

O. E. Vasina, V. A. Maslennikova,  
and N. K. Abubakirov

UDC 547.926

The review gives a table of 47 withasteroids isolated from plants of the genus *Physalis*. The biogenetic relationship between the different structures of the compounds is discussed on the basis of an analysis of literature material. An assignment of some C-methyl groups of the physalins is made.

The genus *Physalis* (family Solanaceae) includes about 120 species of plants growing mainly in South and North America. A small number of species has been recorded in Europe and in the countries of southeastern and central Asia [1]. Six species of *Physalis* are found in the Soviet Union.

The first chemical investigation of a plant of this genus, namely *Ph. alkekengi* L. was made as early as 1852. A bitter amorphous substance called physalin with the empirical formula  $C_{28}H_{30}O_9$ , was isolated from the leaves. Only more than a century later, on the basis of its IR spectrum, was the presence of a  $\gamma$ -lactone moiety in this compound established, and in 1969 T. Matsuura et al. [2], making use of a whole arsenal of physicochemical methods of proof including an x-ray structural analysis of an acetoxybromotetrahydrophysalin A, came to the conclusion that the physalins were 13,14-seco-16,24-cyclosteroids. Thus, physalins A and B opened up a peculiar series of steroid compounds which now includes about 15 substances. Later, from the *Ph. ixocarpa* and *Ph. peruviana*, in addition to 13,14-seco-16,24-cyclosteroids (physalins), withasteroids of the so-called "correct" structure having a carbon skeleton of the ergostane type, were isolated [3, 4]. In the term withasteroids we include the withanolides proper, i.e., compounds of the ergostane type with various lactone and lactol groups in the side chain, and also physalins and withaphysalins. The latter can be considered as modified withanolides [5].

The present review is devoted to withasteroids of *Physalis* (ground cherry). In the Solanaceae — the only plant family in which withasteroids have been detected — this genus is the richest in compounds with various types of structures. The following groups have been isolated from the ground cherry: withanolides (compounds 1-28, 47); withaphysalins containing an additional five-membered lactone ring or a lactone ring formed by the oxidation of the C-18 methyl group (compounds 29-31); and physalins (compounds 32-45) having the 13,14-seco-16,24-cyclo structure, a five-membered lactone ring and, as a rule, containing an ether bond between C-14 and C-27. In *Physalis* are also found withasteroids with a five-membered lactone ring in the side chain (compounds 24-27), with a six-membered lactol ring (compound 28) and, in addition, chlorine-containing withanolides (compounds 12 and 13) (Table 1).

As a result of the analysis of the 70 withanolides known in 1976, Glotter et al. [6] suggested a scheme of the biogenetic link between the withasteroids with different types of substitution in rings A and B. On the basis of these ideas we shall attempt to analyze the mutual relationships of the withasteroids of *Physalis* which, at the moment of drawing up the review (including literature up to January, 1984), numbers almost 50 compounds.

The key structure with which all the other types of substitution are biogenetically connected is apparently (III). The hydration of the latter in position 4 followed by epoxidation at the double bonds forms compounds substituted in rings A and B. A 4 $\beta$ -hydroxy-5 $\beta$ ,6 $\beta$ -epoxy grouping (substitution of type V) is found in many withasteroids (compounds 1, 5, 10, 15, 18, 20, 26, and 28). Substitution of type VI, obtained by the epoxidation at the double bond in ring A is found rarely (compound 15 from *Ph. viscosa*). Substitution of type VII is biogenetically connected with it (compound 18 isolated from the same plant). A 5 $\alpha$ -hydroxy-6 $\alpha$ ,7 $\alpha$ -epoxy grouping is also encountered rarely in *Physalis* (product XII, compound 22).

---

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from *Khimiya Prirodnykh Soedinenii*, No. 3, pp. 263-277, May-June, 1986. Original article submitted October 11, 1984.

