A. I. BAN' KOVSKII, M. E. PEREL' SON, V. A. SHEVELEV

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A. I. BAN' KOVSKII, M. E. PEREL' SON, V. A. SHEVELEV

ALKALOIDS OF *ECHINOPS*

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According to the literature, the seeds of many species of *Echinops* contain echinopsine as the principal alkaloid ([1], [2]). The structure of echinopsine (N-methyl-γ-quinolone) was established by Späth and Kolbe ([3]) and confirmed by synthesis. The content of other alkaloids was considered insignificant, and they were not subjected to chemical study. In isolating echinopsine from the seeds of *Echinops ritro* L., we observed large fluctuations in its yields depending on the method used ([4]). We encountered similar phenomena in developing a semiplant-scale method for obtaining echinopsine from the seeds of *Echinops sphaerocephalus* L. In the quantitative determination of echinopsine in the raw material by the two proposed methods, which differed from one another only in the conditions of alkalization, its content was found to be 0.47% (ammonia) and 1.87% (sodium hydroxide).

Such substantial differences in the yields of echinopsine prompted us to carry out a series of experiments to clarify the causes producing these fluctuations. Experiments with echinopsine nitrate showed that, upon alkalization of its aqueous solutions with alkali or ammonia, no substantial differences were observed in the yield of echinopsine base. It could therefore be assumed either that echinopsine in the raw material is present in a bound state and, on treatment of aqueous or aqueous-alcoholic extracts with alkali, is liberated, as a result of which its yield sharply increases, or that the seeds of *Echinops* contain other alkaloids which, under the corresponding conditions of alkali treatment, are converted into echinopsine.

The investigations carried out established that the total alkaloids isolated from the seeds of *Echinops* upon alkalization with ammonia consist of echinopsine (0.40–0.48%) and other alkaloids (1.67–1.80%); at the same time, when they are treated with alkali, the echinopsine content reaches 2.02% and accompanying alkaloids are almost completely absent. These experiments clearly showed that, when *Echinops* seeds are treated with alkali, the alkaloids contained in them are converted into echinopsine. The isolation of alkaloids from the seeds of *Echinops sphaerocephalus* was carried out by the following method: from crushed and defatted seeds the alkaloids were extracted with isopropyl alcohol. The alcoholic extracts were evaporated in vacuo to a small volume, alkalized with ammonia, and the alkaloids were extracted with chloroform and then with a mixture of chloroform and butanol. The extracts were thoroughly dried and the solvents distilled off in vacuo. The resulting alkaloid fractions were chromatographed on alumina. Elution with chloroform gave echinopsine, while elution with alcohol gave an alkaloid with R_f 0.65 (butanol—acetic acid—water (4 : 1 : 5)). Echinopsine, twice recrystallized from water and alcohol, had m.p. 149.5-151.5°; hydrochloride m.p. 193-195°; nitrate m.p. 152-153°; and picrate m.p. 229°; a mixed melting-point test of echinopsine with a known sample showed no depression. The alkaloid with R_f 0.65 is readily soluble in water and alcohols, practically insoluble in petroleum ether and diethyl ether,

chloroform, benzene, dioxane, and other organic solvents; after recrystallization from ethanol it had m.p. 311-314° (decomp.), optically inactive; readily forms salts. Hydrochloride, m.p. 314-315° (decomp.).

Found, %: C 62.13, 62.26; H 6.05, 6.06; N 14.13, 14.16; Cl 18.15, 18.98
$C_{10}H_{10}N_2 \cdot HCl$. Calculated, %: C 61.76; H 5.66; N 14.39; Cl 18.23

Picrate, m.p. 217-218° (decomp.).

Found, %: C 49.44, 49.82; H 3.56, 3.47; N 18.12, 17.92
$C_{10}H_{10}N_2 \cdot C_6H_3O_7N_3$. Calculated, %: C 49.59; H 3.35; N 18.08

Molecular weight by Rast: 401, 411; determined spectrophotometrically—380. Calculated molecular weight: 387.1.

Picrolonate, m.p. 288-289° (decomp.); **nitrate**, m.p. 279-280° (decomp.); **sulfate**, m.p. 216-218° (decomp.); and **tartrate**, m.p. 197-197.5° (decomp.); **hydroiodide**, m.p. 223-225° (decomp.); **chromium derivative**, m.p. 238° (decomp.). Thus, from the results of analyses of the hydrochloride and picrate, it follows that the alkaloid has the composition $C_{10}H_{10}N_2$. On comparison of the UV spectra of the isolated alkaloid and echinopsine (Fig. 1), their great similarity is noteworthy, indicating that the chromophoric systems of both compounds are of the same type. Proceeding from the empirical formula of the base $C_{10}H_{10}N_2$ and taking into account the UV-spectrum data, the following structure may be proposed for it (1-methylquinolon-(4)-imide):

[[structural formula: 1-methylquinolon-(4)-imide, quinoline ring with NH at position 4 and N—CH_3]]

Fig. 1. UV spectra of alkaloids from *Echinops* (in 95% ethanol): 1—echinopsine, 2—1-methylquinolon-(4)-imide; 3—native base with R_f 0.55 (approximate concentration)

Small differences in the spectra of echinopsine and the isolated base (splitting of the short-wavelength band into two components and a slight bathochromic

Fig. 2. Paper chromatography of alkaloids of Echinops. 1 —alcoholic extract, 2 —alcoholic extract after treatment with sodium carbonate; 3 —pure alkaloids; 4 —alcoholic extract after treatment with sodium hydroxide, 5 —alcoholic extract after treatment with ammonia

Figure 1: Fig. 2. Paper chromatography of alkaloids of Echinops. 1 —alcoholic extract, 2 —alcoholic extract after treatment with sodium carbonate; 3 —pure alkaloids; 4 —alcoholic extract after treatment with sodium hydroxide, 5 —alcoholic extract after treatment with ammonia

shift of the long-wavelength bands) may be due to replacement of the $>C=O$ group by the $>C=NH$ group.

