Voltammetric Studies on Some Antihypertensive Drugs at Platinum test Electrode

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Summary: Labetalol (I) [36894-69-6] and methyldopa (II) [555-30-6] were determined in pharmaceuticals by performing voltammetry at platinum test electrode vs Ag/AgCl reference electrode in sodium hydroxide, potassium hydroxide, hydrochloric acid and acetic acid systems. These compounds followed Ilkovic equation linearly upto 5×10^{-4} mole/dm^3 with 98% reproducibility based on their oxidation potentials. Labetalol showed higher sensitivity in potassium hydroxide and sodium hydroxide, while methyldopa showed higher sensitivity in acetic acid system. Gold did not work when used as a test electrode. This method can be preferred to the reported methods for the determination of these drugs due to its better detection limits, reproducibility of the results, and less interference from dissolved oxygen.

Introduction

The history of labetalol (all-rac-2-hydroxy-5-(1-hydroxy-2-(1-methyl-3-phenylpropylamino)-eth -yl)benzamide hydrochloride) and methyldopa (3-(3, 4-dihydroxyphenyl)-2-methyl-L-alanine sesqui hydrate) is not so long. They have been used as antihypertensive drugs. Their characteristics were established with the development of modern drug research while searching knowledge about hypertension, a disease related to cardiac disorder [1]. Since blood pressure is controlled by cardiac output (related to heart beats/blood volumes) or total peripheral resistance (the arteriol resistance), an antihypertensive drug serves to maintain normal blood pressure by controlling resistance offered by these small arteries [2].

Labetalol and methyldopa as an antihypertensive agent in human plasma and urine were determined with different analytical methods like TLC, HPLC, GLC, and Mass spectroscopy [3-7]. Labetalol has shown antihypertensive action (in the cardiac muscles) when administered to dogs [8]. Different spectroscopic and electroanalytical methods have been used in the determination of these compounds [9-13]. In the electroanalytical methods, various techniques like pulse voltammetry and cyclic voltammetry have been reported in the determination of these drugs [14,15]. However, this determination was done at carbon paste electrode coupled with HPLC method. No direct voltammetric determination has been reported so far on these drugs while using platinum test electrode. The present study includes the determination of labetalol and methyldopa at platinum test electrode vs Ag/AgCl reference electrode. These compounds were also analysed quantitatively when their raw materials were used for pharmaceutical formulation.

Results and Discussion

Voltammetric study on labetalol in acetic acid, sodium hydroxide, and potassium hydroxide and methyldopa in hydrochloric acid and acetic acid showed oxidation potentials at platinum test electrode vs Ag/AgCl reference electrode. No reduction potential of these compounds was found in these supporting electrolytes at platinum test electrode. Similarly, gold electrode was found to be incapable for determining oxidation or reduction of these compounds in the above mentioned supporting electrolytes. Figure-1 shows the profiles of various concentrations of labetalol in acetic acid. Figure-2 gives the profiles of oxidation of Labetalol in potassium hydroxide. Figure-3 shows the profiles of oxidation of Labetalol in sodium hydroxide. The profiles of various concentrations of Methyldopa in hydrochloric acid are given in Figure-4. The profiles of oxidation of Methyldopa in acetic acid are shown in Figure-5. The values of I_d vs concentration of these compounds are given in Table-1 and 2. Figure-6 represents the comparison of the sensitivity of the determination of Labetalol in different supporting electrolytes for calibration pur-

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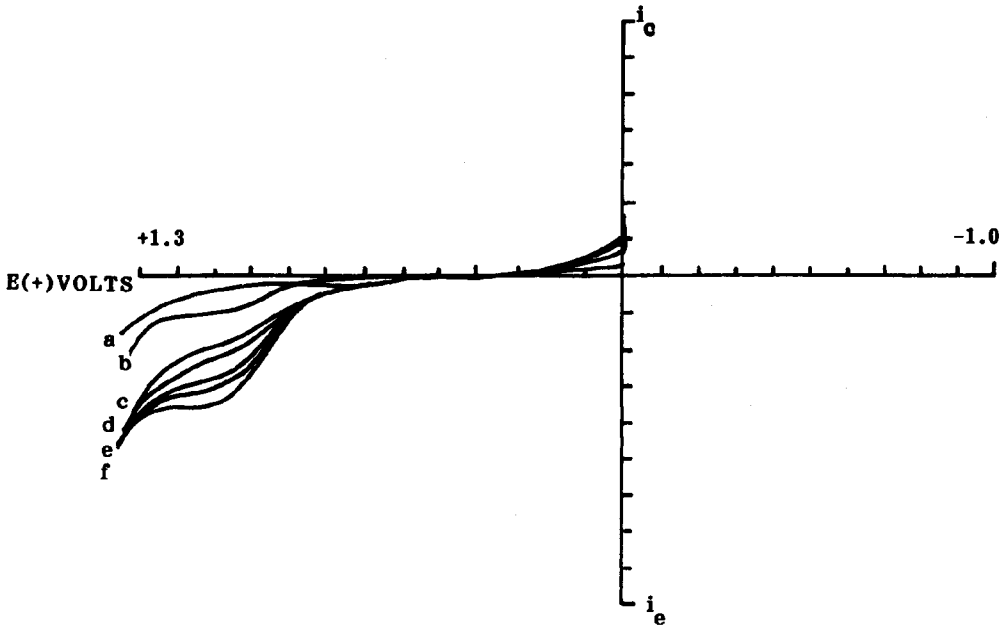