TABLE 1. Withasteroids Isolated from Plants of the Genus *Physalis* (family Solanaceae)

| Name, composition  | Structure | mp, °C;<br>[α] <sub>D</sub> , deg                              | Source   | Literature   |
|--|-----------|--|--|--------------|
| 1. Withaferin A<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub>                  |           | 252—253;<br>+125<br>(chloroform)                               | Ph. viscosa,<br>Withania<br>somniafer L.<br>Dum., Acni-<br>stus arbores-<br>cens | 9, 15,<br>37 |
| 2. Withanolide E<br>C <sub>28</sub> H <sub>38</sub> O <sub>7</sub>                 |           | 167—168;<br>+103,5<br>(chloroform)                             | Ph. peruviana,<br>Withania som-<br>nifera  | 4, 38        |
| 3. Withaphysanolide<br>C <sub>28</sub> H <sub>38</sub> O <sub>7</sub>              |           | 215;<br>+95±2<br>(dioxane)                                     | Ph. viscosa  | 13, 39       |
| 4. Withaperuvin C<br>C <sub>28</sub> H <sub>38</sub> O <sub>7</sub>                |           | 190;<br>+4,5<br>(pyridine)                                     | Ph. peruviana,<br>Ph. viscosa  | 20           |
| 5. 4β-Hydroxy-<br>withanolide E<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub>  |           | 197—198,<br>205—214,<br>229—230;<br>+95,8,<br>+107±1,5,<br>+87 | Ph. peruviana,<br>Ph. viscosa  | 4, 40,<br>41 |
| 6. Withaperuvin B<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub>                |           | 269—270;<br>+215<br>(pyridine)                                 | Ph. peruviana  | 20           |
| 7. 28-Hydroxywith-<br>aperuvin C<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub> |           | 185—186;<br>+152±2<br>(methanol)                               | Ph. viscosa  |              |

TABLE 1 (Continued)

| Name, composition  | Structure | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg | Source                                     | Literature |
|--|-----------|--|--|------------|
| 8. 28-Hydroxy-withaphysanolide<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub> |           | 237  | Ph. viscosa                                | 13         |
| 9. Withanolide S<br>C <sub>28</sub> H <sub>40</sub> O <sub>8</sub>               |           | 272;<br>+95,5                              | Ph. peruviana,<br>Withania soft-<br>nifera | 42,<br>38c |
| 10. Visconolide<br>C <sub>28</sub> H <sub>38</sub> O <sub>9</sub>                |           | 232-233;<br>+119,5±2<br>(methanol)         | Ph. viscosa                                |            |
| 11. Withaperuvin<br>C <sub>28</sub> H <sub>40</sub> O <sub>9</sub>               |           | 225-227;<br>+156,8<br>(acetoni-<br>trile)  | Ph. peruviana                              | 8          |
| 12. 4-Deoxyphysalolactone<br>C <sub>28</sub> H <sub>39</sub> O <sub>7</sub> Cl   |           | 207-209;<br>+103<br>(acetoni-<br>trile)    | Ph. peruviana                              | 8          |
| 13. Physalolactone<br>C <sub>28</sub> H <sub>39</sub> O <sub>8</sub> Cl          |           | 227-228;<br>+29,4<br>(pyridine)            | Ph. peruviana                              | 43         |
| 14. Pubescenol<br>C <sub>28</sub> H <sub>42</sub> O <sub>8</sub>                 |           | 180-182                                    | Ph. pubescens                              | 44         |

TABLE 1 (Continued)

| Name, composition  | Structure | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg | Source        | Literature |
|--|-----------|--|---------------|------------|
| 15. Viscosalactone A<br>C <sub>28</sub> H <sub>38</sub> O <sub>7</sub>         |           | 184—186;<br>-27,4<br>(methanol)            | Ph. viscosa   | 10         |
| 16. Physolanolide<br>C <sub>28</sub> H <sub>38</sub> O <sub>7</sub>            |           | 170—175;<br>0+3                            | Ph. viscosa   | 41         |
| 17. 2,3-Dihydrowithanolide E<br>C <sub>28</sub> H <sub>40</sub> O <sub>7</sub> |           | 264—265;<br>-42                            | Ph. peruviana | 4          |
| 18. Viscosalactone B<br>C <sub>28</sub> H <sub>40</sub> O <sub>7</sub>         |           | 184—186;<br>-19,4<br>(methanol)            | Ph. viscosa   | 10         |
| 19. Physalolactone B<br>C <sub>30</sub> H <sub>44</sub> O <sub>8</sub>         |           | 252—254;<br>+14,2<br>(methanol)            | Ph. peruviana | 45         |
| 20. Physalactone<br>C <sub>29</sub> H <sub>40</sub> O <sub>8</sub>             |           | -4.3<br>(methanol)                         | Ph. viscosa   | 13, 46     |
| 21. Withaperuvin D<br>C <sub>28</sub> H <sub>40</sub> O <sub>9</sub>           |           | 209—211;<br>+12<br>(acetone)               | Ph. peruviana | 47         |
| 22. Ixocarpanolide<br>C <sub>28</sub> H <sub>40</sub> O <sub>6</sub>           |           | 252—253;<br>+27±4<br>(chloroform)          | Ph. ixocarpa  |            |

