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Short Communication

Silver electrode in direct potentiometric determination of propylthiouracil in pharmaceutical dosage form*

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Introduction

Propylthiouracil (6-propyl-2-thiouracil) and a number of thiourea type compounds inhibit the formation of thyroid hormones and are used for the treatment of hyperthyroidism. Several different analytical methods for the determination of propylthiouracil have been described. Polarographic [1, 2], conductometry [3], potentiometric [3–5] and spectrophotometric [6, 7] methods are particularly suitable for the assay of small amounts of propylthiouracil in pharmaceutical formulations. In biological fluids propylthiouracil has been determined by liquid chromatography [8–10] and by spectrophotometric [11].

Experimental

Reagents

Propylthiouracil (Aldrich, USA) was commercially available. The compounds were recrystallized from hot water and dried at 80°C, m.p. 220°C. IR spectrum in cm^{-1} (Nujol mull) at 3100 (NH); 1650 (C=O); 1550, 1240, 1190. The substance was characterized by UV, IR, NMR and elemental analysis, as 99.8%.

Propiultiouracil tablets. The tablets were obtained from Alkaloid (Skopje). Each tablet nominally contained 50 mg of propylthiouracil. All other chemicals were analytical grade (Merck). Double-distilled water was used.

Solutions

For analytical purposes a freshly prepared 10^{-2} M aqueous solution of pure propylthiouracil in 0.4 M NaOH was used as the standard solution. It was stable for several days. Britton–Robinson buffer solutions [12] and standard palladium(II) chloride solution [13] were the same as those described previously.

Apparatus

A PHM 62 Standard pH-meter (Radiometer, Copenhagen) with a silver indicator electrode connected to saturated calomel reference electrode by an electrolytic agar bridge was used.

To analyse the tablets, ten tablets were powdered. A weighted amount of powder was dissolved in water, 0.21 ml 0.4 M NaOH was added and diluted with water to 25 ml. The solution was 10^{-2} M. An aliquot (0.3 ml) of the tablet solution containing about 0.511 mg propylthiouracil was used in the same procedure as described for the calibration curve.

Procedure

Aliquots of the standard propylthiouracil

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Table 1
Potentiometric determination of propylthiouracil with palladium(II) chloride

Substance	Taken (mg)	Found ($\bar{x}$)	SD*	S$\bar{x}$†	RSD‡ (%)
Propylthiouracil§	0.340	0.3915	0.0051	0.0023	1.31
	0.511	0.504	0.0063	0.0028	1.25
	1.022	0.979	0.031	0.014	3.21
	1.360	1.371	0.042	0.019	3.10
Propiltiouracil‖ tablets	0.511	0.512	0.015	0.0048	2.99

* Standard deviation.
† Standard error of the mean value.
‡ Relative standard deviation.
§ Mean values of five titrations.
‖ Mean values of 10 titrations.

solution (0.05–1.00 ml) were taken in to a potentiometric cell, 20 ml Britton–Robinson buffer solution (pH 4.64) was added, the solution was diluted with 20 ml water and titrated against standard 10^{-2} M palladium(II) chloride. During the titration the solution was stirred continuously, the stirring being interrupted intermittently for readings. The end point was taken as the volume corresponding the maximum dE/dV, and was used in calculations. Between successive titrations the Ag electrode was rubbed with a clean towel to remove only formed film, then immersed 1–2 min in KCN solution (5×10^{-2} M) and finally rinsed with water.

Results and Discussion

Potentiometric titration of propylthiouracil with palladium(II) chloride have been performed in Britton–Robinson buffer solutions at pH range 2.55–8.07 forming a stable yellow water soluble complex. During the complex formation the potential of the electrode changed, and the most pronounced change was at the titration end point at which the stoichiometric ratio prophylthiouracil to palladium(II) was 1:1. A typical titration curve for this compound is shown in Fig. 1.

The effect of pH on potential changes during the titration were studied (Fig. 2). The most pronounced differences in potential were obtained in Britton–Robinson buffer at pH 4.64, and for that reason further work was done at this pH. The potential jump at the equivalent point of the titration under these conditions was about 120 mV.

