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Voltammetric determination of droperidol and benperidol

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Abstract

In this study two butyrophenones, droperidol and benperidol were voltammetrically investigated using platinum and specially activated glassy carbon electrodes. The behaviours of the substances were investigated in various electrolyte solutions having different pH values and by different scan rates. As a result of the studies it was shown that the quantitative determinations of the substances from their pharmaceutical preparations could be made rapidly and simply without any separation from the excipients. © 1997 Elsevier Science B.V.

Keywords: Droperidol; Benperidol; Platinum electrode; Glassy carbon electrode; Determination

1. Introduction

Droperidol and benperidol, the structure of which are given below, are the two members of the butyrophenone group. These widely used major tranquillisers are particularly useful in schizophrenic patients. The papers published relating to the electrochemical behaviour of butyrophenones generally cover studies of electro-reduction [1–3]. Bishop et al. [4] investigated the electro-oxidation of butyrophenones using rotating Pt and Au disc electrodes, and they reported that droperidol and benperidol showed anodic activity but, because of the adsorption of reaction products on the electrode surface, voltammetry was not a useful analytical method for a group of butyrophenones including droperidol and benperidol (Scheme 1).

Pap et al. [5] succeeded in voltammetric determination of droperidol and benperidol using a modified carbon electrode. Determinations have been reported with ion selective electrodes [6], by coulometry [7] spectrophotometry [8,9], high performance liquid chromatography [10–13]. Papers relating to the electro-oxidation of butyrophenones are very few.

In the present study electro-oxidation of benperidol and droperidol was investigated using platinum and specially activated glassy carbon electrodes in 0.1 M H_2SO_4 and phosphate and acetate buffers and a rapid and simple voltammetric method was developed for the determination of these drugs and applied to the pharmaceutical preparations.

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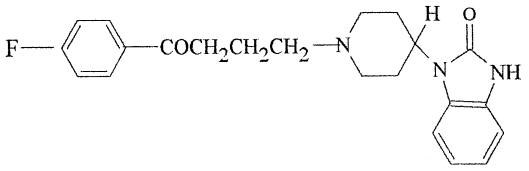
2. Experimental

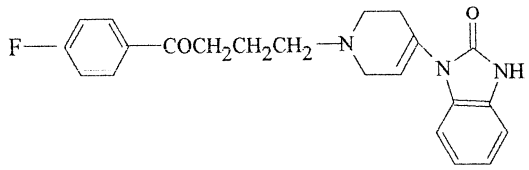
The measurements were taken and voltammograms were recorded with a PRG-3 polarograph and an EPL 2 recorder (Tacussel Electronique). A Pt wire electrode 1 mm in diammeter and 15.7 mm in length (Tacussel), and a glassy carbon electrode (Tacussel XM 540, area 1.013 cm^2) were used as working electrodes and a saturated calomel electrode (SCE) and a Pt wire electrode were used as the reference and counter electrodes respectively.

A special pretreatment procedure was applied to the glassy carbon electrode by means of a Wenking model 70 HP 10 potentiostat and Exact type 250 function generator.

Droperidol and benperidol were of drug standard grade. All other chemicals were of analytical grade. All solutions were prepared using doubly distilled water.



Benperidol



Droperidol

Scheme 1

Scheme 1. Molecular structure of droperidol and benperidol.