TABLE 1 (Continued)

| Name, composition   | Structure | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg | Source                | Literature |
|---|-----------|--|-----------------------|------------|
| 23. Withaphysarpin<br>C <sub>28</sub> H <sub>40</sub> O <sub>7</sub>    |           | 275—278;<br>+20<br>(chloroform)            | Ph. ixocarpa          | 3          |
| 24. Perulactone B<br>C <sub>28</sub> H <sub>40</sub> O <sub>7</sub>     |           | 217—218;<br>+56,5<br>(acetone-trile)       | Ph. peruviana         | 12         |
| 25. Ixocarpalactone B<br>C <sub>28</sub> H <sub>38</sub> O <sub>8</sub> |           | Acetate:<br>170—172;<br>+47,2              | Ph. ixocarpa<br>Brot. | 49         |
| 26. Ixocarpalactone A<br>C <sub>28</sub> H <sub>40</sub> O <sub>8</sub> |           | 294—295;<br>+84<br>(acetone-trile)         | Ph. ixocarpa          | 49         |
| 27. Perulactone<br>C <sub>30</sub> H <sub>46</sub> O <sub>7</sub>       |           | 239—240;<br>-3,2<br>(acetone-trile)        | Ph. peruviana         | 11         |
| 28. Physapubescin<br>C <sub>30</sub> H <sub>42</sub> O <sub>8</sub>     |           |  | Ph. pubescens L.      | 50         |
| 29. Withaphysalin A<br>C <sub>28</sub> H <sub>34</sub> O <sub>6</sub>   |           | 222—223;<br>+43,6                          | Ph. minima            | 23         |
| 30. Withaphysalin B<br>C <sub>28</sub> H <sub>36</sub> O <sub>6</sub>   |           | 161—162                                    | Ph. minima            | 23         |

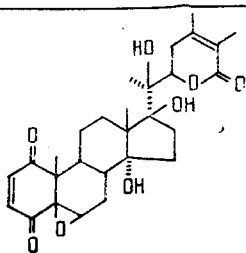
TABLE 1 (Continued)

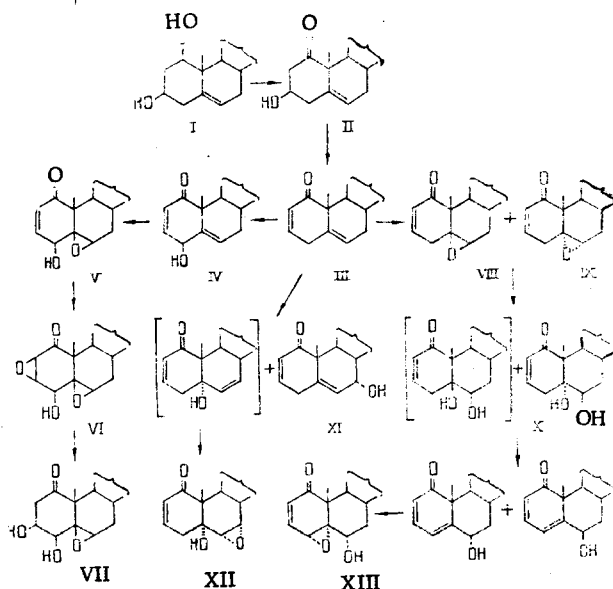
| Name, composition  | Structure | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg | Source  | Literature      |
|--|-----------|--|---|-----------------|
| 31. Withaphysalin C<br>C <sub>28</sub> H <sub>36</sub> O <sub>7</sub>                                  |           | 202–203;<br>+33,4                          | Ph. minima  | 23              |
| 32. Physalin C<br>C <sub>28</sub> H <sub>30</sub> O <sub>9</sub>                                       |           | 274–277;<br>–160<br>(acetone)              | Ph. alkekengi<br>var. Francheti   | 51              |
| 33. Physalin A<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub>                                      |           | 265–266;<br>–126<br>(ethanol)              | Ph. alkekengi<br>var. Francheti   | 52              |
| 34. 25, 26-Epidihydrophysalin C<br>C <sub>28</sub> H <sub>32</sub> O <sub>9</sub>                      |           | 230–234;<br>–114<br>(ethanol)              | Witheringia<br>coccoloboides<br>(Dammer)  | 21              |
| 35. Physalin B<br>C <sub>28</sub> H <sub>30</sub> O <sub>9</sub>                                       |           | 250  | Ph. alkekengi<br>var. Francheti,<br>Ph. ixocarpa,<br>Witheringia<br>coccoloboides<br>(Dammer) | 52, 53<br>3, 21 |
| 36. Physalin G<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub>                                      |           | 295–296;<br>+17<br>(acetone)               | Ph. lancifolia  | 54              |
| 37. 6-Hydroxy-<br>6-7-dihydrode-<br>hydrophysalin B<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub> |           | 270–274                                    | Ph. minima  | 24, 55          |
| 38. Physalin H<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub>                                      |           | 238–240                                    | Ph. angulata  | 56              |