Fig. 1: Profiles of voltammograms of various concentrations of labetalol in acetic acid a = base-line b - f = concn 0.5 - 2.7 x 10^{-3} mole/dm^3

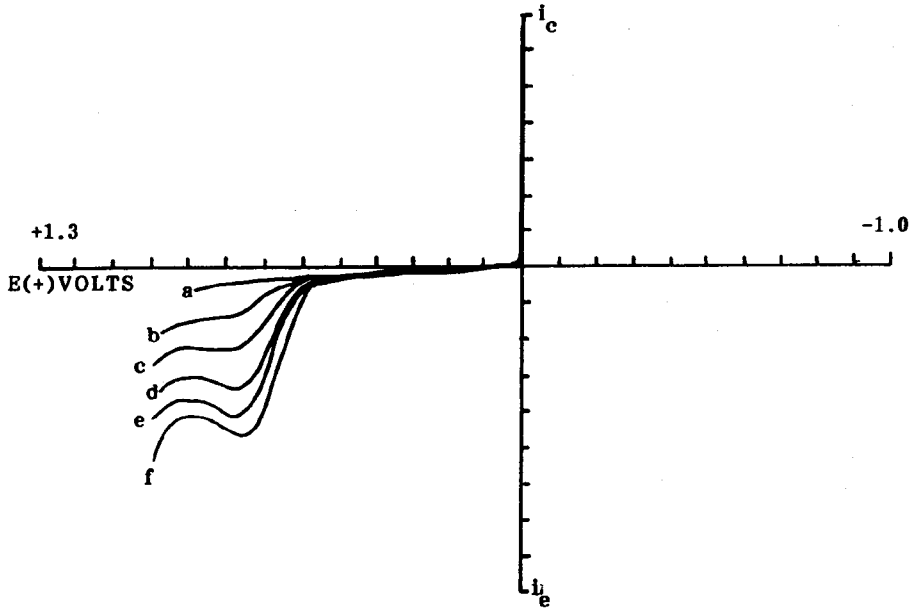

Fig. 2: Profiles of various voltammograms of labetalol in potassium hydroxide a = base-line b - f = concn 0.5 - 2.7 x 10^{-3} mole/dm^3