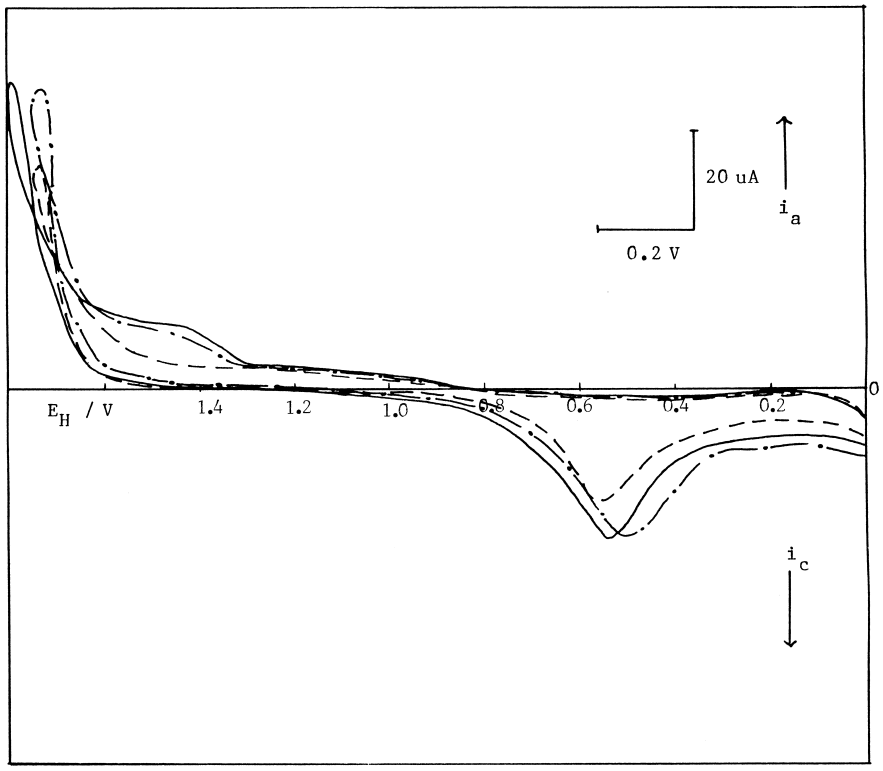


Fig. 1. Cyclic voltammograms recorded in 0.1 M H_2SO_4 with a platinum electrode. Scan rate 10 mV s^{-1}. – – – Supporting electrolyte; —— 4.10^{-4} M benperidol; -.-.-. 4.10^{-4} M droperidol.

