19-CH_3), 1.86 s (3 H, 21-CH_3), 2.02 s (3 H, acetate), 5.0 m (2 H, 3-H, 16-H). The remainder consisted of an complex mixture of substances difficult to separate (TLC). When the experiment was repeated under the same conditions, 280 mg of (VII) was obtained in the form of an oil with R_f 0.4 [benzene—acetone (9:1)]. IR spectrum (ν, cm^{-1}): 1230, 1380, 1460, 1550, 1690, 1750. Mol. wt. 354. Mass spectrum (m/z): 354 (M), 336 (M − 18), 326, 125 ($C_7H_9O_2$). PMR spectrum (δ, ppm): 0.65 m (cyclopropane), 0.88, 0.94 s (6 H, 18-CH_3, 19-CH_3), 1.78 s (3 H, 21-CH_3), 4.95 m (1 H, 16-H). The lactone of the i-steroid (VII) (50 mg) in 0.5 ml of CH_3COOH containing 2% of H_2SO_4 was additionally heated at 65°C for 9 h, and after treatment similar to that described above the mixture of products was acetylated under the usual conditions. After working up and chromatographic separation, a series of products was obtained one of which coincided in terms of R_f with (VII). No formation of (VIII) was observed.

SUMMARY

The δ-lactone of 3β-acetoxy-16-hydroxy-6-oxo-24-nor-5α-chol-17(20)-en-23-oic acid — the $\Delta^{17(20)}$-16α analog of natural chiogralactone — has been synthesized.

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WITHASTEROIDS OF *Physalis*.

III. PHYSANOLIDE AND 4β-HYDROXYWITHANOLIDE E

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Two withanolides have been isolated from the epigeal part of *Physalis viscosa* L. One of them with the compositions $C_{28}H_{38}O_8$ has been identified as 4β-hydroxywithanolide E, and for the second, which has been called physanolide, the structure of 14α,17β,20R-trihydroxy-1,4-dioxo-22R-witha-5,24-dienolide has been proposed on the basis of its UV, IR, PMR, and mass spectra, and also the results of a partial synthesis of 14α-hydroxyandrost-5-ene-1,4,17-trione, obtained by its oxidation.

Continuing a study of *Physalis viscosa* L. [1, 2], from an aqueous extract of the epigeal part of the plant we have isolated two more compounds which have been assigned to the withanolide group on the basis of their UV, IR, PMR, and mass spectra.

Analysis of the spectral characteristics and physicochemical constants of the withanolide (I) $C_{28}H_{38}O_8$, and of its acetate and oxidation products (III, IV) has enabled us to identify this substance as the 4β-hydroxywithanolide E isolated previously from *Ph. peruviana* L. [3, 4].

The detection in the UV spectrum of compound (VIII), $C_{28}H_{38}O_7$, which has been called physanolide, of an intense maximum at 233 nm (log ε 4.1), in the PMR spectrum of two three-proton singlets at δ 1.86 and 1.90 ppm, and in the mass spectrum of a fragment with m/e 125 shows the presence of an unsaturated lactone ring in the side-chain of the new withanolide.

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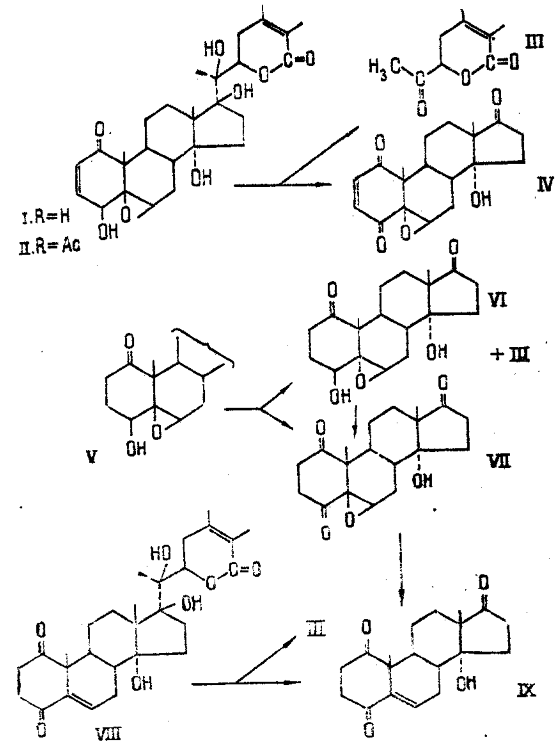

