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(Received 19 February 1986)

DIRECT POLAROGRAPHIC DETERMINATION OF EDTA IN OPHTHALMIC PRODUCTS BASED ON THE ANODIC OXIDATION OF THE DROPPING MERCURY ELECTRODE

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SUMMARY

A direct polarographic method for EDTA determination based on the measurement of the anodic wave (DCP) or peak height (DPP) observed at +0.100 V,vs SCE, in the oxidation of the dropping mercury electrode in the presence of EDTA at pH=6.0 is described. The conditions for a simple and reproducible method using the standard additions technique for the analysis of this chelating agent in ophthalmic products are studied. Finally, the differential pulse polarographic method is applied to the analysis of EDTA in eye drops and contact lens wetting and cleaning solutions.

INTRODUCTION

The pronounced ability of aminopolycarboxylic acids, mainly ethylenediaminetetraacetic acid (EDTA), as chelating agent of cations is used in many practical applications. The masking of metal ion impurities by EDTA improves the stability of foods, pharmaceutical and personal care products, etc.(1).EDTA is often added to ophthalmic products in order to avoid precipitates and to maintain clarity; it is also added because it prevents the development of resistance to many common antibacterial agents by removing calcium and magnesium ions from the outer cell wall of the bacteria, particularly *Pseudomonas* (2).

The oxidation of the dropping mercury electrode in the presence of EDTA has been studied by several authors. GOFFARD et al.(3) ascribe the observed anodic wave to a polarographic process controlled by the diffusion of EDTA towards the mercury electrode with the formation of HgY^{2-} . NIKI et al.(4) using alternating current polarography describe the adsorption onto the electrode surface of the HgY^{2-} complex. JACKSON and OSTERYOUNG (5)

using normal and differential pulse polarography indicate that the oxidation of mercury in the presence of EDTA, EGTA and DCTA are reactions which are generally irreversible and complicated by adsorption, but which are at the same time diffusion controlled; STOJEK and OSTERYOUNG (6) employ one-drop square-wave polarography for the determination of chelons at trace levels.

A titrimetric method with a spectrophotometric end point (7) and an indirect polarographic method, based on the decrease in the peak height of Cd(II) or Zn(II) in ammonia buffer have been employed by CARLSON and HABEGGER (8) for the analysis of EDTA in ophthalmic products. In this polarographic method surfactants commonly present in this type of sample, such as methylcellulose, polyvinyl alcohol, etc., interfere and should be completely removed.

In the present paper the polarographic wave (DCP) or peak (DPP) observed in the anodic oxidation of the dropping mercury electrode in the presence of EDTA at pH=6.0 is used for EDTA determination. The most sensitive DPP technique was applied to the determination of EDTA in ophthalmic products.

EXPERIMENTAL

Apparatus.— Polarecord (Metrohm E-506) with E-505 polarographic stand; Metrohm EA-1029/1 dropping mercury electrode, Metrohm EA-285 platinum counter electrode and a saturated calomel electrode. pH values were measured with a Crison pH-meter equipped with a Metrohm AG 9100 combined glass electrode. The temperature of the solution was controlled by a P.Selecta thermostat.

Reagents.— EDTA solutions were prepared from the solid disodium salt (Merck). All other chemicals used were of analytical grade.

Preliminary procedure.— Different aliquots of aqueous solutions of EDTA are placed into 50.0 ml flasks; the necessary amounts of acetic acid, sodium acetate, Britton-Robinson buffer or sodium hydroxide are added to obtain the desired pH of the medium and volume is brought up with bidistilled water. This solution is placed in the polarographic cell and thermostatted;

after eliminating the oxygen from the solution with purified nitrogen, the voltage is scanned from -0.400 to +0.600 V (vs SCE). A pulse of 50 mV is used in the DPP technique. Drop time is 2 sec/drop in both techniques.

RESULTS AND DISCUSSION

Anodic behaviour of the dropping mercury electrode in the presence of EDTA

In DCP, direct oxidation of the dropping mercury electrode in the presence of EDTA yields a well-defined anodic wave in the 3<pH<10 range (Fig.1). At higher pH values the wave is poorly defined because of interference by OH⁻ ions. The half-wave potential values shift with pH according to the electrode reaction (Table 1) determined by the predominant EDTA species.