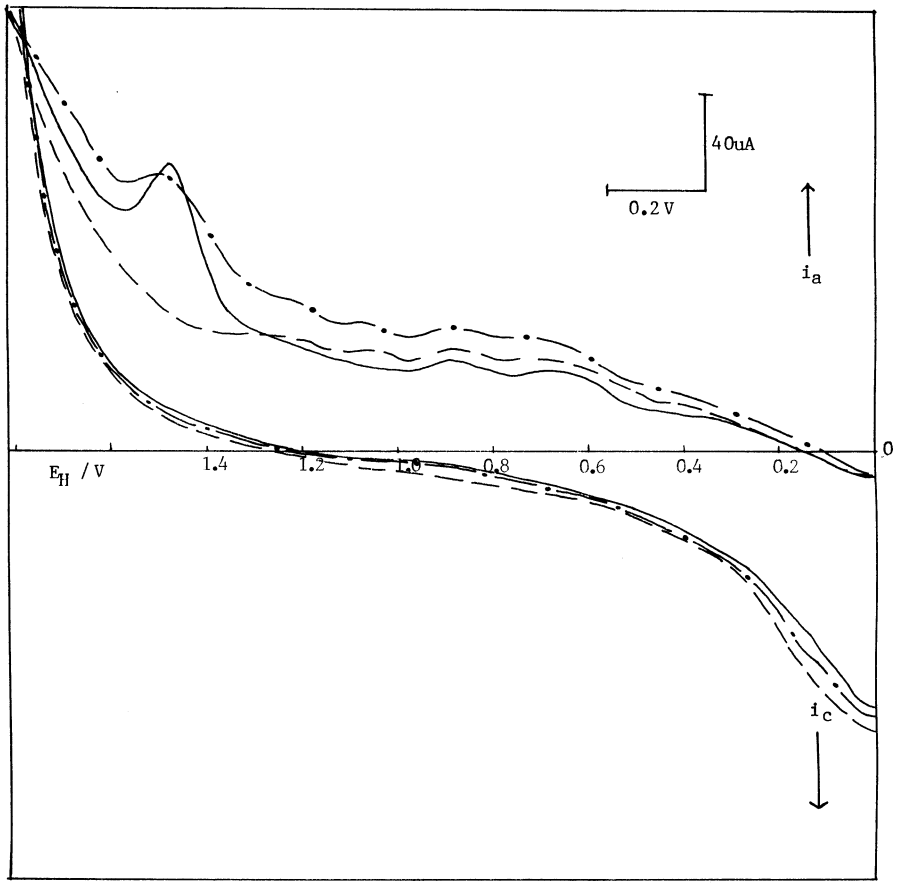


Fig. 2. Voltammograms recorded using a specially activated glassy carbon electrode in 0.1 M H_2SO_4. Scan rate 100 mV s^{-1}. – – – Supporting electrolyte; —— 2.10^{-4} M benperidol; -.-.-. 2.10^{-4} M droperidol.

3. Pretreatment of the electrodes

Glassy carbon electrode was pretreated mainly by the application of high frequency square wave and triangular potential signals repeatedly and an active and permanent surface state was obtained. Before each experiment the electrode was reactivated by applying a potential of 1500 mV for 5 min and -1000 mV for 2–3 s in 0.1 M KNO_3 solution. A detailed description of this pretreatment was given elsewhere [14].

The Pt electrode was electrochemically pretreated by the application of $+1250$ mV for 5 min and then maintaining a potential of $+150$ mV until the current became zero.

4. Results and discussion

Sulphuric acid solution of 0.1 M was chosen as the strong acidic medium. 10, 25, 50 and 100 mV s^{-1} were tested as scan rates and 10 mV s^{-1} was found as the optimum scan rate for the Pt electrode. The behaviours of droperidol and benperidol were found to be similar as their structures are quite similar. With the Pt electrode the oxidation begins at about 1300 mV and a limiting current region appears between 1400–1550 mV (Fig. 1). On the reduction branch a peak at about 550 mV was

The peak current of this peak was higher in the solutions of droperidol and benperidol than the

