THE QUANTITATIVE DETERMINATION OF FOETIDINE

D. A. Rakhimova, E. K. Dobronravova,
and T. T. Shakirov

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The alkaloid foetidine, isolated from the epigeal part of Thalictrum foetidum, family Ranunculaceae [1], is used in medicine in the form of the dihydrochloride.

In the present paper we give the results of a chromatopolarographic determination of foetidine in a chloroform extract from plant raw material and of a spectrophotometric determination of the preparation in tablets.

A study of the electrochemical properties of foetidine at a dropping mercury electrode showed that the alkaloid does not give diffusion waves but forms distinct catalytic waves in $(C_2H_5)_4NOH$. The existence of a linear relationship between the magnitude of the limiting current and the concentration of catalyst in the solution permits quantitative determination to be performed. In the range of concentrations of 0.3 to 0.03 mM on a support of 0.01 N $(C_2H_5)_4NOH$ in 5% ethanol the polarographic indices of foetidine and its dihydrochloride are identical (Table 1).

We have established that the limiting current of the catalytic wave of foetidine does not depend on the height of the mercury column above the dropping electrode, and it decreases with an increase in the concentration of the supporting electrolyte and of the organic solvent.

The polarographic waves of foetidine have a characteristic humped shape; for analytical purposes we measured the maximum current of the wave, which is proportional to the limiting current [2]; the concentration of the alkaloid was determined by the method of standard solutions [3]. The identical polarographic behaviors of foetidine and its salt in the range of working concentrations in $(C_2H_5)_4NOH$ permitted us to use as standard a sample of foetidine dihydrochloride satisfying the requirements of MRTU (Interrepublican Technical Specification). The appropriate correction factor, equal to the ratio of the molecular weights of the alkaloid and its salt, was introduced into the calculation formula.

To separate the foetidine from the accompanying alkaloids [1, 4] we used thin-layer chromatography on a nonfixed layer of neutral alumina [5] in the benzene–ethanol–acetone (8 : 0.5 : 5) system. On elution with chloroform, 98-100% desorption was achieved. The chromatographic separation of the extract freed

TABLE 1

c, mM	Foetidine				Foetidine dihydrochloride			
	c, mg/ml	i, μA	$K=\frac{i}{c}$	$E_{1/2}$, V	c, mg/ml	i, μA	$K=\frac{i}{c}$	$E_{1/2}$, V
0,40	0,280	5,41	13,42	−2,02	0,308	6,04	15,08	−2,02
0,32	0,224	4,24	13,25	−2,03	0,246	4,45	14,03	−2,03
0,28	0,198	3,87	13,82	−2,03	0,214	3,87	13,82	−2,04
0,24	0,168	3,34	13,92	−2,05	0,187	3,34	13,92	−2,05
0,16	0,112	2,22	13,87	−2,04	0,123	2,22	13,87	−2,03
0,10	0,070	1,38	13,80	−2,05	0,077	1,38	13,80	−2,03
0,08	0,056	1,11	13,87	−2,04	0,061	1,12	13,60	−2,05
0,06	0,042	0,82	13,67	−2,05	0,046	0,82	13,67	−2,03
0,04	0,028	0,53	13,25	−2,04	0,031	0,56	13,60	−2,05
0,03	0,021	0,41	13,67	−2,05	0,023	0,41	13,67	−2,05

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TABLE 2

Growth site of the sample	Repetition	Amt. of extract taken for analysis, ml	Foetidine content	Mean	Deviation from the mean
			%		
Chon-Kemin, KirgSSR			1970		
	1	0,3	0,148	0,153	±3,27
	2	0,4	0,158		
			1971		
	1	0,5	0,085	0,090	±5,55
	2	0,3	0,095		
Susamyr, KirgSSR			1970		
	1	0,3	0,180	0,170	±5,88
	2	0,5	0,160		
			1971		
	1	0,3	0,210	0,215	±2,32
	2	0,5	0,220		

the foetidine from foreign alkaloids but did not completely eliminate other extractive substances; the chloroform eluates in our experiments were always colored. To check the influence of the extractive substances on the polarographic indices of foetidine, extracts with different amounts of these substances from the raw material from different growth sites were analyzed (Table 2).