An intense fragment with m/e 169 shows the presence of a diol grouping at C-17 and C-20. This is confirmed by the fact that the oxidation of compound (IV) formed a lactone (III) and an oxosteroid (IX). The size of the molecular ion and the nature of the fragmentation in mass-spectrometric decomposition permits the assumption of the presence of three hydroxyls in physanolide. The withanolide (VIII) was not acetylated when it was heated with acetic anhydride in pyridine, and, consequently, does not contain secondary hydroxy groups. As stated above, two of the hydroxy groups form a diol grouping, and the most probable position of the third hydroxyl is at C-14.

In the PMR spectrum of physanolide (VIII) at δ 6.71 ppm the signal appears of only one vinyl proton. This value is characteristic for a proton at C-6. A singlet at 2.64 ppm (see below) corresponds to four equivalent protons at C-2 and C-3 adjacent to carbonyl groups. Similar facts have been given by Lavie et al. [5] for some products of the degradation of withaferin A, having precisely the same structure of rings A and B.

The facts given above permit structure (VIII) to be suggested for physanolide.

In order to convince ourselves of the correctness of the proposed structure, we undertook a partial synthesis of 14α-hydroxyandrost-5-en-1,4,17-trione (IX), obtained together with the lactone (III) by the oxidation of physanolide (VIII). The synthesis started from the 4β-hydroxy withanolide E (I) found in the same plant.

The reduction of compound (I) (M^+ 502) gave the dihydro compound (V) (M^+ 504), on the oxidation of which two other compounds, in addition to the lactone (III), were detected: 4β,14α-dihydroxy-5β,6β-epoxyandrostane-1,17-dione (VI) and 14α-hydroxy-5β,6β-epoxyandrostane-1,4,17-trione (VII). When the triketo compound (VII) was boiled in glacial acetic acid with potassium iodide, the epoxide ring was eliminated with the formation of 14α-hydroxyandrost-5-ene-1,4,17-trione (IX). Their spectral characteristics and also a direct comparison with the product of the oxidation of physanolide showed their complete identity.

Below we give details of the PMR spectra of the compounds (solvent $CDCl_3$ or — indicated by square brackets — C_5D_5N):

Compound	2-H	3-H	4-H, d	6-H, m	22-H, m	18-CH_3, s	19-CH_3, s	21-CH_3, s	27; 28-CH_3, s s
I	[6,32d]	[7,08 q]	[3,92]	[3,20]	[5,10]	[1,22]	[1,64]	[1,65]	[1,77; 1,88]
II	[6,37d]	[7,00 q]	[4,95]	[3,40]	[5,15]	[1,20]	[1,66]	[1,65]	[1,77; 1,90]
IV	6,79c			3,46		0,89	1,39		
VI	3,22 m			3,40		0,88	1,20		
VII	2,94 s			3,15		0,90	1,11		
VIII	2,64 s			6,71	4,84	1,08	1,20	1,39	1,86; 1,90
	[2,62 s]			[6,84]	[5,15]	[1,30]	[1,22]	[1,68]	[1,67; 1,85]
IX	2,65 s			6,71		0,98	1,22		

The change in the shifts of the signals of the 18-CH_3 and 22-H protons on passing from $CDCl_3$ to C_5D_5N as solvents in taking the PMR spectra ($\Delta_{CDCl_3-C_5D_5N}$ = −0.22 ppm for 18-CH_3 and −0.31 ppm for 22-h) permit the β orientation to be assigned to the 17-OH group [2, 4]. The CD curve ($\Delta\varepsilon_{254}$ + 3.07) shows the 22R configuration. Consequently, physanolide has the structure of 14α,17β,20R-trihydroxy-1,4-dioxo-22R-witha-5,24-dienolide.

