THE POLAROGRAPHIC BEHAVIOR OF THALSIMINE

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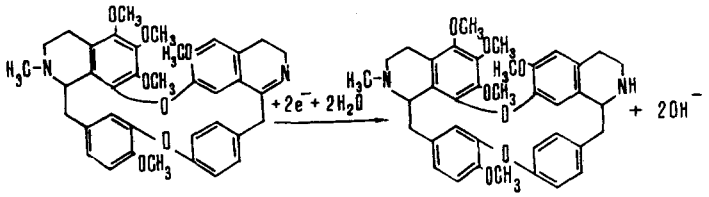
UDC 547.944/945+543.253.422

Thalsimine, isolated from the epigeal part of Thalictrum simplex [1, 2], is a pharmacologically active alkaloid [3]. The present paper gives the results of a polarographic study of thalsimine and of a chromatopolarographic determination of its amount in plant raw material.

In a study of the electrochemical properties of thalsimine at a dropping mercury electrode we found that, on a support of tetraethylammonium hydroxide in an aqueous alcholic medium, the alkaloid forms two waves: a diffusion wave with $E_{1/2} = -(1.40\text{-}1.45)$ V and a catalytic wave with $E_{1/2} = -(2.20\text{-}2.25)$ V. For analytical purposes we used the first wave, the limiting current of which is proportional to the concentration in the range from $1.5 \cdot 10^{-3}$ to $1.5 \cdot 10^{-4}$ M. The similar polarographic behaviors of thalsimine and its dihydrochloride in the region of working concentrations in $(C_2H_5)_4NOH$ enabled us to use a sample of thalsimine dihydrochloride as standard. In this case, in the calculation formula a correction factor is introduced which is equal to the ratio of the molecular weights of the alkaloid and its salt.

The number of electrons participating in the reaction of thalsimine was determined by polarographic microcoulometry [4] and was found to be two. Then it was assumed that it is the double bond of the dihydroisoquinoline ring that undergoes reduction and the product of the electrode reaction may be dihydrothalsimine. This assumption was confirmed by a comparison of the polarographic behavior of thalsimine and its synthetic dihydroderivative [5]. The latter showed no diffusion wave but retained the catalytic wave. The electrode process can be expressed by the following scheme:



It is characteristic that the reduction of the >C=N bond of thalsimine – a bimolecular compound – takes place at the same value of $E_{1/2}$ as the reduction of monomolecular compounds such as 3,4-dihydropapaverine and 3,4-dihydropapaveraldine [6]. Just like the latter, the alkaloid under investigation formed distinct two-electron diffusion waves in Britton–Robinson buffer solutions in the pH range from 3 to 10. The second, catalytic, wave of thalsimine on a support of $(C_2H_5)_4NOH$ decreased with an increase in the concentration of ethanol and supporting electrolyte and did not depend on the height of the mercury column above the dropping electrode.

To separate the thalsimine from accompanying alkaloids [7] we used thin-layer chromatography in a nonfixed layer of alumina in the benzene–acetate (8 : 2) system. On elution with chloroform, desorption amounted to 98-100 %. By this method we determined the amount of thalsimine in chloroform extracts from plant raw material (Table 1).

EXPERIMENTAL METHOD

The experiments were performed on an LP-55A polarograph. The characteristics of the capillary at h_{Hg} 45 cm were: $m = 0.76$ mg/sec^{-1}, $t = 3.5$ sec in 1 N KCl. An electrolyzer with an internal anode was used, and the temperature of the determinations was $25 \pm 0.5°$ C.

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR. Translated from Khimiya Prirodnykh Soedinenii, No. 3, pp. 387-389, May-June, 1975. Original article submitted March 26, 1974.