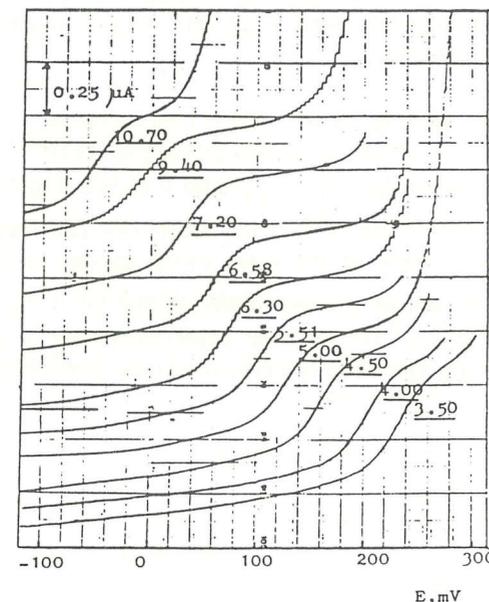


Fig.1.—Anodic oxidation of dropping mercury electrode in the presence of EDTA. Influence of pH on the anodic wave morphology. [EDTA]: 2×10^{-4} M. The pH is indicated on each polarogram.

Table 1

Anodic oxidation of d.m.e. in the presence of EDTA
Influence of pH on the half-wave potential

pH range	Electrode reaction	$E_{1/2}$ (V) = f(pH)
3-6	$Hg + YH_2^{2-} \rightarrow HgY^{2-} + 2H^+ + 2e^-$	$E_{1/2} = 0.427 - 0.060pH$
6-10	$Hg + YH^{3-} \rightarrow HgY^{2-} + H^+ + 2e^-$	$E_{1/2} = 0.229 - 0.026pH$

On the other hand, the limiting current is independent of the pH of EDTA solution in the $3 < pH < 9$ range. Bearing in mind that the major objective of this work is the determination of EDTA in ophthalmic products, an acetic acid-sodium acetate medium, pH=6.0, is chosen because the polarographic wave appears well-defined and at pH>6 precipitates may be originated with solutions of real samples.

In DCP the limiting current-EDTA concentration relationship shows good linearity in low EDTA concentration ranges (1×10^{-5} - 10^{-4} M) in which the adsorption prewave appears, $E_{1/2}=0.00$ V vs SCE (Fig.2). For higher EDTA concentrations (8×10^{-5} - 6×10^{-4} M) the adsorption prewave is not observed and the diffusion current of the wave which appears at $E_{1/2} = +0.10$ V is also a linear function of concentration. In the EDTA concentration range studied (1×10^{-5} - 6×10^{-3} M), a linear dependence may be observed between the limiting current sum of both waves and EDTA concentration.

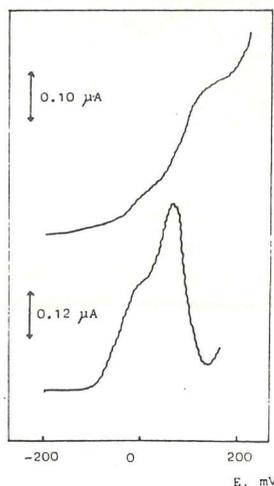


Fig.2.-Direct current and differential pulse polarograms of 1×10^{-4} M EDTA solutions showing the adsorption prewave and prepeak. pH=6.0

Using the DPP technique an adsorption prepeak (2×10^{-6} M<EDTA/< 1×10^{-4} M) and a diffusion peak (8×10^{-5} M<EDTA/< 5×10^{-4} M) are observed also (Fig.2) showing linearity between the height of each peak ($i_{p(a)}$ and $i_{p(d)}$, respectively) and EDTA concentration.

From the analytical point of view calibration graphs are linear over a wide range of EDTA concentrations employing both DCP and DPP techniques (Table 2). In all cases, the correlation coefficients of the current-concentration linear plots are above 0.999.

The influence of temperature on the prewave and prepeak currents confirms the existence of an adsorption process on the electrode. Likewise, the electrocapillary curve obtained from solutions with EDTA shows characteristic distortions caused by adsorption phenomena.

Table 2

Calibration Graphs

Current-Concentration Relationships

<u>/EDTA/ range</u>	<u>Linear Dependence*</u>
<u>DCP Technique</u>	
$1 \times 10^{-5}M - 1 \times 10^{-4}M$	$i_l = -0.0137 + 2.02 \times 10^3 C$
$8 \times 10^{-5}M - 6 \times 10^{-4}M$	$i_d = -0.119 + 2.27 \times 10^3 C$
$1 \times 10^{-5}M - 6 \times 10^{-4}M$	$i_l + i_d = -0.023 + 2.29 \times 10^3 C$
<u>DPP Technique</u>	
$2 \times 10^{-6}M - 1 \times 10^{-4}M$	$i_{p(a)} = -0.008 + 5.1 \times 10^3 C$
$8 \times 10^{-5}M - 5 \times 10^{-4}M$	$i_{p(d)} = -0.404 + 8.44 \times 10^3 C$

*The limiting current of the prewave (i_l) and wave (i_d) and the intensities of the prepeak ($i_{p(a)}$) and peak ($i_{p(d)}$) are expressed in μA ; the EDTA concentration (C) is expressed in Molarity.