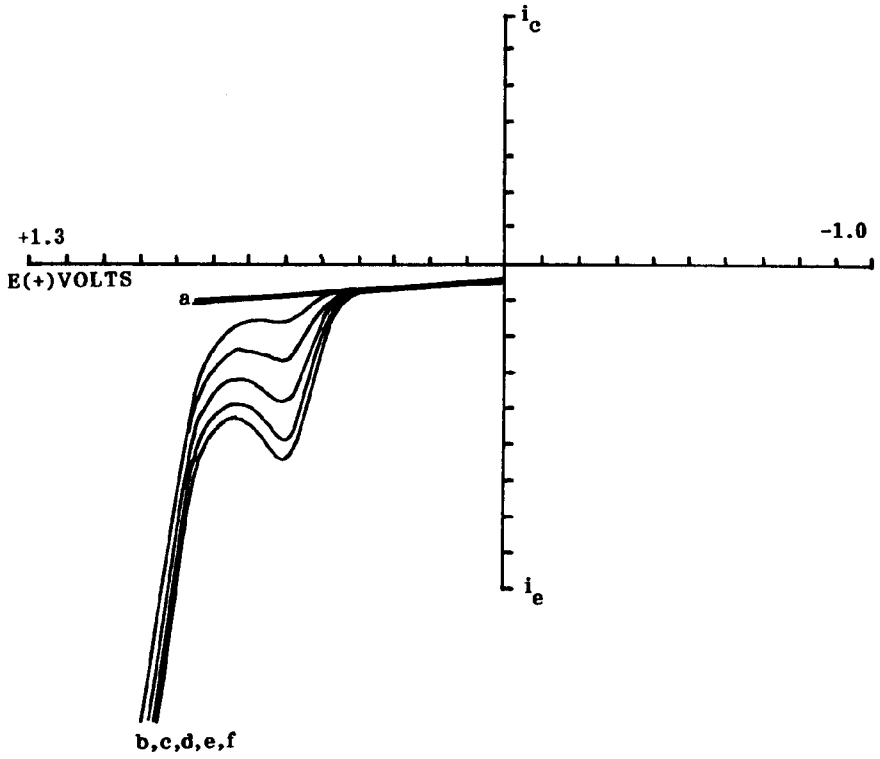

Fig. 3: Profiles of various voltammograms of labetalol in sodium hydroxide a = base-line b - f = concn 0.5 - 2.7 x 10^{-3} mole/dm^3

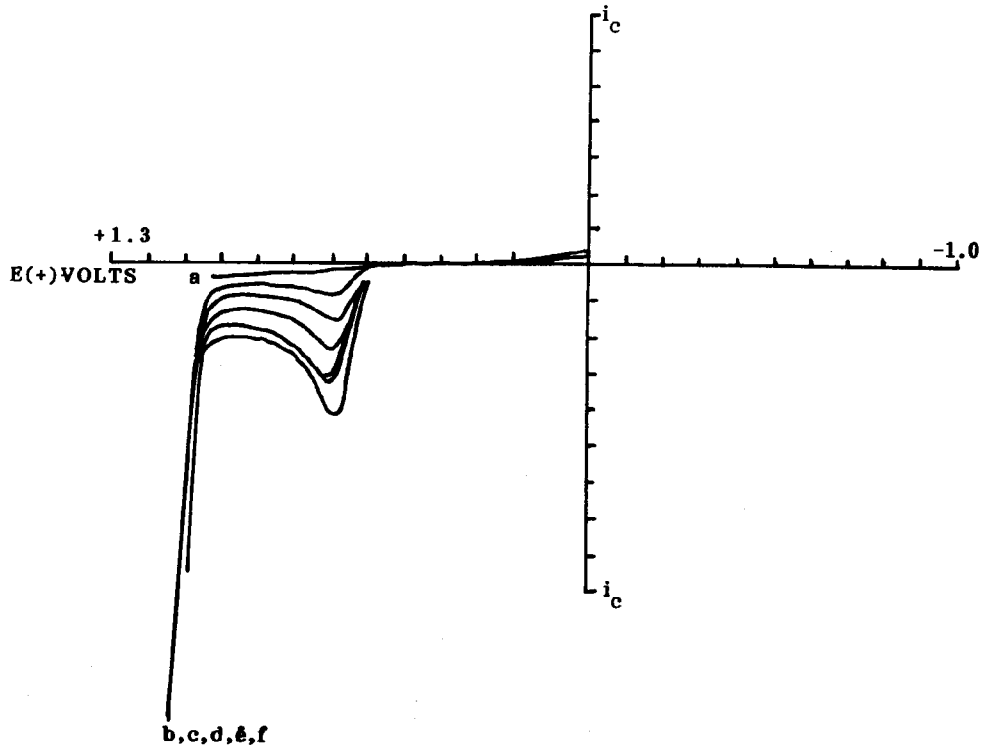

Fig.. 4 : Profiles of various voltammograms of methyldopa in hydrochloric acid a = base-line b - f = concn 0.8 - 4.2 x 10^{-3} mole/dm^3

