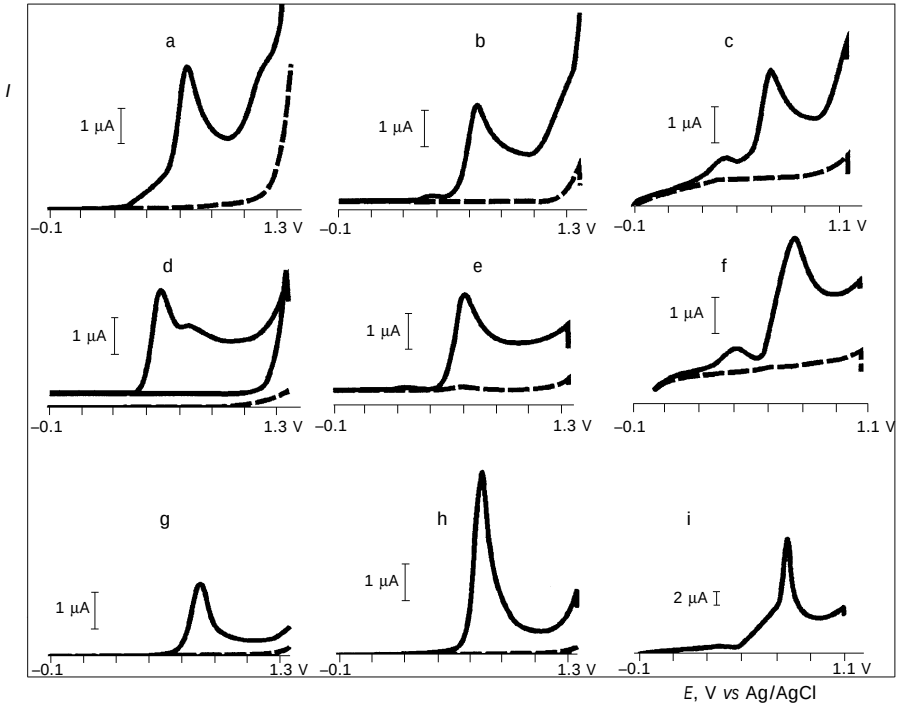


FIG. 2

Linear sweep voltammograms of $1.25 \cdot 10^{-4}$ M (e–i) and $2.5 \cdot 10^{-4}$ M (a–d) promethazine maleate aqueous-alcoholic solution (1 : 1) using CP (a, d, g), SCP (b, e, h) and GCE (c, f, i) at 50 mV s^{-1} scan rate (- - - - baseline). Horizontal axes represent potentials *vs* Ag/AgCl reference and vertical axes currents

The voltammetry of promethazine maleate revealed similar shaped curves and products (S-oxide) due to almost identical molecular structure. Differences can be found only in the side chain, which is not involved in the oxidation reactions. Thus, at pH 1.0 promethazine maleate shows two peaks, the first at +0.68 ± 0.01 V and the second as a shoulder between +1.10 and +1.15 V (Fig. 2a). At pH 6.0 the oxidation potential decreases to +0.54 ± 0.01 V and +0.72 ± 0.01 V, respectively, while at pH 6.0 the current increases (Fig. 2d) loosing reproducibility. At pH 9.0 there is only one, 10–20 times larger, nonreproducible peak at +0.70 ± 0.05 V (Fig. 2g).

Levomepromazine showed also two oxidation peaks (Fig. 3a) at +0.55 ± 0.01 V and at +1.00 ± 0.03 V (pH 1.0), with the current about five times lower than for the other two phenothiazines. At higher pH values, only one