As is well known, the group of compounds described acquired their generalized name "withanolides" from the plant *Withania somnifera* Dun., where they were first found. At the same time, at present not less than 15 substances have been described for which the term withanolide with the addition of the letters of the Latin alphabet (from D to R) has been used to denote concrete chemical compounds. In order to avoid the possibility of confusion, in our opinion, it is desirable to name this group of compounds "withasteroids". Collective names of the same type, such as "cardiosteroids" and "ecdysteroids" have rapidly gained acceptance in the scientific literature.

EXPERIMENTAL

For thin-layer chromatography we used the following systems 1) n-hexane—acetone (1:1); 2) n-hexane—acetone (3:2); and 3) chloroform—benzene—methanol (5:5:1). Mass spectra were recorded on an MKh-1310 mass spectrometer. For general information see [2].

Isolation of the Withasteroids. A chloroform extract (for its preparation see [1]) of an aqueous extract (10 g) was chromatographed on a column of silica gel. Elution was carried out with mixtures of chloroform and benzene (1:1) containing gradually increasing amounts of methanol from 2 to 5%. Fractions with a volume of 300 ml each were collected. The process was monitored by TLC in systems 1 and 3. Fractions 18-29 (2% methanol) showed the presence of, mainly, physanolide. After evaporation of the solvent, the residue was recrystallized from methanol. The yield was about 0.001% on the weight of the raw material. Fractions 60-70 (3-4% of methanol) consisted of a mixture of withaphysanolide [2] and 4β-hydroxywithanolide E. After the solvent had been distilled off, the withanolides were rechromatographed on silica gel with elution by n-hexane—acetone (1:1) and monitoring by TLC in the same system. The fractions containing 4β-hydroxywithanolide E were combined and evaporated, and the residue was recrystallized from ethyl acetate. Yield 0.05%. R_f in system 1: physanolide 0.48; withaphysanolide 0.36; and 4β-hydroxywithanolide E 0.22.

Physanolide (VIII). $C_{28}H_{38}O_7$, mp 170-175°C (from methanol), $[\alpha]_D^{20}$ 0 ± 3° (c 2.86; methanol); $\lambda_{max}^{C_2H_5OH}$ 233 nm (log ε 4.1); ν_{max}^{KBr}: 3500-3200, 1710, 1690, 1630 cm^{-1}. CD (c 1.01; methanol): $\Delta\varepsilon_{224}$ = −10.60, $\Delta\varepsilon_{254}$ = +3.07, $\Delta\varepsilon_{300}$ = −1.81, $\Delta\varepsilon_{335}$ = +0.51. Mass spectrum, m/e (%): M^+ 486 (2), 468 (38), 450 (11.5), 432 (3.5), 343 (17), 325 (17), 299 (13), 281 (11), 169 (47), 152 (100), 125 (86), 109 (86).

4β-Hydroxywithanolide E (I). $C_{28}H_{38}O_8$, mp 229-230°C (from ethyl acetate), $[\alpha]_D^{21}$ +87.8 ± 5° (c 1.48; ethanol); $\lambda_{max}^{C_2H_5OH}$ 220 nm (log ε 4.1); ν_{max}^{KBr} 3650-3300, 1710, 1675 cm^{-1}. CD (c 1.10; methanol): $\Delta\varepsilon_{213}$ = +18.02, $\Delta\varepsilon_{248}$ = +4.95, $\Delta\varepsilon_{338}$ = +1.74. Mass spectrum, m/e (%): M^+ 502 (1.5), 484 (20), 466 (80), 448 (86), 359 (37), 341 (47), 323 (10), 315 (40), 297 (40), 169 (80), 152 (70), 125 (100).

4β-Acetoxywithanolide E (II) was obtained in the form of an amorphous powder when compound (I) was allowed to stand in a mixture of acetic anhydride and pyridine at room temperature for a day. The acetate (II) could not be obtained in the crystalline state. λ_{max}^{KBr} 3500, 1740, 1700, 1675, 1210 cm^{-1}. Mass spectrum, m/e (%): M^+ 544 (1.5), 526 (4.5), 508 (11), 484 (4.5), 466 (54), 448 (100), 341 (34), 321 (48), 297 (45), 279 (70), 169 (100), 152 (63), 125 (100).