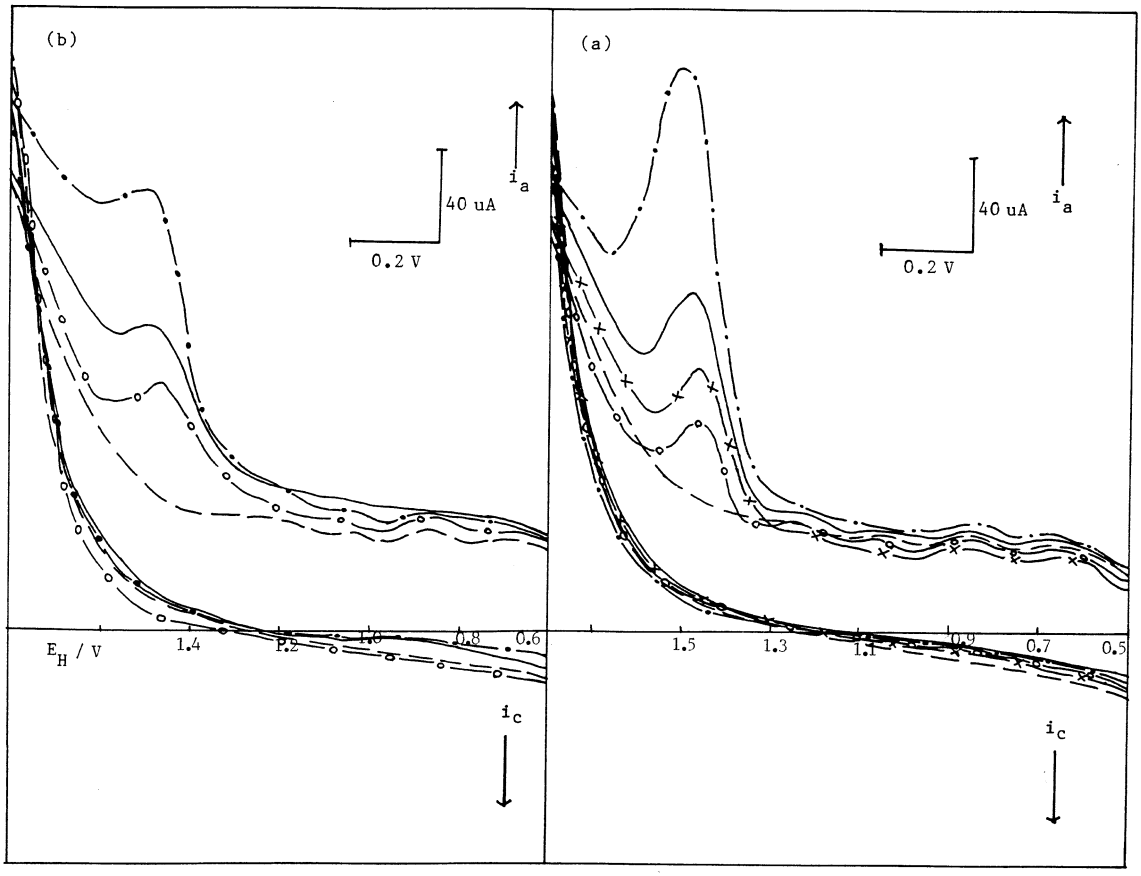


Fig. 3. Voltammetric curves obtained using a specially activated glassy carbon electrode in 0.1 M H_2SO_4 having different concentrations. Scan rate 100 mV s^{-1}. (a) - - - -, Supporting electrolyte; - o - o -, 6.10^{-5}; - x - x -, 1.10^{-4} M; ——, 2.10^{-4} M; -. -. -, 6.10^{-4} M benperidol. (b) - - - -, Supporting electrolyte; - o - o -, 8.10^{-5} M; ——, 2.10^{-4} M; -. -. - 6.10^{-4} M droperidol.

one related to the reduction of the surface oxides of Pt obtained in 0.1 M H_2SO_4. This indicates that the reduction of the substances took place together with the reduction of the surface oxides and the reactions are not completely irreversible.

The voltammogram recorded in 0.1 M H_2SO_4 having droperidol and benperidol in different concentrations showed that when the concentration was increased in the order of 2.10^{-4}, 4.10^{-4}, 6.10^{-4}, 8.10^{-4} and 1.10^{-3} M the increase in current was very small and an analytical evaluation was not possible. In acetate and phosphate buffers, also, good results could not be obtained.

The glassy carbon electrode was subjected to different pretreatments such as polishing with alumina, electrochemical oxidation and reduction and after each pretreatment voltammograms were taken and it was observed that the best results could be obtained with the specially pretreated glassy carbon electrode mentioned in [14]. With the glassy carbon electrode the optimum scan rate was 100 mV s^{-1}. Fig. 2 shows the voltammograms of droperidol and benperidol in 0.1 M H_2SO_4 solution. The oxidation potentials of the substances are the same but the shapes of the curves on Fig. 2 are different, in the case of benperidol a sharp peak is seen whereas droperidol shows a broad peak. The oxidation peak of droperidol has the same shape as that of the corresponding peak in Fig. 1. No peak appears on the reverse scan. The peak currents are linearly dependent on the concentration (Fig. 3a

Table 1
Characteristics of droperidol and benperidol calibration plots

Compound	Medium	Linearity range (M)	Slope μA M^{-1}	Intercept μA^{-1}	Correlation coefficient	S.E. of slope μA M^{-1}	S.E. of Intercept μA^{-1}
Droperidol	0.1 M H_2SO_4	8.10^{-5}–8.10^{-4}	1.11×10^5	49.64	0.9999	8.14×10^2	0.37
Benperidol	0.1 M H_2SO_4	6.10^{-5}–6.10^{-4}	3.02×10^5	18.95	0.9999	2.58×10^3	0.803
Benperidol	acetate buffer pH 5.2	8.10^{-5}–8.10^{-4}	1.88×10^5	2.85	0.9988	4.67×10^3	2.09

and b). The results of the statistical analysis of these linear relationships reveal that quantitative determinations of droperidol and benperidol can be made voltammetrically in 0.1 M H_2SO_4 solutions using a glassy carbon electrode (Table 1).