TABLE 1 (Continued)

| Name, composition   | Structure | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg         | Source  | Literature        |
|---|-----------|--|---|-------------------|
| 39. 5 $\beta$ , 6 $\beta$ -Epoxy-physalin B (physalin F)<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub> |           | 262—264;<br>—60, 7<br>295—296;<br>—20<br>(acetone) | Ph. minima<br>Ph. angulata,<br>Ph. lancifolia     | 23<br>57          |
| 40. Physalin J<br>C <sub>28</sub> H <sub>30</sub> O <sub>10</sub>   |           | 263—270;<br>—60<br>(acetone)                       | Ph. angulata                                      | 57                |
| 41. Physalin K<br>C <sub>28</sub> H <sub>30</sub> O <sub>11</sub>   |           | 280—282  | Ph. angulata                                      | 54                |
| 42. Physalin E<br>C <sub>28</sub> H <sub>32</sub> O <sub>11</sub>   |           | 305—307<br>—83<br>(chloroform)                     | Ph. angulata,<br>Ph. lancifolia,<br>Ph. pubescens | 56, 44            |
| 43. Dihydroxy-physalin B<br>C <sub>28</sub> H <sub>32</sub> O <sub>11</sub>                                 |           | 302—304  | Ph. minima  | 28                |
| 44. Physalin D<br>C <sub>28</sub> H <sub>32</sub> O <sub>11</sub>   |           | 262—263;<br>—68<br>(methanol)                      | Ph. minima,<br>Ph. angulata                       | 34, 58,<br>59, 54 |
| 45. Physalin I<br>C <sub>29</sub> H <sub>31</sub> O <sub>11</sub>   |           | 305—307;<br>+12<br>(acetone)                       | Ph. angulata                                      | 54                |
| 46. Physalolactone B 3-O- $\beta$ -D-glucopyranoside<br>C <sub>36</sub> H <sub>54</sub> O <sub>11</sub>     |           | +3, 7<br>(pyridine)                                | Ph. peruviana                                     | 60                |

TABLE 1 (Continued)

| Name, composition  | Structure   | mp, °C;<br>[ $\alpha$ ] <sub>D</sub> , deg | Source                 | Literature |
|--|---|--|------------------------|------------|
| 47. Withaperuvin E<br>C <sub>28</sub> H <sub>36</sub> O <sub>8</sub> |  | 248–250;<br>–72,7<br>(acetoni-<br>trile)   | Ph. peruviana<br>Linne | 61         |



Another route for the conversion of a product with structure III is direct epoxidation without the introduction of additional hydroxy groups. As a result, compounds of type VIII are formed which are also found fairly frequently among the *Physalis* withasteroids (compounds 2, 17, 30, and 39). The trans-hydroxylation of epoxides with the partial structures VIII and IX leads to products X, XIII, and XIV (compounds 9, 43, 44, and 45, and 4, 7, and 41, respectively). As can be seen from the scheme, the formation of other compounds substituted in rings A and B can easily be explained on the basis of the key structures.