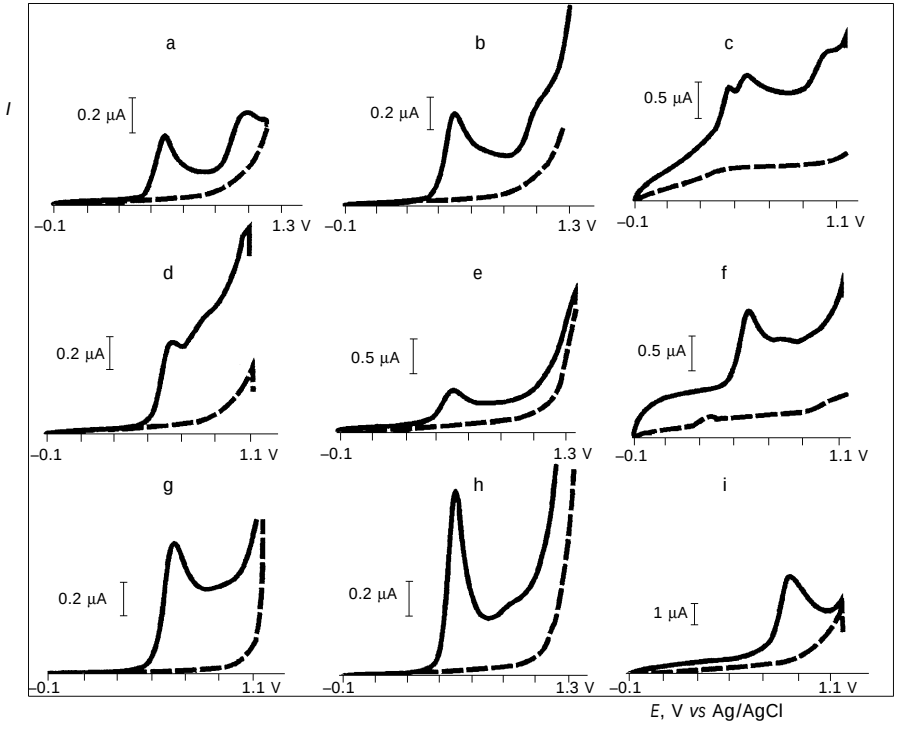


FIG. 3

Linear sweep voltammograms of $5 \cdot 10^{-5}$ M (g, h), $1.25 \cdot 10^{-4}$ M (b, d), $3.75 \cdot 10^{-4}$ M (e), $6.25 \cdot 10^{-4}$ M (a, f, i) and $1.25 \cdot 10^{-3}$ M (c) levomeprazine in alcoholic solution using CP (a, d, g), SCP (b, e, h) and GCE (c, f, i) at 50 mV s^{-1} scan rate (- - - - baseline). Horizontal axes represent potentials *vs* Ag/AgCl reference and vertical axes currents

peak appears, the oxidation potential shifts to more positive values, and the current increases, but the reproducibility is poor (Figs 3d and 3g).

Solid Carbon Paste Electrodes

At pH 1.0, promazine maleate shows two reproducible oxidation peaks (Fig. 1b) at +0.54 ± 0.01 and 1.10 ± 0.012 V. At pH 6.0 a reproducible oxidation peak appears at +0.56 ± 0.02 V (Fig. 1e), while the second is substantially attenuated. The peak current does not change significantly, but with increasing phenothiazine concentration, a slow drift of the oxidation peak to higher potentials was observed. At pH 9.0 (Fig. 1h) the shift becomes larger, but the reproducibility is poor.

The current–potential plot for promethazine maleate shows three oxidation peaks at +0.43 ± 0.01, +0.70 ± 0.01 V and the last one as a shoulder between 1.15 and 1.20 V (Fig. 2b). At pH 6.0 the peak current decreases and the peaks are shifted to higher potential values (Fig. 2e). At pH 9.0, only a single peak appears at +0.70 ± 0.05 V (Fig. 2h), the oxidation peak is well defined, but not reproducible.

At pH 1.0, the current–potential plot for levomepromazine shows two peaks, one well defined at +0.55 ± 0.01 V and a shoulder at approximately 1.0 V (Fig. 3b). The same behavior was observed at higher pH values (Figs 3e and 3h) for levomepromazine.

Glass-Like Carbon Electrodes

The current–potential curves for promazine maleate at pH 1.0 show two oxidation peaks (Fig. 1c) at +0.52 ± 0.01 and 1.10 ± 0.05 V. At pH 6.0 (Fig. 1f) the oxidation peaks shift convergently, the first to higher and the other to lower potential values (see Table I). The peak current increases for the first peak and decreases for the other, better defined peak, and shifts to lower E_{ox} as the concentration decreases. At pH 9.0 (Fig. 1i) a single large oxidation peak appears at +0.78 ± 0.02 V. In the case of GCE the shift of the E_{ox} has opposite direction, *i.e.* to lower potential values (+0.70 ± 0.01 V) with increasing concentration.

Promethazine maleate has a similar behavior at pH 1.0 with two oxidation peaks at +0.40 ± 0.01 and +0.65 ± 0.01 V (Fig. 2c). The same increase of the current and shift of the oxidation potential occurs at higher pH values (Figs 2f and 2i, Table I).

At pH 1.0, levomepromazine shows three oxidation peaks at +0.43 ± 0.01, +0.52 ± 0.02 (main peak) and 0.95 ± 0.03 V (Fig. 3c). At pH 6.0, in spite of a

current increase, the reproducibility is poor and the curve presents only two peaks, the first, well defined at +0.55 ± 0.01 V and the other, less pronounced at +0.75 ± 0.05 V (Fig. 3f). At pH 9.0 the current is further increased, but the reproducibility of the single peak at +0.78 ± 0.02 V is poor (Fig. 3i).

