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Short communication

# Anodic voltammetric assay of lansoprazole and omeprazole on a carbon paste electrode

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**Abstract**

The electrochemical oxidations of lansoprazole and omeprazole have been studied at a carbon paste electrode by cyclic and differential-pulse voltammetry in Britton–Robinson buffer solutions (0.04 M; pH 6.0–10.0). The drug produced a single oxidation step. By differential-pulse voltammetry, a linear response was obtained in B–R buffer pH 6.0 in a concentration range from $2.0 \times 10^{-7}$ to $5.0 \times 10^{-5}$ M for lansoprazole or omeprazole. The detection limits were $1.0 \times 10^{-8}$ and $2.5 \times 10^{-8}$ M for lansoprazole and omeprazole, respectively. The method was successfully applied for the analysis of omeprazole and lansoprazole in capsules. The results were comparable to those obtained by spectrophotometry.
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*Keywords:* Lansoprazole; Omeprazole; Pharmaceutical analysis; Voltammetry; Carbon paste electrode

## 1. Introduction

Lansoprazole (**L**) (±)2-[[[3-methyl-4-(2,2,2-trifluoro-ethoxy)-2-pyridinyl]methyl]sulfinyl]-1*H*-benzimidazole and omeprazole (**O**) (5-(difluoromethoxy)-2-{[3,4-dimethyloxy-2-pyridinyl) methyl]sulfinyl}-1-*H*-benzimidazole, structural formulae are shown in Scheme 1, are benzimidazole derivatives which act as proton pump inhibitors (PPIs) being introduced for the management of duodenal ulcers, gastric ulcers or pathologic hypersecretory conditions [1,2].

Gastric PPI is prodrug that requires an acid-induced activation. It is a weak base that is converted to the active form by gastric acid before acting on the proton pump. It inhibits gastric acid secretion by covalently binding to the proton pump ($H^+/K^+$ ATPase) [3].

Lansoprazole and omeprazole break down rapidly in an acidic medium and thus must be administrated in the form of enteric-coated granules in capsules to prevent gastric decomposition and improve their systematic bioavailability [4,5].

There have been several reports for the determination of lansoprazole or omeprazole in formulations including colorimetric or spectrophotometric methods [6–11], TLC densitometry [12,13] and high-performance liquid chromatography [14].

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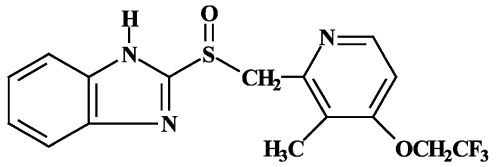
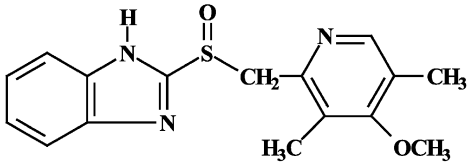


(L)



(O)

Scheme 1.

The development of new methods capable of determining drug concentration in pharmaceutical formulations is important. Electroanalytical techniques have been used for the determination of a wide range of pharmaceuticals with the advantages that there is in most instances, no need for derivatization, and that these methods are less sensitive to matrix effects than other analytical techniques [15].

The reduction process and quantitative determination of lansoprazole and omeprazole have been studied by means of several polarographic techniques [16–20], but up to now; nothing has been published concerning electrochemical oxidation of lansoprazole or omeprazole at solid electrodes. The oxidation behavior of these drugs on carbon paste electrode is, therefore, described and voltammetric method was developed for quantitative determination of lansoprazole or omeprazole in capsules.

## 2. Experimental

### 2.1. Reagents

Lansoprazole and Lanzor® capsules were kindly supplied by Hoechst Orient (Cairo, Egypt); Omeprazole and Gastrazole® capsules by Amriya (Alexandria, Egypt). Each Lanzor® capsule was labeled to contain 15 mg lansoprazole, magnesium carbonate, neutral microgranules (Saccharose and corn starch), saccharose, corn starch, low substitution hydroxypropyl cellulose, hydroxypropyl cellulose, endragit L 30 D-SS, talc, polyethyleneglycol, titanium dioxide, polysorbate 80, anhydrous colloidal silica. Each Gastrazole® capsule was labeled to contain 40 mg omeprazole, starch, sucrose, eudragit L 100. A stock solution of $1.0 \times 10^{-3}$ M lansoprazole or omeprazole was prepared in 0.02 M sodium hydroxide solution and more dilute solutions were prepared daily with de-ionized water just before use. Britton–Robinson buffers (0.04 M, pH 6.0–10.0) were used as supporting electrolytes. Carbon paste was prepared containing 5 g of graphite powder (Aldrich, Milwaukee, WI, US 1–2 μm) and 1.8 ml of Nujol (Sigma, $d = 0.84$ g ml$^{-1}$). All chemicals used were of analytical-reagent grade. Ultra-pure water was used throughout.

