

DETERMINATION OF PROBUCOLE BY SQUARE-WAVE VOLTAMMETRY

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1. Introduction

Today's medicine applies a lot of drugs as a preventative against different maladies. The amount of these substances must be strictly controlled in human bodies since their abnormal usage often produces undesirable effects. In this paper, a square-wave voltammetric method for quantitative determination of probucole is developed. Probucole (4,4'-[1-methylethylidene]bis(thio)]bis[2,6-bis(1,1-dimethyl)phenol] propionamide) (Figure 1) is an important drug which has been extensively used as a cholesterol lowering agent [1].

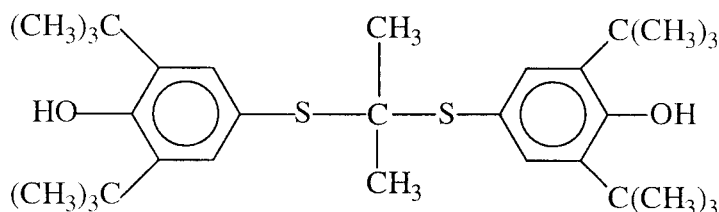


Figure 1. Molecular structure of probucole

Recently, its redox properties were investigated [2]. It was shown that probucole is both an electroactive and a surface active compound. The electrode reaction of probucole at the HMD electrode in an aqueous medium exhibits all characteristic properties of a redox reaction in which both species of the redox couple are strongly immobilized to the electrode surface. On the base of these features, an adsorptive stripping method for quantitative determination of probucole, applying square-wave voltammetry is developed.

2. Experimental

All chemicals used were of an analytical grade (MERCK). Water was doubly distilled. A stock solution was prepared by dissolving an appropriate amount of probucole in 96 % methanol. The supporting electrolyte was 0.1 mol/L solution of KNO_3 . All measurements were performed at room temperature. All experiments were carried out with a multi-mode polarographic analyzer PAR 384B equipped with PAR 303A Static Mercury Drop Electrode Assembly. The auxiliary electrode was Pt wire and Ag/AgCl (saturated KCl) was the reference electrode.

3. Results and discussion

Developing an adsorptive stripping voltammetric method, the most important parameters which affect the sensitivity of the proposed method appear to be the type and composition of the supporting electrolyte, accumulation time and potential as well as the parameters of the excitement signal.

The adsorptive stripping square-wave (ASSW) voltammetric response of probucrole was recorded in the following solutions: 1 mol/L KNO₃, 0.1 mol/L KNO₃, 0.1 mol/L CH₃COONa, 0.1 mol/L KOH, 0.1 mol/L KI, 0.1 mol/L KCl, 0.1 mol/L H₂SO₄ and 0.2 mol/L NaClO₄. In all these supporting electrolytes the ASSW voltammetric response of probucrole consisted of a single sharp peak at a potential of about -1.00 V. It should be emphasized that the peak potential E_p of the response is almost the same in all supporting electrolytes. However, the peak current i_p and half-peak width $\Delta E_{p/2}$ were sensitive to the type of the supporting electrolyte. The maximum ratio between the peak current and the half-peak width was observed in 0.1 mol/L KNO₃ indicating that this supporting electrolyte provides the most suitable conditions for quantitative determination of probucrole.

Figure 2 shows the dependence of the peak current of the ASSW voltammetric response of probucrole recorded in 0.1 mol/L KNO₃ on the accumulation time.