Investigations made on above-mentioned phenothiazines demonstrated that the current and oxidation potential are strongly related to the pH, whatever is the working electrode used. The first peak shifts to higher and the second to lower E_{ox} values as pH increases. Meanwhile, the first oxidation peak is pH independent, the formation of dication diradical or sulfoxide by irreversible hydrolysis of cation radical strongly depends on pH. Generally, the current intensity increases significantly with the increase of pH, but at the same time the reproducibility is lost. The best reproducibility of electroanalysis of phenothiazines using carbon paste, solid carbon paste or glass-like carbon electrodes was found at pH 1.0–5.0.

TABLE I
The influence of pH and electrode type on the oxidation potential

Electrode type	pH	Oxidation potential, V		
		promazine maleate	promethazine maleate	levomepromazine
Carbon paste electrode	1.0	+0.55 ± 0.02 +1.12 ± 0.02	+0.68 ± 0.01 +1.10 to +1.15	+0.55 ± 0.01 +1.0 ± 0.03
	6.0	+0.56 ± 0.01 +0.95 to +1.00	+0.54 ± 0.01 +0.72 ± 0.01	+0.62 ± 0.01
	9.0	+0.65 ± 0.01 +0.84 ± 0.01	+0.70 ± 0.05	+0.60 ± 0.01
Solid carbon paste electrode	1.0	+0.54 ± 0.01 +1.10 ± 0.02	+0.43 ± 0.01 +0.70 ± 0.01	+0.55 ± 0.01
	6.0	+0.56 ±0.02	+0.65 ± 0.02	+0.59 to +0.70
	9.0	+0.55 to +0.60	+0.75 ± 0.05	+0.55 ± 0.03
Glass-like carbon electrode	1.0	+0.52 ± 0.01	+0.65 ± 0.01	+0.43, +0.52, +0.95
	6.0	+0.55 ± 0.01	+0.30 +0.70	+0.55 ± 0.02
	9.0	+0.70	+0.77	+0.78 ± 0.02

Influence of Electrode Type

The current–potential curves for promazine maleate (Fig. 1) are similar on all three studied carbon electrodes at pH 1.0 and 6.0. Some differences appear only at pH 9.0. Thus, in the case of "soft" carbon paste (made with paraffin oil), two oxidation peaks are convergently shifted, and for the GCE, only a well defined, retrograde peak appears. A less modified behavior was observed when solid carbon paste electrode was used.

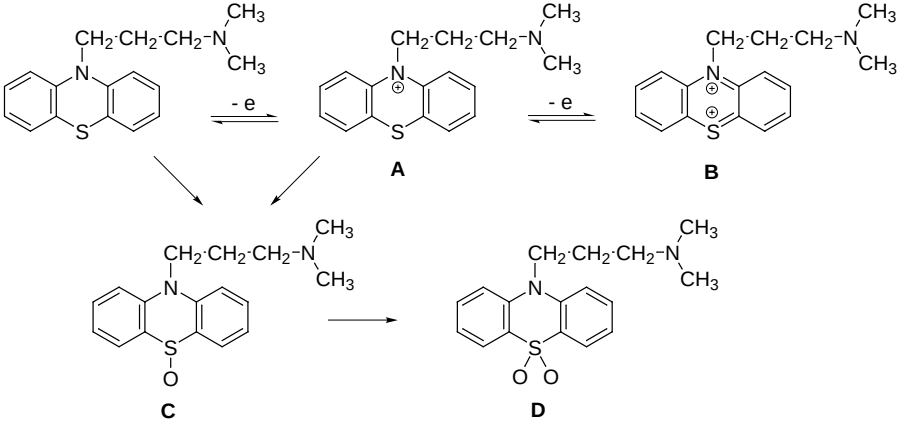
In the case of promethazine maleate, the current–potential curves (Fig. 2) were quite similar for pH 1.0 and 9.0, differences can be found only in E_{ox} values (see Table I). The greatest differences between the three electrodes were found at pH 6.0, with two shifted peaks for CPE, a single nonreproducible peak for SCPE and two nonreproducible, continuously shifting peaks for GCE.

Levomepromazine (Fig. 3) shows at pH 1.0 identical oxidation curve shapes, but different E_{ox} values. At pH 6.0 the shapes of curves were different, but the oxidation peak around +0.60 ± 0.05 V was poorly reproducible. At pH 9.0 the shape of oxidation curves was similar, but potentials E_{ox} were different, +0.60 ± 0.02 V for CPE, +0.55 ± 0.03 V for SCPE and +0.78 ± 0.02 V for GCE (see Table I).

