QUANTITATIVE DETERMINATION OF DEOXYPEGANINE HYDROCHLORIDE

A. Kh. Sattarova, E. K. Dobronravova,
and T. T. Shakirov

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A procedure has been developed for the quantitative determination of deoxypeganine hydrochloride by nonaqueous titration without the use of mercury acetate. A chromatospectrophotometric method of determining the oxypeganine hydrochloride in technical products has been developed.

Deoxypeganine is an alkaloid isolated from the herb *Peganum harmala* L. (harmel peganum), family Zygophyllaceae [1]. The hydrochloride of this alkaloid is used in medicine [2]. According to the existing standardization and technical documentation (STD), the quantitative determination of deoxypeganine hydrochloride (DH) is performed by an acidometric method based on the titration of the preparation in perchloric acid in glacial acetic acid with Crystal Violet as indicator. To eliminate interfering action of chloride ions mercuric acetate is added to the solution being titrated [3]. A disadvantage of this method of determination is the high toxicity of mercury salts.

In the present communication we give the results of the quantitative determination of DH as such and in medicinal form without the addition of mercuric acetate and propose a procedure for determining the main substance in the technical product.

Cases of the titration of salts of hydrohalic acids without a mercury salt have been described in the literature [3]; the determination was carried out in acetic anhydride. DH is practically insoluble in acetic anhydride, and we therefore used a mixed solvent: acetic acid—acetic anhydride with the optimum ratio of 1:25. The equivalence point of potentiometric indication coincides with the change in the color of the indicator. Results have been obtained by the method developed which did not differ from those of analysis carried out in accordance with the NTD:

Batch of a preparation	According to the STF	Concentration, %, according to the method developed	Metrological characteristics
11280	99.35	99,23	$n=6$, $f=5$
20581	99,90	99,38	$\bar{X}=99,85\%$
30681	99,86	99,23	$S^2=0,0379$
40482	99,15	99,15	$S=\pm 0,195$
50582	99,28	99,25	$P=95\%$
60982	99,27	99,42	$t\ (P,\ f)=2,57$
71282	99,60	99,32	$X=\pm 0,50$
80383	99,75	99,58	$E=\pm 0,50\%$
90383	100,07	100,08	
100583	99,50	100,00	

In the process of manufacturing the drug [4] the necessity arises for the analytical control of the process of purifying the technical product. We have developed a chromatospectrophotometric method which envisages the chromatographic separation of deoxypeganine from the accompanying alkaloids with its subsequent spectrophotometric determination in the eluate. A high-quality chromatogram of technical DH showed the presence of five alkaloids: deoxypeganine, peganine, vasicinone, deoxyvasicinone, and harmine. The separation of the DH from the accompanying alkaloids was effected in a fixed layer of silica gel in the solvent system chloroform—95% ethanol—ammonia (25:5:0.25); the revealing agent was the Dragendorff reagent, and the sensitivity of detection was 5 μg.

We have reported previously [5] that in the TLC of halide salts of alkaloids on alumina the salts decompose to form the bases, which migrate, and halide ion, which remains at the start. We have detected a similar phenomenon on silica gel. Consequently, on using in

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spectrophotometry as the solution of a standard sample DH satisfying the requirements of the current STD we introduced into the formula for calculation a factor equal to the ratio of the molecular weights of DH and of free deoxypeganin (1.175).

In the UV spectrum of DH (0.002% aqueous solution) in the range from 220 to 320 nm there is an intense absorption band with its maximum at 278 ± 3 nm (log ε 3.82). The absorption of solutions of DH in the range of working concentrations (0.08-0.005 mg/ml) obeys Beer's law.

When a number of solvents were tested for the desorption of DH from a plate, it was found that the most suitable eluent was a mixture of acetic acid and water with the optimum ratio 1:9. The completeness of the desorption of the alkaloid from the silica gel was checked by chromatographing known amounts of the preparation followed by elution and spectrophotometry of the eluate.

The results of the determination of the desorption of DH are as follows:

Eluent	Desorption, %	Absorption, maximum, nm
95% ethanol	52-55	295
Acetic acid	67-70	272
Water	40-45	278
Acetic acid–water (1:9)	98-100	275

The main substance (DH) has been determined by the method developed in samples obtained in the process of purifying the technical product. The results of the determinations are as follows:

Stage of the Process	Concentration of DH, %
Technical DH	75-80
Reprecipitation	80-92
Recrystallization	92-98
Reprecipitation (finished product)	98-100

EXPERIMENTAL

For TLC we used type KSK silica gel (0.09 mm) prepared as described in [6]. Optical densities were determined on an SF-16 spectrophotometer and potentiometric titration was carried out on a EV-74 universal pH-meter with glass and silver chloride electrodes.

Analysis of the Substance. About 0.1 g (accurately weighed) was dissolved in 1 ml of glacial acetic acid, 25 ml of acetic anhydride was added, and titration was performed with a 0.1 N solution of perchloric acid until the color changed from violet to yellow (indicator: Crystal Violet). A control experiment was performed in parallel. 1 ml of 0.1 N perchloric acid solution corresponds to 0.02087 g of DH.

Analysis of a 1% Ampul Solution. In a glass beaker, 10 ml of the preparation was evaporated to dryness on a boiling water bath. The dry residue was analyzed as described above.

Analysis of Technical DH. About 0.025 g (accurately weighed) of technical DH was dissolved in 5 ml of 95% ethanol. A glass plate with dimensions of 24 × 18 cm bearing a fixed layer of silica gel was divided into four equal parts. On each of the first and second bands was deposited 0.1 ml (500 µg) of an ethanolic solution of a standard sample of DH in the form of a strip 4 cm long, and on the third 0.1 ml (500 µg) of an ethanolic solution of the technical sample, again in the form of a strip 4 cm long, and the fourth band was left as control. The plate with the deposited samples was dried for 1 h, chromatographed in the system described above, and the chromatogram was dried in the air and the first band only, was carefully sprayed with the Dragendorff reagent (during spraying the other bands were protected by clean glass). The spot of the DH on the first band was marked. The sections of the sorbent from the second and third bands with spots present at the level of the marked spot of the standard DH and also a section of the sorbent from the fourth (control) band of the same area were transferred quantitatively to 50-ml flasks and covered with 25 ml of acetic acid–water (1:9) and left for 15-18 h and the extracts were filtered through a No. 4 glass filter.

The optical densities of the standard solution and the solution under investigation were measured on a spectrophotometer in cells with a layer thickness of 10 mm at a wavelength of 275 nm, using as comparison solution the eluate from the control band. The amount of DH in the technical sample as a percentage (X) was calculated from the formula

$$X = \frac{D_X \cdot C_0 \cdot 5 \cdot 25 \cdot 100 \cdot 1.175}{D_0 \cdot a \cdot 0.1},$$

where D_0 and D_X are the optical densities of the solution of the standard sample of DH and of the solution under investigation, respectively; C_0 is the concentration of the solution of the standard sample, g/ml; and a is the weight of the technical sample, g.

SUMMARY

1. The method for the quantitative determination of deoxypeganine hydrochloride has been improved.

2. A procedure for the quantitative determination of deoxypeganine hydrochloride in technical samples has been developed.

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