### 2.2. Apparatus

All voltammograms were obtained with a computer driven AEW2 Analytical Electrochemical Workstation with ECprog3 Electrochemistry software (Sycopel, England) in combination with C-2 stand with a three-electrode configuration: a carbon paste electrode (BAS model MF-2010, 3 mm diameter) working electrode, an Ag/AgCl/3 M KCl (BAS model MF-2063) reference electrode and a platinum wire (BAS model MW-1032) counter electrode. MICROCAL ORIGIN (v.4.10) software was used for the transformation of the initial signal. A CG 808 (Schott Gerate, Germany) digital pH-meter with glass combination electrode served to carry out the pH measurements.

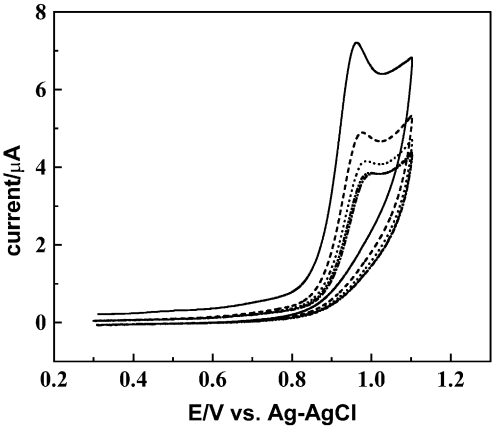



Fig. 1. Repetitive cyclic voltammograms of $5.0 \times 10^{-5}$ M lansoprazole in B–R buffer (0.04 M, pH 6.0). Scan rate = 100 mV $s^{-1}$.

### 2.3. Procedures

Voltammetric analyses were carried out in 10 ml of BR buffer. The accumulation potential (usually open circuit condition) was applied for a selected time while the solution was stirred at 2000 rpm. The stirrer was then stopped, and after 15 s rest period, the drug was removed by stripping anodically using differential-pulse voltammetry (pulse height: 50 mV and scan rate 10 mV $s^{-1}$). After background voltammograms had been recorded, aliquots of the drug standard were introduced and the adsorptive stripping cycle was repeated using a new electrode surface. The peak current was evaluated as the difference between each voltammogram and the background electrolyte voltammogram. All data were obtained at ambient temperature.

#### 2.3.1. Determination of lansoprazole and omeprazole in capsules

The content of ten capsules of Lansor® or Gastrazole® were emptied, weighed and powdered. An accurately weighed amount of powdered content equivalent to a single tablet was dissolved in 50 ml of 0.01 M sodium hydroxide solution. After the non-dissolved excipients have settled down, an aliquot of the clear supernatant liquor was then transferred into a voltammetric cell containing 10 ml of B–R buffer (pH 6.0) to yield a final concentration of $5.0 \times 10^{-6}$ M lansoprazole or omeprazole. The differential-pulse voltammogram was subsequently recorded by employing a pulse height: 50 mV and scan rate 10 mV $s^{-1}$. The content of the drug in capsules was determined referring to the regression equation.

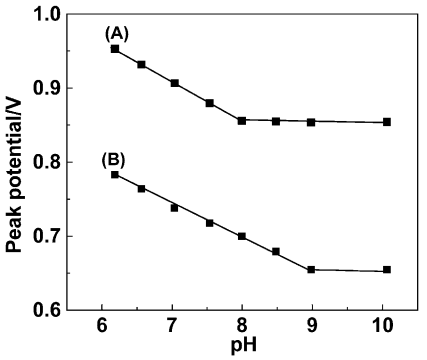



Fig. 2. Dependence of differential-pulse peak potential for on pH for (A) lansoprazole and (B) omeprazole peak at carbon paste electrode. Pulse height = 50 mV; scan rate = 10 mV $s^{-1}$ and $C = 5.0 \times 10^{-6}$ M.