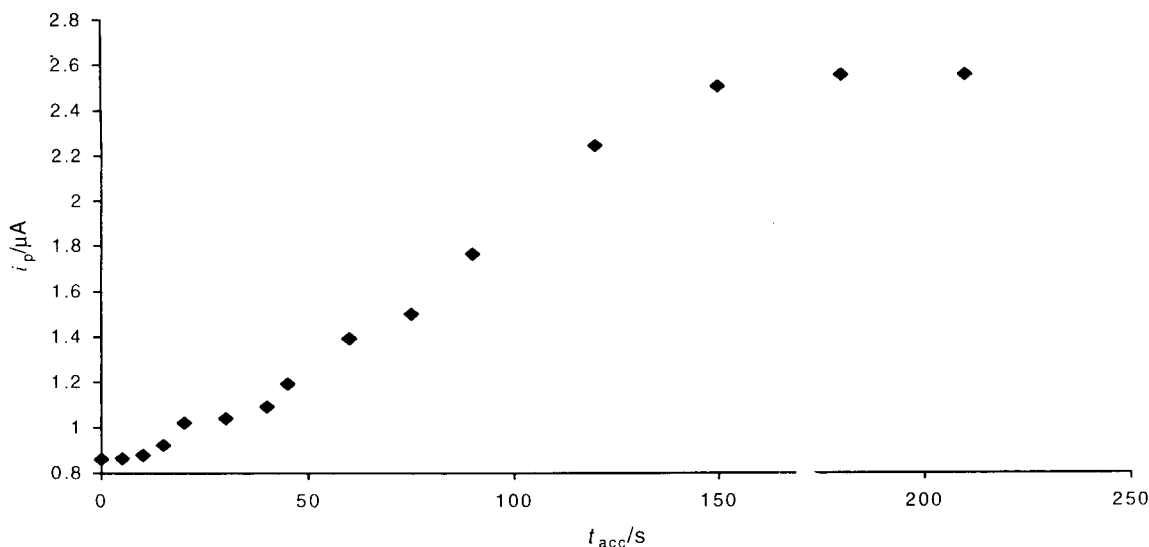


Figure 2. The dependence of the ASSW peak current of 5×10^{-5} mol/L probucrole solution recorded in 0.1 mol/L KNO₃ on the accumulation time. The parameters of the signal are: frequency $f = 120$ Hz, amplitude $E_{sw} = 20$ mV and scan increment $dE = 4$ mV.

The adsorption isotherm shows that after accumulation longer than 150 s the saturation of the electrode surface with molecules of probucrole occurs. The accumulation potential varied within the range from -0.4 to -1.00 V had no significant effect on both the peak currents and peak potentials of the response.

The ASSW voltammetric response of probucrole is rather sensitive on the composition of the supporting electrolyte. Figure 3 represents the effect of various amounts of methanol present in the supporting electrolyte on the ASSW peak current of probucrole. As can be seen from Fig. 3 a complex dependence was observed which can be approximated by a parabolic function. The highest response was obtained in the supporting electrolyte which contains 2.5 % (v/v) of methanol.

The specific effect of methanol on the peak current most probably appears due to its influence on the solubility of probucrole in the supporting electrolyte as well as on the strength of probucrole adsorption onto the HMDE surface. A low amount of methanol added in the supporting electrolyte

increases the solubility of probucole yielding an enhanced response (ascending part of the parabola). However, one should keep in mind that methanol is also a surface active compound. Hence, if the amount of methanol was higher than 2.5 % (v/v), a concurrent adsorption between methanol and probucole occurs causing the peak current to diminish (descending part of the parabola). This is an important result from an analytical point of view since one should expect a similar effect if some other surfactants were present in the sample or in the supporting electrolyte. Therefore, all further experiments were carried out in the 0.1 mol/L KNO₃ containing 0.25 mL methanol since this medium provides the highest sensitivity of the proposed method.

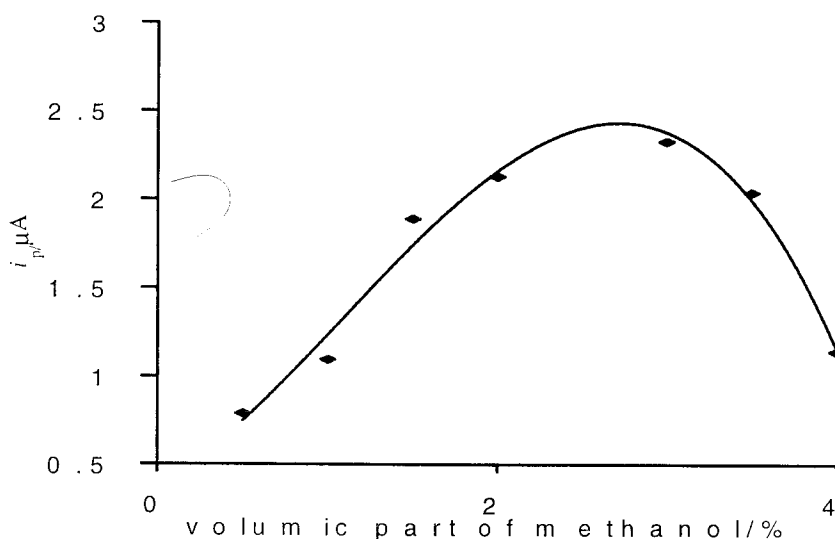


Figure 3. Effect of methanol on the ASSW peak current of probucole. The experimental conditions are the same as in the caption of the Fig. 2.

The ASSW voltammetric response of probucole is also affected by the parameters of the excitement signal such as the SW frequency f and the SW amplitude E_{sw} .

With an increase of the frequency from 10 to 120 Hz the peak current proportionally enhances, while the peak potential slightly shifts in a negative direction. The half-peak width remains virtually the same with the frequency. The ratio between the peak current and the half-peak width increases with the frequency reaching the maximum value at a frequency of 120 Hz. Therefore, this frequency value was explored for further measurements.