Similarities in electrochemical behavior for studied carbon electrodes suggest that redox processes at the electrode/solution interface are also similar. Small differences were found for different phenothiazine derivatives in the pH impact on the curve shape, oxidation potential and current. All electrodes showed good reproducibility in acid (pH between 1–5), because of pH-independent stable radical formed in the first oxidation step, while at pH above 6.0 the reproducibility was substantially worse. The poor reproducibility in neutral and alkaline media is due to the unstable dication diradical and the irreversible hydrolysis of cation radical to sulfoxide, which are dramatically influenced by the pH. The current increase at pH 9.0 indicated also rapid and progressive corrosion of electrode surface in alkaline media. SCPE seems to be more resistant in comparison with "soft" CPE at pH 6.0 probably due to the superior mechanical properties given by the solid paraffin.

Similar current–potential curves of phenothiazines for the same type of electrode and their similar electrochemical behavior suggest that they have similar oxidation mechanisms and also similar oxidation products. Promazine, promethazine and levomepromazine have very similar molecular structures with small differences in the side-chain. Data from literature[1] indicate that the phenothiazine ring is the most sensitive for different oxi-

dation agents such as oxidizing acids, halogens, H_2O_2 forming solid salts, dimers, radicals or S-oxides. Thus, the similar electrochemical behavior is explained by minor structural differences among studied phenothiazines where the moiety responsible for redox properties (thiazinic cycle) is the same. The first oxidation peak can be attributed to the monocation radical (**A**), the second peak to the dication diradical (**B**) or sulfoxide (**C**) formation and the third peak to sulfone (**D**) formation in different redox stages described below.



Voltammetric Determination in Drug Formulations

In order to calculate the regression equation, oxidation curves were recorded using linear sweep voltammetry at pH 1.0, with all the electrodes, in the same concentration range as already mentioned. An example is given for levomepromazine in Fig. 4. Each determination was repeated three times, stirring the solution for 60 s before each determination. The results were statistically processed by the least square method. The calibration curve equations and statistical parameters of voltammetric determination of phenothiazines are given in Table II. The electrochemical method was used for the quantitative determination of promethazine maleate and levomepromazine in several formulations, with good results as illustrated in Table III.

TABLE II
Regression equation and statistical parameters of voltammetric determination of phenothiazines using different electrodes. The symbol *n* represents number of assays

Compound	Electrode	Calibration curve equation	R^2	Concentration mol l^{-1}	RSD %	Accuracy %
Promazine maleate	CPE	$y = 0.65x - 0.68$	0.999	$2.5\cdot10^{-5}$–$5\cdot10^{-3}$	4.5 (n = 6)	98.8 ± 3
	SCPE	$y = 0.85x - 6.88$	0.996		5.7 (n = 18)	100.6 ± 3.1
	GCE	$y = 0.61x + 0.17$	0.999		2.2 (n = 6)	100.6 ± 1.5
Promethazine maleate	CPE	$y = 0.9x + 1.3$	0.997	$2.5\cdot10^{-5}$–$5\cdot10^{-3}$	1.7 (n = 18)	99.6 ±0.9
	SCPE	$y = 0.74x - 1.98$	0.999		4.3 (n = 18)	99 ± 2
	GCE	$y = 0.73x + 0.22$	0.998		5.2 (n = 18)	99 ± 3
Levomepromazine	CPE	$y = 0.26x + 0.38$	0.998	$6.2\cdot10^{-5}$–$1.2\cdot10^{-3}$	7.1 (n = 6)	99 ± 4
	SCPE	$y = 0.19x + 3.88$	0.992		5.1 (n = 18)	100.8 ± 2.8
	GCE	$y = 0.07x + 1.69$	0.996		4.4 (n = 6)	99.4 ± 2.4

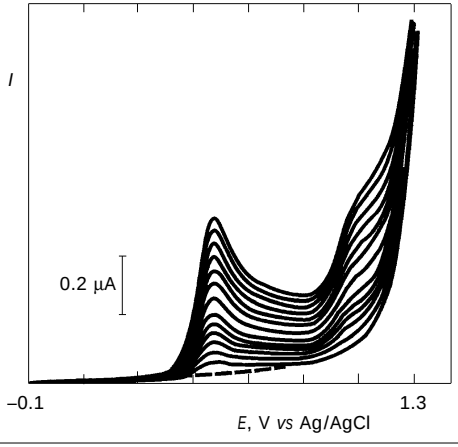


FIG. 4
Linear sweep voltammograms of different concentrations of levomeprazine using a solid carbon paste electrode (50 m Vs^{-1} scan rate (- - - - - baseline), pH 1.0, 0.1 M HCl buffer). The concentration range: $7.5\cdot10^{-5}$–$1.25\cdot10^{-3}$ M levoprazine in alcoholic solution (60–1 000 μl)