## 3. Results and discussion

### 3.1. Electrochemical behavior of lansoprazole

Fig. 1 illustrates cyclic voltammograms for $5.0 \times 10^{-5}$ M lansoprazole solution in B–R buffer at pH 6.0 and scan rate $v = 100$ mV $s^{-1}$, recorded after 5 min of stirring (2000 rpm) at open circuit potential. A well-defined oxidation peak appears at 0.963 V and no reduction peak is observed in the cathodic branch, which shows that drug oxidation is irreversible. The second and successive scans show substantially smaller peak that indicates the passivation of the electrode surface by the polymeric oxidation product. The $\log i_p - \log v$ graph was linear over the scan rate range 25–500 mV $s^{-1}$ with a slope of 1.08, close to 1.0, the value expected for an ideal reaction of surface species [21]. The peak potential shifted to the anodic direction when the scan rate increased according to the following equation: $E_p$ (V) = 0.979 + 0.749$v$

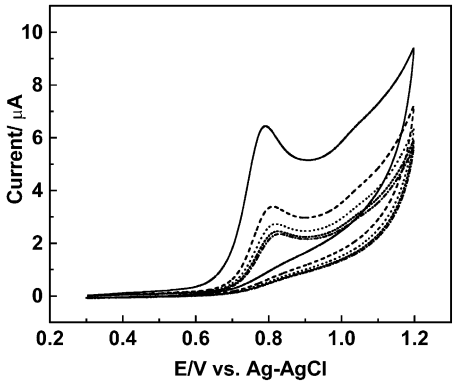



Fig. 3. Repetitive cyclic voltammograms of $5.0 \times 10^{-6}$ M omeprazole in B–R buffer (0.04 M, pH 6.0). Scan rate: 100 mV $s^{-1}$.

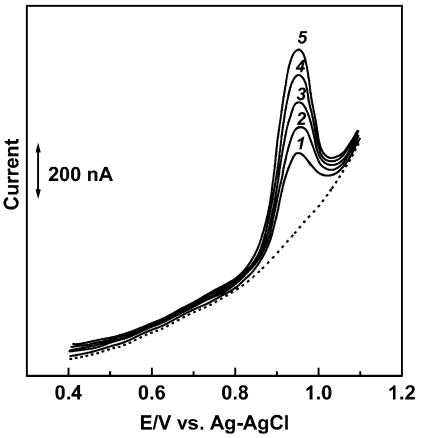



Fig. 4. Differential-pulse voltammograms for different lansoprazole concentrations in BR buffer (0.04 M, pH 6.0), (1) $2.0 \times 10^{-7}$ M (2) $4.0 \times 10^{-7}$ M (3) $6.0 \times 10^{-7}$ M (4) $8.0 \times 10^{-7}$ M and (5) $1.0 \times 10^{-6}$ M. (b) The dotted lines is the blank response.

(mV $s^{-1}$), $r = 0.998$, which confirms the irreversibility of the electrode process.

The adsorption of lansoprazole can be used as an effective pre-concentration step prior to its voltammetric determination and it is necessary to select the variables affecting the adsorptive process. The effect of variables on peak current was examined for $1.0 \times 10^{-5}$ M lansoprazole using differential pulse voltammetry. The peak stripping current is independent on accumulation potential, thus the adsorption stage was carried out at open circuit potential. The effect of pre-concentration period on differential pulse voltammograms for $5.0 \times 10^{-6}$ M lansoprazole stirring at 2000 rpm at open circuit potential showed an optimum value of 5 min. This value was selected for optimization of other variables and for the analytical determination.

Differential pulse voltammetry was used to study the effect of pH varying from 6.0 to 10.0 to avoid degradation phenomena. The peak current reaches its maximum value at pH 6.0, which was selected as optimum value to carry out its qualitative determination. The peak potential shifts towards less positive values with a slope of 52 mV/pH up to pH 8.0, then becomes pH-independent (Fig. 2A). The intercept of two segments, which occurs at pH 8.0, may be correlated to the p$K_a$ of lansoprazole.

### 3.2. Electrochemical behavior of omeprazole

Electrochemical studies of omeprazole have been performed under identical conditions as lansoprazole. Differential pulse voltammetry studied as function of pH closely resembles those of lansoprazole. One anodic peak was observed, whose potential is shifted to less positive values by increasing the pH with slope of 46 mV/pH until pH 9.0, then remains practically pH independent (Fig. 2B).

Cyclic voltammetry experiment conducted at pH 6.0 exhibits a single anodic peak at 0.791 V with no peak on the reverse scan, indicating the irreversible nature of the electrode reaction. Continued scanning results in a drift of the peak potential towards more positive values and large decrease in the peak current (Fig. 3). This suggests a possible role of adsorption. The peak current change linearly with scan rate ($v$) as expected for adsorption-controlled reaction.