Lavie et al. [7] made a summary of investigations at the molecular level of the mechanism of the inheritance of the enzyme systems responsible for the oxidative processes of withanolide-containing plants. On the basis of an analysis of their withasteroid compositions it can clearly be seen that *Ph. angulata*, *Ph. minima*, *Ph. alkekengi*, and *Ph. lancifolia* are plants containing an enzyme system directing processes to the formation of 4-deoxy compounds. The enzymes of *Ph. viscosa* and *Ph. ixocarpa*, conversely, promote the formation of 4 $\beta$ -hydroxy groups; in *Ph. peruviana* the two systems act in competition, as has been observed in *Withania somnifera* of an Indian chemotype [7].

Among known withasteroids the majority have the  $\beta$  configuration of the C-17–C-20 bond, and withasteroids with the  $\alpha$  orientation of the side chain are few in number and have been isolated mainly from two species of *Physalis*: *Ph. viscosa* and *Ph. peruviana* (see Table 1). It has been reported [8] that *Ph. peruviana* specimens collected in two regions of India differ with respect to their withanolide composition, but in both varieties withasteroids with a 17 $\alpha$  side chain have been found.

*Ph. viscosa* is being studied by two groups of workers. Pelletier et al. have isolated from plants of North American origin compounds 1, 15, and 18 containing no hydroxy groups in the C-14, C-17, and C-20 positions and with  $\beta$ -oriented side chains [9, 10]. We have detected eight withasteroids (3, 4, 5, 7, 8, 10, 16, and 20), each having a 14 $\alpha$ ,17 $\beta$ ,20-trihydroxy grouping and an  $\alpha$ -oriented side chain in *Ph. viscosa* of Central Asian origin.



We have not been in a position to compare the morphological characteristics of these populations, but since they differ in their chemical composition it is not excluded that they are different chemotypes of a single species.

In addition to this, *Ph. viscosa* from the village of Kara-Kala (Turkmen SSR) possesses another distinguishing feature. This is the first plant of the genus *Physalis* in which compounds with a C-28-hydroxy group attached to a lactone ring have been found. Before this, two compounds — perulactone (27) and perulactone B (24) — in which an oxidized C-28 carbon atom forms the closure of a five-membered lactone were known [11, 12]. Three compounds with a 28-hydroxy function have been isolated from *Ph. viscosa*: 28-hydroxywithaphysanolide [13], visconolide, and 28-hydroxywithaperuvin C. In association with other withasteroids from the same plant, they form three pairs: withaphysanolide (3)—28-hydroxywithaphysanolide (8), 4 $\beta$ -hydroxywithanolide E (5)—visconolide (10), and withaperuvin C (4)—28-hydroxywithaperuvin C (7) in which the second compound is the C-28-hydroxy derivative of the first. Similar pairs of compounds but with hydroxy groups only at C-27 have been isolated from *Withania somnifera*: withaferin A [15] and 27-deoxywithaferin A [16], and withanolide D and 27-hydroxywithanolide D [14, 17].

Among the withasteroids so far known no compounds have been recorded in which an  $\alpha$ -oriented side chain has been combined with a 27-hydroxy group in an unsaturated lactone ring. Apparently, in the *Ph. viscosa* growing in Turkmenia there is an oxidative enzyme system having recessive characteristics which, because of spatial factors ( $\alpha$  side chains) oxidizes not the methyl group at C-25 but that at C-24.

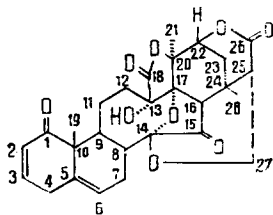
It has been possible to establish the position of the primary hydroxy group at C-28 in 28-hydroxywithaphysanolide with adequate reliability only with the aid of  $^{13}\text{C}$  NMR [13]. PMR spectra showed only the presence of a  $-\text{CH}_2\text{OH}$  group — signals at 7.05 ( $^2J = 12.1$  Hz), 4.40 (14.5 and 6.5 Hz), and 4.71 ppm (14.5 and 5.61 Hz) from a primary hydroxy group and two geminal methylene protons. But it was not clear to which of the atoms — C-24 or C-25 — the hydroxymethyl group was attached and to which the methyl group.