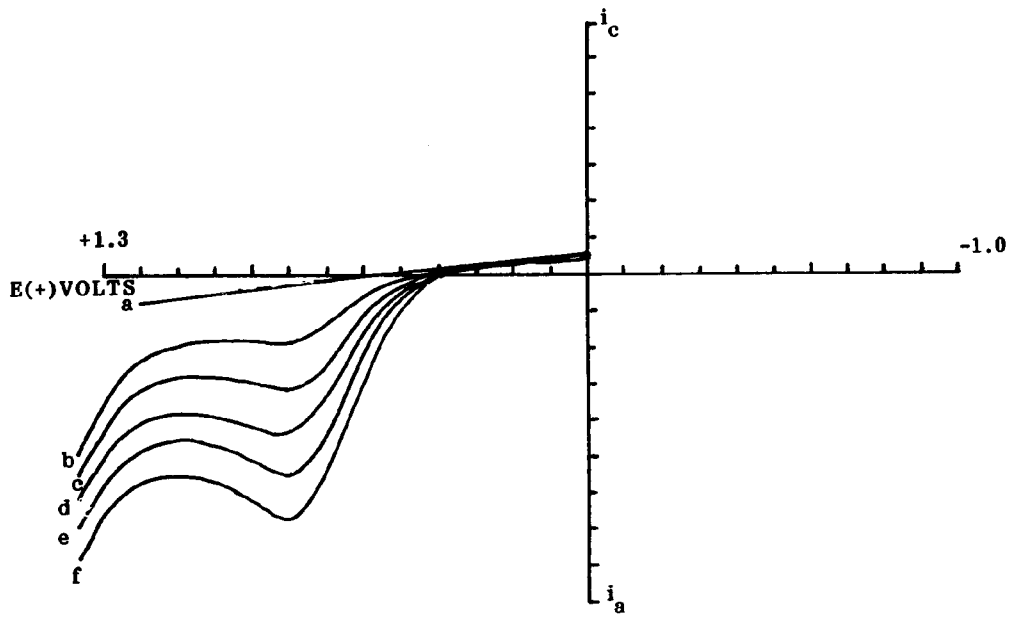

Fig.-5: Profiles of various voltammograms of methyldopa in acetic acid a = base-line b - f = concn 0.8 - 4.2 x 10^{-3} mole/dm^3

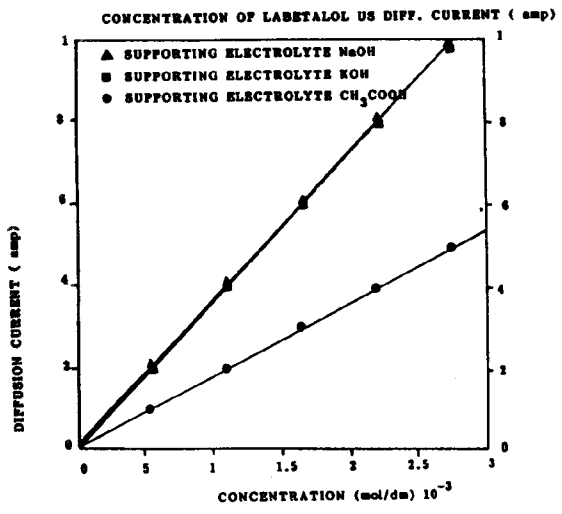

Fig.6

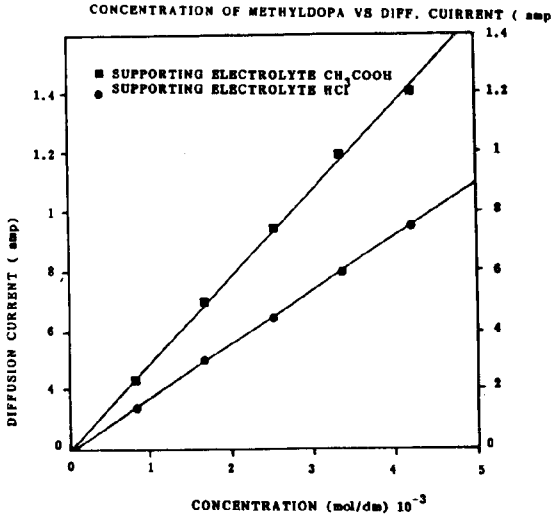

Fig.7

pose, while the sensitivity of Methyldopa in HCl and acetic acid is given for calibration purpose in Figure-7.

The base-lines obtained in these supporting electrolytes at gold and platinum test electrodes are straight and extended enough to determine oxidation of these compounds voltammetrically. In the comparison of lower detection limits of Labetalol in these supporting electrolytes, potassium hydroxide and sodium hydroxide showed higher sensitivity while acetic acid showed least response towards its determination as given in Figure-6. In these cases, the Ilkovic Equation was followed linearly upto 5 x 10^{-4} mole/dm^3 with 98% reproducibility (except in acetic acid). The sensitivity of detection of Methyldopa in acetic acid is high as compared to hydrochloric acid. Ilkovic Equation in this case was

Table 1: The response of diffusion current in various concentrations of Labetalol in given supporting electrolytes at platinum (test electrode) vs Ag/AgCl (reference electrode) at 30°C.