The parallel behavior of the $E_p$–pH plots for omeprazole and lansoprazole suggests an identical mechanism. The amine function of benzimidazole moiety is the most easily oxidizable group in drug molecule. The voltammograms are typical of irreversible oxidations. It is likely that the radical cation generated from oxidation of lansoprazole

Table 1
Data of DPV and UV-spectrophotometric methods for determination of lansoprazole and omeprazole in capsules

| Preparations technique | Lansor® | | Gastrazole® | |
|---|---|---|---|---|
| | DPV | UV | DPV | UV |
| $\bar{x}$ | 29.69 | 29.53 | 19.82 | 19.91 |
| $S$ | 0.59 | 045 | 0.48 | 0.23 |
| $s_r$ | 1.99 | 1.52 | 2.42 | 1.16 |
| CL | 0.73 | 0.56 | 0.60 | 0.29 |
| $t$-test significance $t$ $(P = 0.05) = 2.78$ | 0.48 | | 0.38 | |
| $F$-test significance $F(P = 0.05) = 6.39$ | 1.72 | | 4.36 | |

or omeprazole at the electrode undergoes rapid decomposition (e.g. rearrangement [22], fragmentation, or addition of water [23]) before it can be reduced back to neutral.

### 3.3. Analytical characteristics and applications

Qualitative evaluation is based on the linear correlation between the stripping peak current and concentration. For example, differential pulse voltammetry (pulse heights: 50 mV and scan rate 10 mV $s^{-1}$) for five different concentrations of lansoprazole after a pre-concentration period of 5 min is shown in Fig. 4. Good correlations were obtained in differential pulse voltammetry of lansoprazole or omeprazole in supporting electrolyte consisting of 0.04 M B–R buffer at pH 6.0 for concentration between $1.0 \times 10^{-7}$ and $5.0 \times 10^{-5}$ M; then the plot leveled off at higher concentration, as expected for a process that is limited by adsorption of analyte. The calibration equations were found to be the following: $i_p$ (nA) = (200.7 ± 10.5) + (540.3 ± 15.8) $C$ (μM) with $r = 0.998$ for lansoprazole and $i_p$ (nA) = (145.2 ± 7.10 + (490.6 ± 10.7) $C$ (μM) with $r = 0.998$ for omeprazole, respectively. the detection limits, defined as $a + 3S_{yx}$, [24] were $1.0 \times 10^{-8}$ M for lansoprazole and $2.5 \times 10^{-8}$ M for omeprazole. The precision determined by performing ten scans in $1.0 \times 10^{-5}$ M of each drug. After each scan, the electrode surface was renewed by wiping on a filter paper. The relative standard deviations were 2.3 and 3.4% for lansoprazole and omeprazole, respectively.

The differential-pulse voltammetric technique (DPV) has been applied to determine lansoprazole or omeprazole in commercially available capsules: Lansor® and Gastrazole®. The results of the proposed technique have been evaluated statistically as compared with results of UV-spectrophotometeric method (Table 1). The UV-spectroscopic method was based on the absorption of lansoprazole and omeprazole in methanol at 287 and 302 nm, respectively. There was no significant difference between the mean values and precision of the two methods at 95% confidence level.

It is well established that omeprazole and lansoprazole are stable at high pH but degrade under acidic conditions to afford the corresponding sulfenamide, sulfide and other products [25–27]. The response of omeprazole or lansoprazole and their degraded products are similar suggesting that they all undergo similar oxidation pathways at the electrode. It is likely that oxidation occurs mainly on the benzimidazole. The degraded products can not be differentiated from the intact compounds using voltammetric method since the relative inductive and resonance effects of the sulfur groups does not modify the oxidation potential of the benzimidazole ring, as previously demonstrated [28]. Hence, to apply the proposed method for analysis of omeprazole or lansoprazole and their degraded products in aqueous solutions during stability study, a separation step may be needed.

## 4. Conclusion

It can be concluded that the voltammetric methods are more versatile and easy to apply than the colorimetric and chromatographic methods. Colorimetric methods are time consuming and need special reagents and have been proved to be inaccurate due to matrix interference. The chromatographic methods need a slightly expensive instrumentation and running costs. The disadvantage of the proposed methods is that they cannot be applied for analysis of omeprazole or lansoprazole and their degraded products in aqueous solutions during stability study.

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