A linear relationship between quantities of palladium(II) chloride and propylthiouracil consumed up to the end-point has been established over the range 0.08–1.70 mg. The

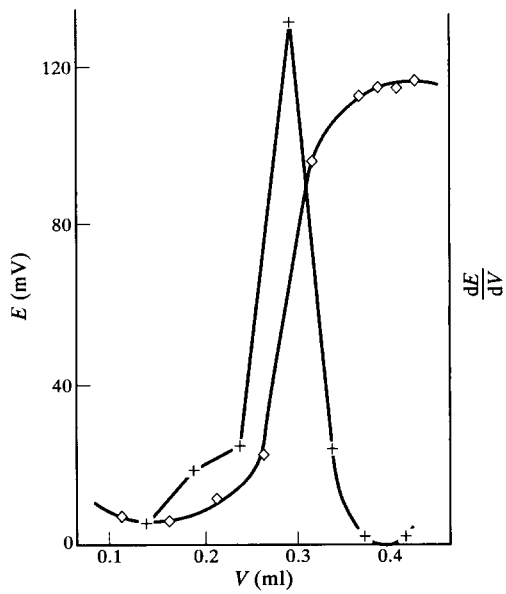

Figure 1
Potentiometric titration curve: 0.3 ml 10^{-2} M of propylthiouracil obtained by titration with 10^{-2} M palladium(II) chloride in Britton–Robinson buffer pH 4.64.

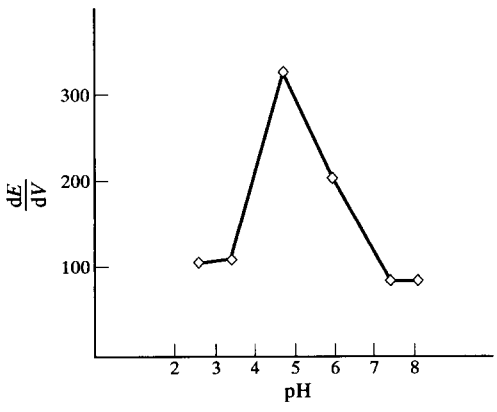

Figure 2
dE/dV dependence on pH at equivalent point of 0.3 ml 10^{-2} M propylthiouracil solution titrated with palladium(II) chloride 10^{-2} M in Britton–Robinson buffer solutions (pH 2.55–8.07).

regression line equation was $y = 2.29476x - 0.0192379$. The correlation coefficient, R, being equal to 0.9999 indicates excellent linearity.

The precision of the proposed method has been checked in a number of experiments carried out at four different concentration levels. The results of the analysis of propylthiouracil are presented in Table 1. The relative standard deviation varied from 1.25–3.21% for concentrations from 0.34 to 1.36 mg.

The applicability of the method for the assay of sample dosage forms was examined by analysing tablets *Propiltiouracil*. The results confirm the suitability of the proposed method for the routine analysis of propylthiouracil in a pure substance and in the dosage form.

References

[1] N.B. Tadros, A. Besada and Y.A. Gawargions, *Egypt. J. Pharm. Sci.* **30**, 241–250 (1989).

[2] J.M. Lopez, C. Gonzales Posa and P. Sanz. Pedrero, *An. R. Acad. Farm.* **47**, 161–169 (1981).

[3] K. Nikolić, B. Stanković and M. Bogavac, *J. Serb. Chem. Soc.* **59**, 385–389 (1994).

[4] M. Kucharski, H. Sikorska-Tomicka and T.H. Szumilo, *Zesz. Nauk. Politech. Biolostockiej, Mat. Fiz. Chem.* **7**, 81–88 (1981).

[5] S. Pinzauti, G. Papeschi and E. La Porta, *J. Pharm. Biomed. Anal.* **1**, 47–53 (1983).

[6] E.M. Mohamed, S.M. Tawakkol and Y.H. Aboul-Enein, *Chem. Biomed. Environ. Instrum.* **11**, 241–250 (1981).

[7] A. Besada, N.B. Tadros and Y.A. Gawargions, *Egypt. J. Pharm. Sci.* **30**, 251–261 (1989).

[8] C. Kim, *J. Chromatogr.* **272**, 376–379 (1983).

[9] H.G. Giles, R. Miller and E.M. Sellers, *J. Pharm. Sci.* **68**, 1459–1460 (1979).

[10] T. Onkubo, T. Uno and K. Sugawara, *J. Liq. Chromatogr.* **14**, 2745–2753 (1991).

[11] C.R. Ratliff and P.F. Grilliland, *Clin. Chem.* **18**, 1373–1378 (1972).

[12] J.A. Coch-Frugoni, *Gazz. Chim. Ital.* **87**, 403–407 (1957).

[13] T. Jovanović, B. Stanković and Z. Koričanac, *J. Serb. Chem. Soc.* **59**, 315–321 (1994).

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