S.No.	Concenration	Diffusion Current I_d (μ amp)		
	$mol/dm^3 \times 10^3$	NaOH	KOH	CH_3COOH
1	0.5481	0.193	0.205	0.100
2.	1.0962	0.395	0.405	0.197
3.	1.6443	0.597	0.609	0.297
4.	2.1924	0.798	0.804	0.392
5.	2.7405	0.980	0.980	0.491

Table 2: The response of diffusion current in various concentrations of methyldopa in given supporing electrolytes at platimum (test electrode) vs Ag/AgCl (reference electrode) at 30°C.

S.No.	Concentration	Diffusion current I_d (μ amp)	
	$mol/dm^3 \times 10^3$	HCl	CH_3COOH
1.	0.8396	0.140	0.235
2.	1.6790	0.302	0.500
3.	2.5189	0.450	0.740
4.	3.3590	0.602	0.998
5.	4.1982	0.750	1.206

Table 3: comparison between reported methods and the present method for the determination of antihypertensive drugs.

No.	Drug's name	Detection limits	Method
1	Labetalol	25 μ g/ml	Colorimetry [9]
2	Labetalol	10 - 80 μg/ml	Fluorimetry [18]
3	Labetalol	1 ng/ml	HPLC [17]
4	Methyldopa	0.4 - 0.06 ng/ml	HPLC(Pulse voltam.[15]) (Fluorescence det.[19])
5	Labetalol	20 μg/ml	Present method
6	Methyldopa	20 μg/ml	Present method

followed upto 8×10^{-4} mole/dm^3. Labetalol showed $E_{1/2}$ = + 0.98 V in acetic acid but in sodium hydroxide and potassium hydroxide. The peak potential (E_p) is found to be + 0.6 and + 0.75 V respectively. Methyldopa showed E_p = + 0.79 V in acetic acid and + 0.68 V in hydrochloric acid. The interference from dissolved oxygen was not found to be significant as compared to other methods where it is much pronounced and needs special attention. The samples of these antihypertensive drugs (as raw material) were obtained from different pharmaceutical companies and were successfully determined voltammetrically at platinum test electrode. In Table-3, a comparison was made between the reported methods and the present method. This shows that the voltammetry at platinum test electrode meets lower detection limits as reported in spectrophotometric method [9]. However, HPLC technique coupled with voltammetric or other detectors improved the lower detection limits (upto 0.06 ng/mL see ref. [15]). On the basis of above results, voltammetric method can be used in the determination of these antihypertensive drugs in pharmaceutical formulations at platinum test electrode.

Experimental

Equipment

CV-1B Cyclic Voltammograph from Bioanalytical Systems (BAS), Inc., USA, was used for recording voltammograms. However, linear scan voltammetry was performed at this instrument. An XY chart recorder Omnigraphic, Houston Instruments, USA, was coupled with cyclic voltammograph. Platinum and gold test electrodes and Ag/AgCl reference electrodes (BAS) were used in this study.

Reagents

Stock solution of Labetalol 3.0×10^{-3} mole/dm^3 (E. Merck) was prepared in acetic acid 10^{-2}mol/dm^3(E.Merck), potassium hydroxide 10^{-2} mole/dm^3 (E. Merck), and sodium hydroxide 10^{-2} mole/dm^3 (E. Merck). Methyldopa 4.5×10^{-3} mole/dm^3 (E. Merck) was prepared in HCl 10^{-1} mole/dm^3 (E. Merck) and acetic acid 10^{-2} mole/dm^3(E. Merck). All reagents used were of analytical reagent grade and the solutions were prepared in double-distilled water.

Procedure

The three electrodes assembly consisting platinum or gold test electrode, platinum counter electrode, and Ag/AgCl reference electrode alongwith purge and blanket tubes (for nitrogen flushing) were placed in the voltammetric cell vial. Supporting electrolyte was taken in the cell and nitrogen was purged for three minutes to have inert atmosphere. The scan rate was kept at 100 mv/s, initial potential at 0 volt and current sensitivity at 2 micro ampere. The key was turned to blanket position (to blanket the surface of test solution) before starting the potential scan. The scan direction was turned to +ve. (for oxidation). Base-lines were recorded in each supporting electrolyte before

studying the voltammetric behaviour of these drugs at 30 + 1°C. Each time fresh solution was taken in the cell. After taking each voltammogram, the surface of the platinum or gold test electrode was renewed (cleaned)by placing the test electrode in chromic acid solution [16] for five minutes followed by repeatedly washing with distilled water and finally drying with Whatman 42 filter paper.

Conclusion

The present method was found to be easy and useful due to its better detection limits as required in pharmaceutical formulations. Platinum test electrode offered less interference from dissolved oxygen, ease in surface renewal, and reproducibility of the results.

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