Analysis of EDTA in ophthalmic products

Considering that sodium chloride is usually present in ophthalmic products, and that the chloride anion also causes an anodic wave in the oxidation of the dropping mercury electrode with the formation of mercurous chloride (9), the influence of chloride ($2 \times 10^{-5} \text{M}$ - 0.8M range) on the EDTA anodic wave was studied. Interference was only observed when chloride concentration was greater than 0.1M (Fig.3).

It was ascertained that NaCl present in the samples of ophthalmic products analyzed does not cause interference in the determination of EDTA; no distortions were observed in the EDTA anodic waves, most probably because the concentration of NaCl was below 0.1M .

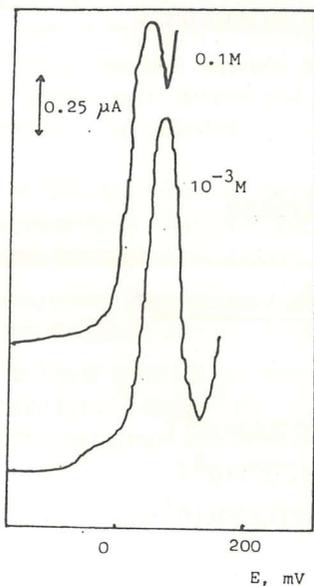


Fig.3.-Effect of chloride concentration on the morphology of EDTA differential pulse polarographic peak. /EDTA/: $2 \times 10^{-4} \text{M}$. NaCl concentration is indicated on each polarogram.

According to the polarographic viewpoint of EDTA determination in ophthalmic products, the surfactants commonly present in these samples cause matrix effects, as has been mentioned. For this reason, it was ascertained that the method of standard additions minimizes these effects and that it can be used advantageously over the calibration graph standardization technique (Fig.4).

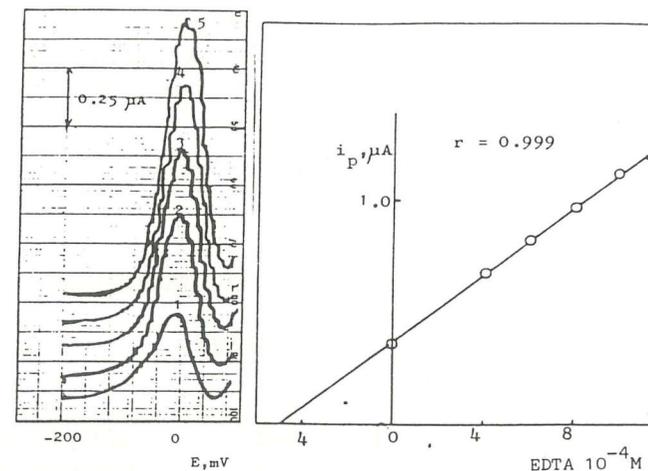


Fig.4.-Differential pulse polarograms of a sample of contact-lens preserving solution with different amounts of EDTA standard added and graphic plots to determine the EDTA concentration in the samples.

Recommended procedure.-One or two ml aliquots of the samples, according to the EDTA contained in the ophthalmic products, are placed into five flasks of 50.0 ml; 25.0 ml of 1M acetic acid-sodium acetate solution (pH=6.0) are also added to each flask. To four of the flasks are added 2.0, 3.0, 4.0 and 5.0 ml of $1 \times 10^{-3} \text{M}$ EDTA standard solution after which the volume of the five flasks is made up with bidistilled water. Each solution is placed in a polarographic cell and thermostatted; after eliminating the oxygen from the solution with purified nitrogen, the voltage is scanned anodically from -0.400 to $+0.600 \text{V}$ vs SCE. When DPP is used, a pulse of 50 mV is employed; drop time is 2 sec/drop in both techniques.

Precision.-Relative standard deviation, calculated by applying the recommended procedure 10 times to an eyewash sample containing 0.42 mg/ml of disodium salt of EDTA were 5.7% (DCP) and 4.2% (DPP), respectively.

The advantages of DPP over DCP, particularly in the simplicity of peak height measurements, the best precision and the possibility of determining lower concentrations, suggests that the DPP technique is the best for analysis of EDTA in ophthalmic products.

Table 3 summarizes the results obtained by DPP using the standard additions method in various commercial eyewashes, eyedrops and contact lens cleaning solutions. The amount found is the average of three determinations. The results obtained agree with the amount declared except in the case of a contact lens cleaning solution.

Table 3

Results for EDTA determination in commercial ophthalmic products
by differential pulse polarography

Type of sample	EDTA found (disodium salt) mg/ml	EDTA declared (disodium salt) mg/ml
Eye drops	0.46	0.50
Eye drops	0.99	1.0
Eye wash	0.42	---
Contact lens disinfecting and cleaning solution	0.07	0.1
Contact lens cleaning solution	2.24	1.0
Contact lens cleaning solution	0.45	---
Contact lens preserving solution	0.45	---

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(Received 3 March 1986)