This point was cleared up by  $^{13}\text{C}$  NMR spectroscopy, which played the decisive role in the definitive assignment of the tertiary hydroxy group at C-14 in a number of compounds isolated from *Withania somnifera* and *Ph. viscosa* [18, 19, 13]. The  $^{13}\text{C}$  NMR method also proved useful for a reliable assignment of the double bond in ring D of compound 6 [20].

Attention is attracted by the fact that 13,14-seco-6,24-cyclosteroids — the physalins (compounds 32-41) — are found only in plants that do not produce withasteroids with  $\alpha$ -oriented side chains. Apparently the spatial form of the molecule plays a decisive role in the oxidative processes leading to the formation of 13,14-seco compounds.

Until recently, physalin had been found only in *Physalis* plants. In 1981, a report appeared [21] on the isolation of two physalins — physalin B (35) and the new 25,26-epidihydrophysalin C — from *Witheringia coccoboides* (Dammer) A. T. Hunziker (*Solanaceae*). We considered it necessary to include the second compound (34) in our review, although it has not yet been found in *Physalis*.

The biogenesis of the physalins and their possible origins from the withanolides has been reported previously [6, 22]. It appears to us to be rational to number the carbon atoms of the physalins in the same way as has been adopted in the withasteroids of normal structure, namely:



On the basis of the nature of the substitution at the C-25 atom, the physalins can be divided into two groups. The first group, having an ether bond between C-14 and C-27 (compounds 35-45), makes up the majority of physalins. The second group includes compounds 32-34 having a methylene group  $-\text{CH}_2=$  or a methyl group at C-25.

TABLE 2. Assignment of the Individual Signals of the PMR Spectra of Some Withasteroids

| Compound | Resolving power of the instrument, MHz | 13-OH | 22-H               | 19-CH <sub>3</sub> | 21-CH <sub>3</sub> | 27 and 28-CH <sub>3</sub>          | Signals of other protons     | Literature |
|----------|--|-------|--------------------|--------------------|--------------------|------------------------------------|------------------------------|------------|
| 29       | 60                                     |       | 4.62 dd (12; 4,5)  | 1,30s              | 1,51s              | 1,95                               |                              | 23         |
| 30       | 60                                     |       | 4,58 dd            | 1,25s              | 1,28; 1,47         | 1,93                               | 18-H 5,17                    | 23         |
| 31*      | 60                                     |       | 4,32 dd (12; 4)    | 1,27s              | 1,27s              | 1,90s, 1,97s                       | 18-H 5,10                    | 23         |
| 32       |  | 5,90s | 4,55 m             | 1,07s              | 1,80s              | 5,57 br.s, 1,55s                   | 14-OH 6,13                   | 51         |
| 33       |  | 5,63s | 4,58 m             | 1,03s              | 1,72s              | 6,39 br.s, 5,63 br.s, 1,55s        | 7-OH 4,97 (1), 14-OH 6,38    | 52         |
| 34       | 80                                     | 6,12s | 4,46 dd (4; 2,6)   | 1,06s              | 1,74s              | 1,23d(7,9), 1,14s                  | 14-OH 6,40                   | 21         |
| *        | 360                                    |       | 4,56 dd (4,7; 1,3) | 1,18s              | 1,91s              | 1,3 d(7,3), 1,33s                  |                              | 21         |
| 35       |  | 6,26s | 4,57               | 1,12s              | 1,81s              | 4,28dd, (13; 4), 1,12s 3,60d(12)   |                              | 52         |
| 36       |  | 6,36s | 4,54 m             | 1,26s              | 1,78s              | 4,29 dd (14; 4), 1,20s, 3,63d (13) | 6-OH 5,08d (2)               | 54         |
| 37*      | 100                                    | 4,40s | 4,6 m              | 1,52s              | 1,96s              | 4,6m 1,28s, 3,75d                  |                              | 24         |
| 38       |  | 5,96s | 4,58 m             |                    |                    | 4,29 dd (14; 4), 3,61d (14)        | 7-H 3,88m, 7-OH 4,94d (4)    | 56         |
| 39*      | 60                                     | 6,35s | 4,58 m, 4,56 m     | 1,31s              | 1,96s              | 1,26s 4,27 dd, 3,57d (14)          |                              | 23, 57     |
| 40       |  | 6,31s | 4,59               |                    |                    | 4,28dd (14; 4), 3,60d (4)          |                              | 57         |
| 41       |  | 6,54s | 4,58 m             | 1,04s              | 1,82s              | 4,30dd, (12; 4), 1,16s 3,62d (12)  |                              | 54         |
| 42       |  | 5,66s | 4,56 m             |                    |                    | 4,27dd (14; 4), 3,60dd (14; 2)     | 7-H 3,52m, 5-OH 4,22s        | 56         |
| 43       | 60                                     | 5,64s | 4,53 m             | 1,20s              | 1,80s              | 4,06s, 1,13s 3,53d                 |                              | 28         |
| 44       | 60                                     |       | 4,5 dd (14;4)      | 1,17s              | 1,85s              | 4,50 dd (14;4), 1,12s 3,71, (14)   |                              | 59         |
| 45       |  | 5,70s | 4,58 m             | 1,20s              | 1,84s              | 4,29 dd (14; 4) 1,20s              | 6-OH 4,94d (4), 5-O-Me 2,94s | 54         |