Oxidation of 4β-Hydroxywithanolide E. With ice-cooling and constant shaking, 5-6 drops of the Jones reagent was added to a solution of 50 mg of compound (I) in 10 ml of acetone. The reaction was monitored by TLC in system 1 (with iodine as the visualizing agent). After the disappearance of the initial compound, the reaction mixture was poured into water (20 ml) and extracted with chloroform (5 × 10 ml). The chloroform extract was washed with water, dried with Na_2SO_4, and evaporated. The residual light yellow oil was separated on plates with a thin layer of silica gel in the same system. This gave two compounds: the light yellow oil $C_9H_{12}O_3$ (III), $[\alpha]_D^{25}$ +145.0 ± 4° (c 1.20; chloroform) [mass spectrum, m/e (%): 125 (100), 100 (40), 71 (25), 43 (35)], identical with the lactone from withaphysanolide in systems 2 and 3 [2]; and crystals of 14α-hydroxy-5β,6β-epoxyandrost-2-ene-1,4,17-trione (IV) with mp 254°C (from ether), $[\alpha]_D^{25}$ +136 ± 3° (c 1.12; dioxane), $\lambda_{max}^{C_2H_5OH}$ 233 nm (log ε 3.99), ν_{max}^{KBr} 3530, 1745, 1700, 1678 cm^{-1}; mass spectrum, m/e (%): M^+ 330 (88), 312 (86), 298 (100), 294 (84), 284 (50).

4β-Hydroxy-2,3-dihydrowithanolide E (V). A solution of 600 mg of compound (I) in 65 ml of ethanol was treated with 150 mg of $Pd/BaSO_4$, and hydrogenation was performed with hydrogen under constant stirring for 10 min. The reaction mixture was filtered from the catalyst, and the filtrate was evaporated. The residue consisted of a vitrous mass showing a single spot on TLC (systems 1 and 3). Mass spectrum, m/e (%): M^+ 504 (0.5), 486 (12.5), 468 (91), 450 (64), 361 (65), 343 (79), 299 (65), 169 (66), 152 (100), 125 (100).

Oxidation of 4β-Hydroxy-2,3-dihydrowithanolide E (V). The whole of the product obtained in the preceding experiment was dissolved in 90 ml of acetone and, with ice cooling, the Jones reagent was added in drops to the solution. The process was monitored by TLC in system 2. After the disappearance of the initial compound from a chromatogram, the reaction mixture was diluted with water (200 ml), and the subsequent procedure was the same as in the oxidation of 4β-hydroxywithanolide E. The residue consisted of 460 mg of a yellowish oil, which was subjected to chromtographic separation on silica gel (250 g). Elution was performed with mixtures of hexane and acetone with a gradual increase in the amount of acetone (5:1; 5:2.5; 5:3), 50-ml fractions being collected. The process was monitored by TLC in system 2. Fractions 20-60 (5:1) contained a light yellow oil (42 mg) with the composition $C_9H_{12}O_3$, which was identified as the lactone (III). Fractions 92-103 (5:2.5) contained 14α-hydroxy-5β,6β-epoxyandrostane-1,4,17-trione (VII), $C_{19}H_{24}O_5$. Yield 97 mg. After recrystallization from hexane—acetone, it had 222°C, (decomp), $\lambda_{max}^{C_2H_5OH}$ 290 nm (log ε 2.0), ν_{max}^{KBr} 3550, 1745, 1730, 1715 cm^{-1}; mass spectrum m/e (%): M^+ 332 (85), 314 (40), 304 (30), 299 (55), 296 (45), 271 (100). The subsequent washing of the column with hexane—acetone (5:3) yielded the crystalline 4β,14α-dihydroxy-5β,6β-epoxyandroastan-1,17-dione (VI), $C_{19}H_{26}O_5$, in an amount of 120 mg. After recrystallization from hexane—acetone, it had mp 263°C (decomp.). ν_{max}^{KBr}: 3470, 1730, 1695 cm^{-1}. Mass spectrum, m/e (%): M^+ 334 (14), 316 (44), 298 (20), 231 (65), 213 (100).

Oxidation of compound (VI) by the Jones method led to the triketone (XII).