TABLE III
Determination of promethazine maleate and levomepromazine in pharmaceuticals. Here n = number of assays, t = Student criteria, α = probability

Pharmaceuticals	g/unit		Recovery, % of the nominal value
	theoretical	found	
Romergan tablets (Terapia, S.A.)	0.03 promethazine maleate	0.029 ± 0.001	96.8 ± 2.8 (n = 10; t = 2.26; α = 0.95)
Romergan vials (Sicomed S.A.)	0.05 promethazine maleate	0.056 ± 0.002	112 ± 4 (n = 10; t = 2.26; α = 0.95)
Levomeprazin tablets (Terapia S.A.)	0.025 levomeprazine	0.027 ± 0.001	107 ± 3 (n = 10; t = 2.26; α = 0.95)
Levomeprazin vials (Terapia S.A.)	0.025 levomeprazine	0.025 ± 0.01	99 ± 3.6 (n = 10; t = 2.26; α = 0.95)

The Study of CPEs Modified with Phenothiazines

In order to exploit the three studied phenothiazines as mediators, we investigated the electrochemical behavior of carbon pastes modified with 5% of phenothiazine according to the procedure already described.

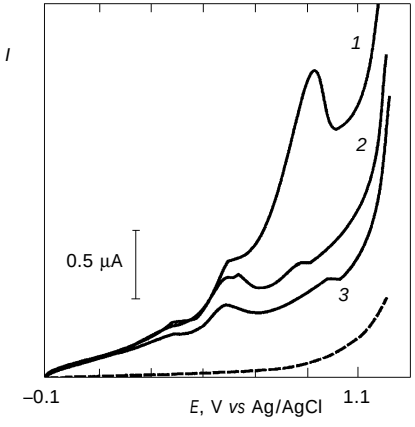


FIG. 5
Three succesive linear sweep voltammetry curves at pH 1.0 of the carbon paste electrode modified with 5% promethazine; scan rate 50 mV s^{-1} (- - - - baseline); numbers indicate successive potential sweeps: *1* 1st record, *2* 2nd replicate, *3* 3rd replicate

Figure 5 illustrates three successive potential sweeps on the CPE modified with 5% promethazine maleate. The current–potential curves show three oxidation peaks which correspond probably to the radical or S-oxide formation. The first bell-shaped peak appears between +0.28 and +0.38 V, the second at +0.54 ± 0.02 V has a shape of shoulder in the first sweep. The third peak due to the main oxidation process has the biggest current intensity, but at the same time is less reproducible. The oxidation potential E_{ox} is different for each sweep, +0.82 ± 0.01 V for the first, +0.78 ± 0.012 V for the second and +0.87 ± 0.02 V for the third.

These first results encourage us to continue the study of phenothiazine-modified CPEs and to develop chemosensors containing NADH for enzyme determination in biological fluids.

CONCLUSIONS

Electrochemical behavior of promazine maleate, promethazine maleate and levomepromazine was studied by linear sweep voltammetry using carbon paste, solid carbon paste and glass-like carbon electrodes.

Oxidation potential and peak current are strongly dependent on pH values, especially in the second and third oxidation steps. Generally, with increasing pH, the oxidation potential shifts towards more positive values and the current increases but, unfortunately, with the loss of reproducibility.

Phenothiazine derivatives studied show similar electrochemical behavior at the same pH value, whatever is the working electrode used. The highest impact on the shape of oxidation curve, E_{ox} or current is caused by pH. Similar electrochemical behavior of the studied phenothiazine derivatives suggest also similar oxidation mechanisms, due to small differences of the molecular structure.

The linear sweep voltammetry within the potential range from –0.1 to +1.3 V, at different current densities and pH 1.0 was used to develop rapid, accurate and reproducible methods for determination of phenothiazines in drug formulations.

The linear sweep voltammetry of carbon paste electrodes modified with 5% of phenothiazine derivatives indicated the possibility of using these phenothiazines as redox mediators in the design of enzyme electrodes.

The authors are indebted to Prof. J.-M. Kauffmann and Dr Ch. Petit from Université Libre de Bruxelles for valuable discussions, and the kind and generous help with instrumentation, accessories and literature.

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