Note. The spectra were taken in DMSO-d<sub>6</sub>, or, where marked with an asterisk, in CDCl<sub>3</sub>. The signals that we have assigned are given in half-bold print.

An analysis of the literature shows that, as a rule, the chemical shifts of the signals of the tertiary methyl groups at C-19, C-21, and C-28 are not assigned in the PMR spectra of the physalins. The environment of the C-21 methyl group is the same in all the physalins, and the signal of this group always undergoes the descreening influence of the neighboring oxygen atom and, consequently, is shifted downfield to the greatest degree [21]. For this reason, on the basis of the facts given in [21] and [23], we have assigned the chemical shifts lying between 1.96 and 1.72 ppm to the signals of the C-21 methyls. The position of the signal of the C-28 methyl in a PMR spectrum depends greatly on the nominal group to which the physalin belongs. In the physalins of the first group the position of this signal depends on the solvent used and it is found either at 1.20-1.12 ppm (if the spectrum is taken in DMSO-d<sub>6</sub>) or at 1.28-1.26 ppm (if the spectrum is taken in CDCl<sub>3</sub>). In the physalins of the second group (compounds 32 and 33) the signal from the C-28 methyl is located at 1.55 ppm in DMSO-d<sub>6</sub>, while for compound 34 it is found at 1.14 ppm in deuterated DMSO and at 1.33 ppm in CDCl<sub>3</sub>.

The remaining unassigned signal, from the C-19 methyl group, which is subjected to the influence of substituents in rings A and B, is located between 1.26 and 1.03 ppm in PMR spectra taken in DMSO-d<sub>6</sub> and shifts downfield by 0.12-0.20 ppm for spectra taken in CDCl<sub>3</sub>.

In compound 37 the chemical shift of the signal from the C-19 methyl is 1.52 ppm [24]. Having analyzed the signal in such a weak field, we came to the conclusion that the hydroxyl at C-6 has the β orientation. Then, from the rule of the additivity of the influence of substituents on the chemical shifts of the signals of angular methyls [25], a theoretical value of 1.6 ppm (combined influence of the 1-oxo and the Δ<sup>2-</sup>, Δ<sup>4-</sup>, and 6β-OH groups) is obtained, which agrees with that actually found - 1.52 ppm.

Making use of just these considerations, in Table 2 we have assigned the signals of the tertiary methyl groups of the physalins in three cases where in the literature source only the magnitudes of the chemical shifts are given.

Plants of the genus *Physalis* have attracted human attention since ancient times: Some species have been cultivated as food plants [26, 27], and others are used in the folk medicine of the countries of Central and South America and South-east Asia [23, 28, 29]. It has been established that the active principle of an extract of *Ph. minima* consists of withasteroids.