In acetate buffer of pH 3.7 and 5.2 the oxidation of both substances begins at less positive potentials than in the 0.1 M H_2SO_4 solution (Fig. 4a and b). In the solution of pH 5.2 the limiting current region for benperidol is well defined and the limiting current linearly increases with concentration in the case of benperidol but as can be seen from Table 1 the S.E. of the intercept is very high and this relationship is not helpful for analytical purposes. For droperidol there is no such linear correlation between current and concentration. In acetate buffer of pH 3.7 the increase in current is not enough for a quantitative evaluation for both substances. Table 1 shows the results of the linear regression analysis of the concentration limiting current relationship for benperidol and droperidol.

In phosphate buffers of pH 5.8 and 7.8 oxidation of benperidol and droperidol was observed at the same potentials as in the acetate buffers although the pH values of the solutions are not same.

The peak of benperidol was sharper than that of droperidol. Although the peak currents increased with concentration these increases for both substances were not enough for analytical purposes in both phosphate buffers.

5. Analytical application

The proposed voltammetric method was applied to the Frenactil® oral solution of benperidol. One ml of the solution corresponds to 1 mg of benperidol. 3.8 ml Of the drug was taken and diluted to 100 ml in a volumetric flask with the supporting electrolyte solution and the voltammogram of the solution was recorded. The voltammetric method was applied to the tablet form of droperidol called Dehidrobenzperidol®. One tablet contains 5 mg of droperidol. Ten tablets were weighed accurately and ground to a fine powder. A proper aliquot of droperidol was