The results of the analysis showed that the catalytic wave of foetidine is sufficiently specific for analytical use. To evaluate the accuracy of the method, foetidine was determined in extracts from plant material with the addition of the pure alkaloid to them. The relative error of three determinations did not exceed ±6.0%.

The UV spectrum of foetidine dihydrochloride, like that of foetidine itself [1], has three maxima, at 220, 280, and 350 nm (log ε 4.80, 4.36, 4.24). We used the maximum at 280 nm. In the range of working concentrations the absorption of solutions of the preparation obey the Bouguer–Lambert–Beer law. The relative error of the spectrophotometric determinations is ±2.0%.

EXPERIMENTAL

The work was performed on an LP-55A polarograph and an SF-4 spectrophotometer. 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±0.5°C.

Analysis of the Raw Material. An accurately weighed 10-g sample of the air-dry raw material previously moistened with 10 ml of 8% ammonia solution was exhaustively extracted with chloroform in a Soxhlet apparatus. The extract was concentrated to a volume of 2-3 ml and was quantitatively transferred to a 10-ml measuring flask and made up to the mark with chloroform. The extract, in amounts of 0.2-0.5 ml, was transferred to a plate (13 × 18 cm) with a nonfixed layer of alumina and was chromatographed in the system mentioned above. A marker (foetidine hydrochloride) was deposited on the same plate, and the spots were revealed in the moist state with Dragendorff's reagent as modified by Munier [6]. The section of the sorbent corresponding to the spot of foetidine in the region of R_f 0.75±0.05 (the R_f values of foetidine and of foetidine dihydrochloride are identical) was eluted with 50 ml of chloroform in a Schott No. 4 funnel. The eluate was evaporated to dryness, and the residue was first dissolved in 1 ml of 50% ethanol, and then 8 ml of water and 1 ml of 0.1 N $(C_2H_5)_2NOH$ were added and polarography was performed with cathodic polarization of the dropping electrode from −1.5 to −2.6 V. A standard solution of foetidine hydrochloride containing 0.05-0.08 mg/ml was polarographed under the same conditions. The heights of the waves obtained with $E_{1/2}$ = −2.0 to −2.10 V were determined. The percentage of foetidine (x) on the dry raw material was calculated from the formula

$$x = \frac{0.905 \cdot 10 \cdot c_{st} H_x \cdot V_1 \cdot V_2}{p \cdot H_{st} V_3 (100 - k)},$$

where c_{st} is the concentration of the solution of the standard sample, mg/ml; H_x is the height of the wave of the substance being determined, mm; H_{st} is the height of the wave of the standard substances, 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; and 0.905 is a factor equal to the ratio of the molecular weights of the alkaloid and its salt (700.60/773.60).

Analysis of the Preparation. An accurately weighed sample of 0.5 g of the powdered tablets was extracted for 10 min with 60-70 ml of water in a 100-ml measuring flask, then water was added to the mark and the solution was filtered. A 1-ml portion of the filtrate was transferred to a 25-ml measuring flask and was made up to the mark with water. The optical density of the solution was measured at a wavelength of 280 nm in a cell with a layer thickness of 1 cm. In parallel the optical density of a solution of a standard sample of foetidine dihydrochloride containing 0.02 mg/ml was measured. This foetidine dihydrochloride was a sample satisfying the requirements of the MRTU. The amount of the substance (x, g) in one tablet was calculated from the formula

$$x = \frac{D_1 \cdot c_0 b \cdot V}{D_0 \cdot a \cdot 10000},$$

where D_1 is the optical density of the solution under investigation; D_0 is the optical density of the solution of the standard sample; c_0 is the concentration of the solution of the standard sample, mg/ml; a is the weight of powder, g; b is the mean weight of a tablet, g; and V is the dilution, ml; in our case V = 100 · 25 ml.

SUMMARY

1. On the basis of a study of the polarographic behavior of foetidine in $(C_2H_5)_4NOH$, a chromatopolarographic method for the quantitative determination of foetidine in the epigeal part of Thalictrum foetidium has been described.

2. A spectrophotometric method for the quantitative determination of foetidine dihydrochloride in tablets has been proposed.

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