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TABLE 1. Results of the Quantitative Determination of Thalsimine in Raw Materials

Growth site and year	Sample	Amount of extract taken for analysis, ml	Thalsimine content	Mean	Deviation from the mean
			%		
Susamyr, KirgSSR, 1970	1	0,5	0,143		
	1	0,7	0,155	0,149	±4,03
	2	0,5	0,167		
	2	0,5	0,173	0,170	±1,76
Chon-Kemin, KirgSSR, 1972	1	0.5	0,155		
	1	0,5	0,152	0,153	±1,30
	2	0,8	0,147		
	2	0,5	0,155	0,151	±2,76

Analysis of Raw Material. A 20-g sample (weighed with an accuracy of 0.01 g) of the comminuted raw material (practicle size 1-40 mm) was wetted with 20 ml of 8% ammonia solution and stirred. The alkaloids were exhaustively extracted with chloroform in a Soxhlet apparatus. The extract was concentrated to 10-15 ml and was quantitatively transferred to 25-ml measuring flask, and its volume was made up to the mark with chloroform. A definite amount (0.5-1.0 ml) of the extract was deposited on a plate (13 × ×18 cm) with a nonfixed layer of alumina (activity grade II) and chromatographed in the system mentioned above. A chromatogram was run under the same conditions on a plate (9 ×18 cm) with a "marker" [0.1 ml of an ethanolic solution of thalsimine dihydrochloride (concentration 0.5 mg/ml)], and this was shown up in the moist state with Dragendorff's reagent. The section of sorbent corresponding to the thalsimine spot in the R_f 0.6 ± 0.05 region was eluted with 50 ml of chloroform in a Schott No. 4 funnel. The eluate was evaporated to dryness and the residue was dissolved in 2.5 ml of 0.1 N $(C_2H_5)_4NOH$ in 50% ethanol and polarographed with cathodic polarization of the dropping electrode of from −1.0 to −1.7 V. A standard solution of thalsimine dihydrochloride containing 0.5-0.8 mg/ml was polarographed under the same conditions. The amount of thalsimine (x, %) referred to the dry raw material was calculated from the formula:

$$x = \frac{10 \cdot 0,897 \cdot C_{st} \cdot H_x \cdot v_1 \cdot v_2}{p \cdot H_{st} \cdot v_3 \cdot (100 - h)},$$

where C_{st} is the concentration of the solution of the standard sample, mg/ml; H_{st} is the height of the wave for the standard substance, mm; H_X is the height of the wave of the substance being determined, mm; p is the weight of raw material, g; h is the moisture content of the raw material, %; v_1 is the volume of the chloroform extract, ml; v_2 is the volume of the solution in the electrolyzer, ml; v_3 is the volume of the chloroform extract deposited on the chromatogram, ml; 0.897 is the factor equal to the ratio of the molecular weights of the alkaloid and its salt (636.7/709.7).

SUMMARY

In a study of the polarographic behavior of thalsimine in an aqueous alcholic solution of $(C_2H_5)_4NOH$ it was found that the product of the electrode reaction is dihydrothalsimine.

A chromatopolarographic method for the quantitative determination of thalsimine in the epigeal part of Thalictrum simplex has been proposed.

LITERATURE CITED

1. Z. F. Ismailov, S. Kh. Maekh, and S. Yu. Yunusov, Dokl. Akad. Nauk UzbSSR, No. 12, 22 (1960).
2. N. M. Mollov, V. St. Georgiev, D. Jordanov, and P. Panov, Dokl. Bolg. Akad. Nauk, 19, No. 6, 491 (1966).
3. F. Sadritdinov, Farmakol. i Toksikol., No. 15, 588 (1969); and in: The Pharmacology of the Alkaloids and Cardiac Glycosides [in Russian], Tashkent (1971), p. 122.
4. A. G. Stromberg and T. M. Markacheva, Zh. Obshch. Khim., 28, 671 (1954).
5. S. Kh. Maekh and S. Yu. Yunusov, Khim. Prirodn. Soedin., 188 (1965).
6. M. Maturova, Tschu Shun, I. Ctvrtnik, and F. Santavy, Collection Czech. Chem. Commun., 25, 3321 (1960).
7. S. Kh. Maekh. Z. F. Ismailov, and S. Yu. Yunusov, Khim. Prirodn. Soedin., 393 (1968).