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USE OF THE PHOTOMETRIC METHOD FOR THE QUANTITATIVE DETERMINATION OF VALIDOL IN TABLETS

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At present the quantitative determination of validol in tablets is conducted by a polarimetric method (State Pharmacopoeia, 10th edn., article 42-1181-78), which is relatively simple to carry out but nonspecific and possesses low sensitivity.

Thermonephelometric [1], UV spectrophotometric [2], and gas chromatographic [3] methods have been proposed for the quantitative determination of validol in tablets; however, for various reasons they have not found use in practice.

Validol (I), representing a 25-30% solution of menthol in the menthyl ester of isovaleric acid, forms a colored product in the reaction with aromatic aldehydes in the presence of concentrated sulfuric acid (State Pharmacopoeia, 10th edn., article 728). Earlier [4-6], a highly sensitive method of photocolorimetric analysis of crystalline menthol and its drug forms was developed using this reaction. The purpose of the present work was to refine the possibility of using a photometric method for the quantitative determination of I in tablets.

EXPERIMENTAL

The work was conducted on Hitachi (Japan) and SF-16a spectrophotometers. The reagents used were 1% solutions of p-dimethylaminobenzaldehyde (II) in concentrated sulfuric acid, diluted in 95% ethanol [4], which in the reaction with I and its components (menthol, menthyl and isomenthyl esters of isovaleric acid, menthyl ester of 2-methylbutyric acid and its isomer) gave colored solutions with absorption maximum at 554 nm.

The maximum color intensity at a 1:1.5 ratio of the volumes of solutions of I and the reagents is noted after 30 min and remains constant for no less than 2 h. At the same time, the color obtained at a 1:1 ratio of the volumes is unstable with time, and the optical density of the solution constantly decreases (see Fig. 1).

In the range of I concentrations in the working solution 2-20 μg/ml, the optical density obeys the Bouguer–Beer–Lambert law (Table 1).

The color observed in the reaction with components with the filler of the tablets (a mixture of powdered sugar and calcium stearate) has practically no effect on the optical density

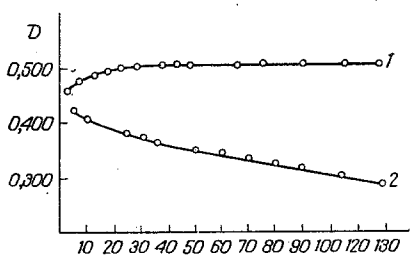

Fig. 1. Dependence of the optical density of colored products of the reaction of I with II at the time of their storage. Along x axis: time (in min); along y axis: optical density at 554 nm. 1) Ratio of the volumes of the investigated solution of I and reagent 1:1.5; 2) ratio of volumes of the investigated solution of I and reagent 1:1.

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TABLE 1. Dependence of the Optical Density of the Colored Product of the Reaction of I with II on the I Concentration

Concentration of solution of I, μg/ml	Optical density; D	Specific index of absorption, $E_{1\%}$	Metrological characteristics
2,0	0,085	425	$\bar{y}$ 428
3,9	0,165	423	
5,8	0,245	424	$S_{\bar{y}}$ 1,6
7,9	0,335	426	$t_p S_{\bar{y}} = 7,6$
10,2	0,430	423	$\bar{y} \pm t_p S_{\bar{y}} = 427 \pm 7,6$
12,2	0,520	425	
14,2	0,615	432	A_{rel} % ±1,8
16,3	0,712	436	
18,4	0,785	428	
20,4	0,890	436	

of the colored product of the reaction of I with II.

Method of Quantitative Determination of Validol in Tablets. About 1 g (exact weighed sample) of ground tablets of I is placed in an Erlenmeyer flask with a ground stopper and extracted with 95% ethanol according to the State Pharmacopoeia, 10th edn., article 42-1181-78. Then 1.3 ml of the extract obtained is transferred to a 60-ml volumetric flask, the volume in the volumetric flask brought up to the mark with distilled water, and the mixture mixed (test solution).

A 3-ml portion of freshly prepared 1% solution II in concentrated sulfuric acid is added to the test tube, then 2 ml of the test solution is added cautiously along the wall and mixed. After 30 min the optical density is determined on a spectrophotometer at 554 nm or on a photoelectrocolorimeter at the same wavelength in a cuvette with 5 mm layer thickness of the liquid. A mixture of 3 ml of a 1% solution of II in concentrated sulfuric acid and 2 ml of distilled water is used as the control solution. The optical density of a standard sample of I, prepared under the same conditions, is measured simultaneously.

Preparation of a Solution of a Standard Sample of Validol. About 0.1 g (exact weighed sample) of liquid I is dissolved in 95% ethanol in a 100 ml volumetric flask and brought up to the mark with alcohol (solution A). Then 1.3 ml of solution A is placed in a 50-ml volumetric flask and brought up to the mark with water (solution B). A 1-ml portion of solution B contains 0.000026 g/ml I.

The content of I in the tablets is calculated according to the formula

$$c = \frac{D_1 \cdot 50 \cdot 0,000026 \cdot a \cdot V}{D_0 \cdot B \cdot 1,3},$$

where D_1 and D_0 are the optical densities of the test and standard solutions, respectively; 0.000026 is the content of I (in g per ml of the standard solution); a is the average mass

TABLE 2. Results of Comparison of Methods of Analysis of I in Tablets

Series of tablets	Validol found, calculated per average mass of tablet									
	spectrophotometric determination, $\bar{y}$, mg	metrological characteristics				polarimetric density, termination, y, mg	metrological characteristics			
		$S_{\bar{y}}$	$E_{0,95}$	A	%		$S_{\bar{y}}$	$E_{0,95}$	A	%
1340677	61,9	0,742	1,91	61,9±1,9	3,08	61,4	1,45	3,73	61,4±3,7	±6,07
1870777	60,5	0,662	1,54	60,5±1,5	2,31	62,3	0,961	2,47	62,3±2,5	±3,97
420377	60,3	0 661	1,57	60,3±1,6	2,27	59,1	1,12	2,88	59,1±2,9	±4,87

Note. Average values of 5-6 determinations are given.

of the tablet (in g); V is the dilution of the solution to be analyzed (in ml); B is the weight of powder of the ground tablets of I (in g).

To establish the accuracy of the proposed method of determining I, an analysis was made of artificially prepared mixtures containing known amounts of I. In this case the relative error of the determination of I at the 0.95 probability level was ±2.39%.

The results of a comparative analysis of tablets of I by standard spectrophotometric and polarimetric methods (according to the State Pharmacopoeia, 10th edn., article 42-1181-78) show that the sensitivity of the spectrophotometric determination is greater (Table 2), and this method can be used for the analysis of I in tablets.

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