14α-Hydroxyandrost-5-ene-1,4,17-trione (IX) from (VI). A solution of 130 mg of the triketone (VII) in 15 ml of glacial acetic acid was heated with 130 mg of KI at 100°C for 1 h. After cooling, 200 ml of water was added to the reaction mixture and the reaction products were extracted with chloroform. The chloroform extract was washed with a dilute solution of $Na_2S_2O_3$ and with $NaHCO_3$, and then with water, and it was dried over Na_2SO_4. Evaporation of the solvent gave 105 mg of a yellowish oil consisting, according to TLC (system 1) of a mixture of three substances. The mixture was separated on plate with a thin layer of silica gel in the same system. The compound present in largest amount was 14α-hydroxyandrost-5-en-1,4,17-trione, $C_{19}H_{24}O_4$, mp 215°C (from acetone—hexane). $\lambda_{max}^{C_2H_5OH}$ 347 nm (log ε 3.7), ν_{max}^{KBr} 3500, 1745, 1720, 1695 cm^{-1}; mass spectrum m/e (%): M^+ 316 (34), 298 (34), 283 (92), 255 (91), 241 (100).

14α-Hydroxyandrost-5-ene-1,4,17-trione (IX) from Physanolide (VIII). Physanolide (30 mg) was dissolved in 10 ml of acetone and oxidized by the Jones method in the same way as compound (V). The mixture was separated preparatively in a thin layer of silica gel (system 1). The feebly polar compound was identified by TLC (systems 2 and 3) and spectral characteristics as the lactone (III). A more polar compound was crystallized from a mixture of acetone and hexane and had mp 215°C, $\lambda_{max}^{C_2H_5OH}$ 247 nm (log ε 3.7), ν_{max}^{KBr} 3500, 1745, 1720, 1695 cm^{-1}; M$^+$ 316. In systems 1 and 3, the R$_f$ values of compound (IX) coincided with those of the 14α-hydroxyandrost-5-en-1,4,17-trione obtained from (VII).

SUMMARY

Two withanolides have been isolated from the epigeal part of *Physalis viscosa* L. — 4β-hydroxywithanolide E and a new one which has been called physanolide. The latter has the structure of 14α,17β-20R-trihydroxy-1,4-dioxo-22R-witha-5,24-dienolide.

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ALKALOIDS OF *Nitraria komarovii*.

IV. TOTAL SYNTHESIS OF KOMAROVINE AND KOMAROVIDINE

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Two alkaloids of a new type — komarovine and komarovidine — have been isolated from the epigeal part of the *Nitraria komarovii*. Their structures — 3-(quinolin-8'-yl)-β-carboline and 3-(quinolin-8'-yl)-5,6-dihydro-β-carboline, respectively — have been established by synthesis.

The isolation of komarovine [1] and komarovidine [2] — alkaloids of the epigeal part of the *Nitraria komarovii* — and the determination of their structures have been reported previously. The identity of komarovine (V) with one of the products of the dehydrogenation of the main alkaloid of *N. schoberi*, nitrarine [3], with selenium and sulfur was shown. Nitrarine has also been isolated from this plant [4].

Analysis of the spectra (PMR, mass, IR, UV) of komarovidine (IV) showed that it is a dihydro derivative of komarovine. The dehydrogenation of (IV) with palladium black led to komarovine.

On the basis of the spectral characteristics of (V), and also taking into account its formation from 14,21-dimethylene-16-azayohimbane (nitrarine) in a dehydrogenation reaction, we put forward the structure of 3-(quinolin-8'-yl)-β-carboline for the alkaloid komarovine. We have synthesized a compound of this structure from quinoline-8-carboxylic acid and tryptamine.

Quinoline-8-carboxylic acid was obtained from anthranilic acid by the Skraup reaction [5]. Tryptamine was synthesized from indole in three stages by a known method [7], and was also obtained in part by the decarboxylation of tryptophan [8].

The amide (III) was synthesized by two methods: by the condensation of (I) and (II) with the participation of dicyclohexylcarbodiimide (DCC) at room temperature [9], and also by the direct thermal reaction of (I) and (II) [10]. It must be mentioned that the yields

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