The SW amplitudes greater than 30 mV produces the phenomenon of a "split SW peak". In our previous publication [2], we demonstrated that if the surface redox reaction is fast and chemically reversible, under suitable experimental conditions the SWV response splits in two symmetrical peaks. This phenomenon was explored for entire characterization and kinetic measurements of the surface redox reaction of probucole [3]. However, from an analytical point of view the splitting of the response is an undesirable feature. Therefore, the amplitude of 20 mV, which produces a single SW peak was used for analytical measurements of probucole.

From the results presented above it can be concluded that the optimal experimental conditions for the determination of probucole with adsorptive stripping square-wave voltammetry are as follows: supporting electrolyte 0.1 mol/L KNO₃ containing 2.5 % (v/v) methanol; accumulation potential -0.8 V; SW frequency $f = 120$ Hz and SW amplitude $E_{sw} = 20$ mV.

With an accumulation of 60 s a linear calibration plot was constructed at a concentration level of 10^{-7} mol/L (Fig. 4). The correlation coefficient of the linear regression line is $R^2 = 0.99$. The detection limit of the proposed method is 2×10^{-7} mol/L and the reproducibility of the results in the term of relative standard deviations are ranged from 1.2 to 4.7 %.

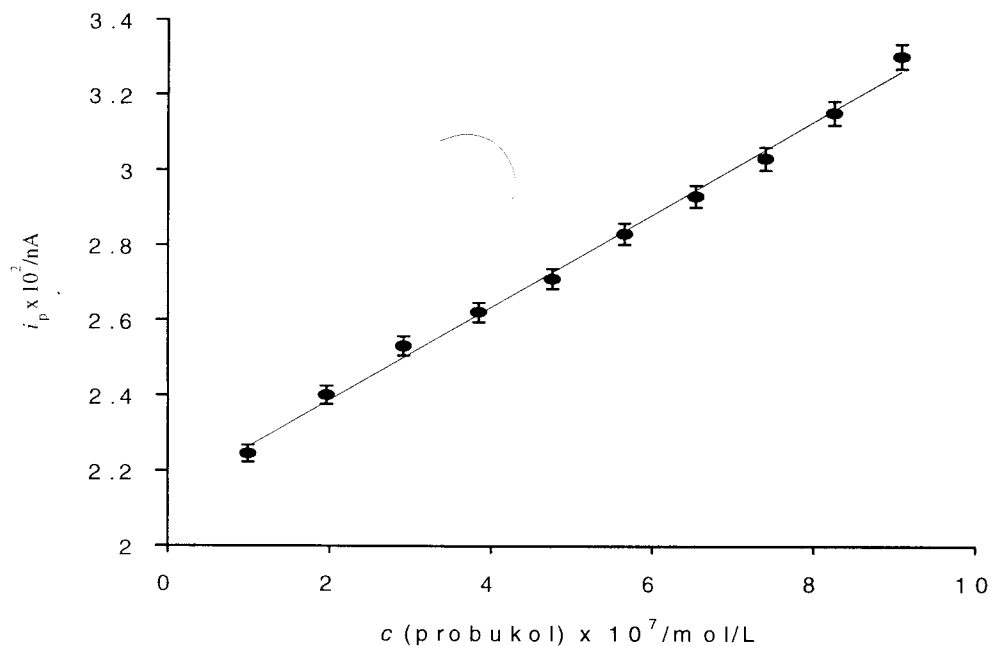


Figure 4. Calibration curve for probucole. Supporting electrolyte was 0.1 mol/L KNO_3 and containing 2.5 % (v/v) methanol. Accumulation time $t_{\text{acc}} = 60$ s. Other conditions as in the figure 2.

References

- [1] E. Mutscheler, H. Derendorf, *Drug. Actions, Basic Principles and Therapeutic Aspects*, MedPharm Scientific Publishers, Stuttgart, 1995, p. 425.
- [2] V. Mirčeski, M. Lovrić, *Electroanalysis*, 9 (1997) 1283.
- [3] V. Mirčeski, M. Lovrić and B. Jordanoski, *Electroanalysis*, 11 (1999) 660.

Апстракт. Разработена е квадратно-бранова волтаметриска метода за квантитативно определување на пробукол на стационарна живина електрода. Пробуколот (4,4'-[(1-methylethylidene) bis (thio)] bis-[2,6-bis (1,1-dimethyl) phenol] претставува важно фармаколошко соединение со антихиперлипипротейнски својства. Пробуколот е електроактивно и површински активно соединение со потенцијал на редукција на стационарна живина електрода од околу $-1,00$ V во однос на Ag/AgCl (заситен раствор од KCl). Механизмот на редукција на пробуколот на стационарна живина електрода спаѓа во редот на површинските редокс реакции. Извршена е оптимизација на експериенталните параметри за квантитативно определување на пробукол. Границата на детекција на пробукол изнесува 3×10^{-7} mol/L, додека репродукцибилноста на методата се движи во граници од 1,2 до 4,7 %.