In the region of stretching vibrations of the N—H and O—H bonds in the IR spectrum of the base (pressed KBr disk) there is a series of bands (3422, 3357, 3307, and 3147 cm^{-1}), caused, in addition to the NH group, evidently also by the presence of water of crystallization, strongly bound by hydrogen bonds ([5]). Similar absorption (3396 and 3252 cm^{-1}) is also found in the case of echinopsine.

Investigation of the 1700-1500 cm^{-1} region in the IR spectra of the isolated base and echinopsine (suspensions in Vaseline oil) also supports the proposed formula. Instead of the carbonyl band of echinopsine at 1653 cm^{-1}, a band at 1674 cm^{-1} appears in the spectrum of the base, which may be due to stretching vibrations of the C=N bond. The band

···position and intensity of the remaining maxima in this region (echinopsine 1621, 1565, 1549, and 1496 cm^{-1}; base 1622, 1568, 1549, and 1514 cm^{-1}) confirm the data of the UV spectrum on the same type of chromophoric systems in both substances. A compound with the proposed structure has been described in the literature ([6,7]). The melting points of its derivatives—the hydrochloride (310°), the hydroiodide (224°), and the chromium derivative (228°)—coincide with our data.

Experiments carried out on the conversion of the alkaloid of composition $C_{10}H_{10}N_2$, in the form of the base and the hydrochloride, into echinopsine showed that such an easy transition as occurs when alcoholic or aqueous extracts are treated with alkali is not observed. Complete conversion of the alkaloid into echinopsine was achieved only after prolonged heating of its aqueous solution alkalized with sodium hydroxide. In this connection the question arose whether the base isolated by us is not a compound formed during treatment of the raw material, or of aqueous or alcoholic extracts, with ammonia. To clarify this, an aqueous-alcoholic extract (70° ethanol) was prepared from the seeds; after distillation of the alcohol it was divided into three parts: I was treated with sodium carbonate, II with ammonia, and III with sodium hydroxide; after 45 min and 24 hours chromatography was carried out on paper in two systems: *n*-butanol—hydrochloric acid—water (5 : 1 : to saturation) and butanol—acetic acid—water (4 : 1 : 5).

Reaction scheme showing compounds (I), (II), and (III)

Figure 2: Reaction scheme showing compounds (I), (II), and (III)

Fig. 2. Paper chromatography of alkaloids of *Echinops*. 1 —alcoholic extract, 2 —alcoholic extract after treatment with sodium carbonate; 3 —pure alkaloids; 4 —alcoholic extract after treatment with sodium hydroxide, 5 —alcoholic extract after treatment with ammonia.

The results of chromatography (Fig. 2) showed that after treatment of the aqueous-alcoholic extract with sodium carbonate there are present: echinopsine with R_f 0.79, a base with R_f 0.69, an alkaloid of composition $C_{10}H_{10}N_2$ with R_f 0.65, and a base with R_f 0.27; after treatment of the extract with sodium hydroxide there is present echinopsine, R_f 0.79, as the principal alkaloid, and a base with R_f 0.27 in trace amounts; after treatment of the extract with ammonia there are present echinopsine, R_f 0.81, an alkaloid of composition $C_{10}H_{10}N_2$ with R_f 0.65 as the principal substance, and an insignificant amount of a base with R_f 0.25; the alcoholic extract without treatment showed only one base with R_f 0.55 (system butanol—acetic acid—water (4:1:5)). The absence of echinopsine and of the base isolated by us in the aqueous-alcoholic extract not subjected to any treatments, and also their presence after treatment of this extract with alkalis, indicates that echinopsine and the base of composition $C_{10}H_{10}N_2$ isolated by us are secondary products formed from the native base (R_f 0.55) in the process of isolating the alkaloids from the raw material. On evaporation of the aqueous-alcoholic extract in vacuo, partial conversion of it into echinopsine and the alkaloid of composition $C_{10}H_{10}N_2$ takes place.

The formation of the alkaloid $C_{10}H_{10}N_2$ upon heating of the aqueous-alcoholic extract and upon its treatment with sodium carbonate indicates that the native alkaloid in its structure must contain two nitrogen atoms.

The literature describes ($^{6-8}$) the formation of methylated quinolone imides and methylquinolones under the action of alkali on hydroxymethylates of 2- and 4-aminoquinolines. It may be assumed that, in the case under consideration, an analogous chain of transformations takes place.

By paper chromatography, a small amount of a substance with R_f0.55 was isolated. Its UV spectrum (Fig. 1) and the presence of optical activity $(\alpha)_D^{20} + 53.8^\circ$ are in full agreement with the assumption that the native substance is present in the plant in the form of salts of a quaternary ammonium base (I).

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