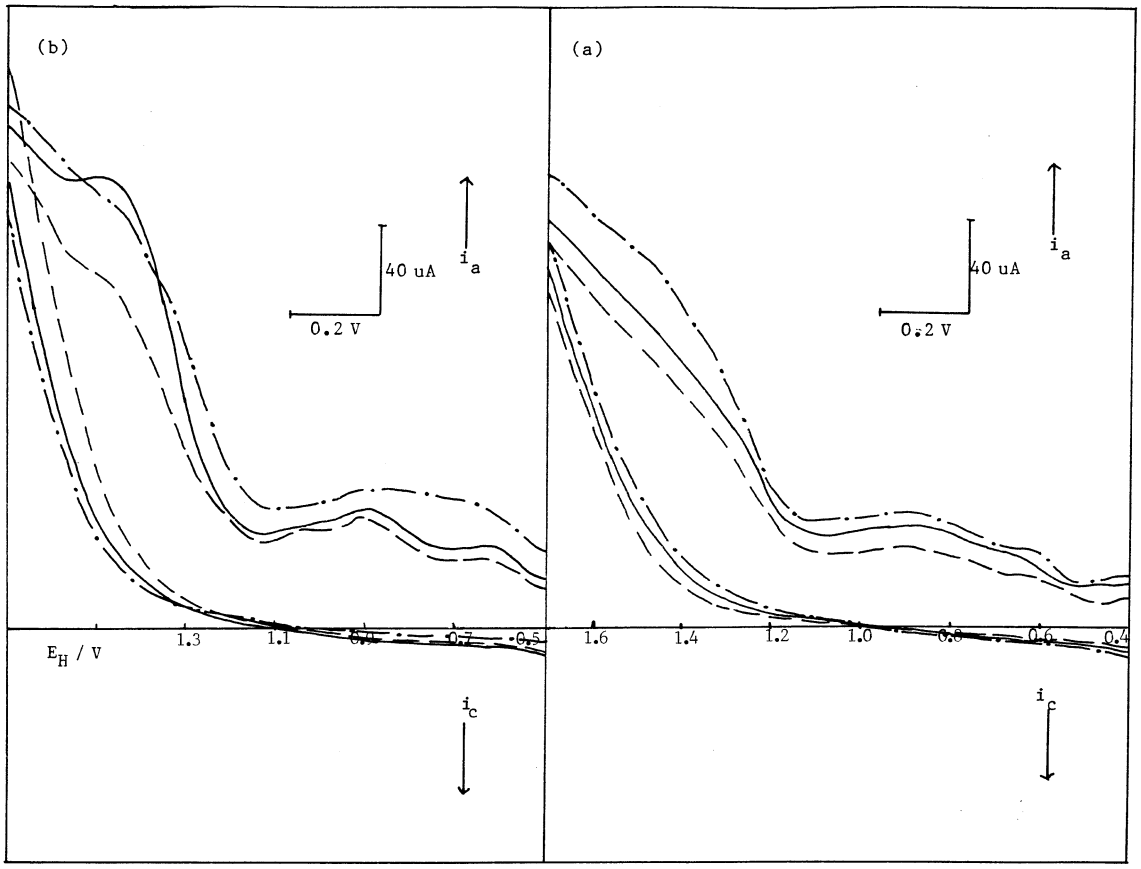


Fig. 4. Voltammograms of the specially activated glassy carbon electrode obtained in acetate buffer (a) pH 3.7; (b) pH 5.2; scan rate 100 mV s^{-1}. – – –, Supporting electrolyte; ——, 2.10^{-4} M, benperidol; -.-.-. 2.10^{-4} M droperidol.

Table 2
Assay of droperidol tablets and benperidol oral solutions by voltammetry at the activated glassy carbon electrode

Compound	Medium	Labelled claim	Amount found[a]	S.D. of amount found
Droperidol	0.1 M H_2SO_4	5 mg	4.9 mg	0.13
Benperidol	0.1 M H_2SO_4	15 mg per 15 ml	14.8 mg per 15 ml	0.44

[a] Each value is the mean of five experiments.

Table 3
Recovery studies by the proposed method at the activated glassy carbon electrode

Compound	Medium	Added (mg)[a]	Found (mg)[a]	S.D. of recovery (%)	Recovery[a] (%)	R.S.D. of recovery (%)
Droperidol	0.1 M H_2SO_4	30.4	29.7	1.45	98.0	1.48
Benperidol	0.1 M H_2SO_4	22.9	22.5	1.42	98.4	1.44

[a] Each value is the mean of five experiments.

weighed and diluted to 100 ml in a volumetric flask with 0.1 M H_2SO_4 solution and a 10^{-3} M droperidol solution was prepared and stirred for 30 min with a magnetic stirrer. Twenty ml of this stock was taken and 2.10^{-4} M of solution was prepared with the addition of 0.1 M H_2SO_4.

The voltammograms were recorded under the same conditions as the voltammograms of the standard substance. Table 2 shows the results of the analysis of droperidol and benperidol.

The method was checked by performing recovery tests as no standard method is given in the pharmacopoeias for both of the substances.

6. Recovery experiments

A portion of the finely mixed droperidol tablets corresponding to 18.9 mg of droperidol was accurately weighed and transferred into 100 ml calibrated flasks containing 70 ml of 0.1 M H_2SO_4 and 30.4 mg pure Droperidol was added and the contents of the flask were stirred for 30 min and diluted to volume with 0.1 M H_2SO_4 and then filtered. The appropriate solution was prepared by taking a suitable volume of this solution and voltammograms were recorded and recoveries after experiments were calculated. A 19.1 ml portion of benperidol formulation corresponding to 19.1 mg benperidol was accurately taken and transferred into 100 ml calibrated flasks, containing 70 ml of 0.1 M H_2SO_4 and 22.9 mg pure benperidol was added to the flask. The flask was stirred for 30 min and diluted with 0.1 M H_2SO_4 to volume. The solution was filtered and suitable aliquots were taken and proper solutions were prepared and voltammograms were obtained. Calculated recoveries are given in Table 3.

7. Conclusion

The proposed method proved to have adequate precision and accuracy to carry out reliable analy
sis of droperidol and benperidol. Moreover, no treatment of the sample is required before the voltammetric analysis. Excipients present in the tablet or oral solution do not interfere with the analyses. Finally, the developed voltammetric method is not time-consuming according to the above characteristics. This method is recommended as a useful tool for the analyses of droperidol and benperidol in pharmaceutical preparations.

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