The physiological action of some individual withasteroids has been studied. Withaferin A (1), first isolated from *Withania somnifera* [15] and later from *Ph. viscosa* [9], has been investigated most fully. It exhibits antifungal [30] and antibacterial [6] activities. Withaferin A is cytotoxic *in vitro* in a culture of KB tissue from a carcinoma of the human nasal pharynx and retards the growth of some tumor systems in mice [48]. It has an influence on the ultrastructure of the tumor cells, causing a retardation of mitosis in the metaphase and vacuolization of the cytoplasm [6]. Another withasteroid - withanolide E (2) - exhibited activity against P 388 leukemia of mice, B-16 melanoma of the mouth, and Lewis's lung carcinoma.

In a study of structure-property relationship using withaferin A and its derivatives as examples it has been shown that the manifestation of antitumoral activity requires the presence of an unsaturated lactone ring, a 1-keto unsaturated grouping [31, 32], a hydroxy group at C-4 [32], and an epoxy group [31]. 4 $\beta$ -Hydroxywithanolide E (5), distinguished by the  $\alpha$  orientation of the side chain at C-17, exhibited a high antitumoral activity in screening performed by a complex scheme in the National Cancer Institute (USA). By this characteristic they form a distinctly isolated group among the other withanolides, which possess an undirected cytotoxic action [33]. The increased activity of 4 $\beta$ -hydroxywithanolide E is apparently due also to the presence of a 14 $\alpha$ -hydroxy group, which is a necessary component of such physiologically active compounds as the cardenolides, bufadienolides, and ecdysteroids.

The biological activity of the withasteroids of the physalin group has been little studied. Physalin D (44) exhibited antitumoral activity in a tissue culture [34] and in B-16 melanocarcinoma [21]. Physalin B (35), which is cytotoxic for 9KB and KPS tumor cells (*in vitro*), just like 25,26-epidihydrophysalin C (34) proved to be moderately active against 3PS murine leukemia (*in vitro*). Confirming the conclusion of the favorable influence of a 5 $\alpha$ ,6 $\alpha$ -epoxy group on the intensification of antitumoral properties [31], Antoun et al. [21] showed that 5 $\alpha$ ,6 $\alpha$ -epoxyphysalin B is more toxic in 9KB but less toxic in 9PS tumor cells than the initial physalin B (35).

There has been a report of an abortive activity of physalin X obtained by modifying the physalins from *Ph. minima* (structure not deciphered) [29]. Some withasteroids of *Physalis* are characterized by insecticidal [35] and antifeedant [36] action.

Their broad spectrum of physiological action is the attractive feature that is responsible for the undiminishing interest in an all around study of *Physalis* withasteroids.

#### LITERATURE CITED

1. Flora of the USSR [in Russian], Vol. 22, (eds. B. K. Shishkin and E. G. Bobrov), Moscow (1955), pp. 62-69.
2. T. Matsuura, M. Kawai, R. Nakashima, and Y. Butsugan, *Tetrahedron Lett.*, 1083 (1969).
3. S. S. Subramanian, P. D. Sethi, *Indian J. Pharmacy*, 35, 36 (1973).
4. I. Kirson, A. Abraham, P. D. Sethi, S. S. Subramanian, and E. Glotter, *Phytochemistry*, 15, 340 (1976).
5. I. Kirson, and E. Glotter, *J. Natural Prod.*, 44, 633 (1981).
6. E. Glotter, I. Kirson, D. Lavie, and A. Abraham, "The Withanolides, a group of natural steroids," in: *Bioorganic Chemistry*, Vol. II (ed. E. E. Van Tamelen), Academic Press, New York (1978), pp. 57-95.
7. D. Lavie, S. S. Nittala, and V. Van de Velde, International Conference on the Chemistry and Biotechnology of Biologically Active Natural Products, 1st. (Proceedings, ed. B. Atanasova), Bulgarian Academy of Sciences, Sofia, Vol. 2 (1982), pp. 407-419.
8. F. Frolov, A. B. Ray, M. Sahai, E. Glotter, H. E. Gottlieb, and I. Kirson, *J. Chem. Soc. Perkin I*, 1029 (1981).
9. S. W. Pelletier, N. V. Mody, J. Nowacki, and J. Bhattacharyya, *J. Natural Prod.*, 42, 512 (1979).

10. S. W. Pelletier, G. Gebeyehu, J. Nowacki, and N. V. Mody, *Heterocycles*, 15, 317 (1981).
11. H. E. Gottlieb, I. Kirson, E. Glotter, A. B. Ray, M. Sahai, and A. Ali, *J. Chem. Soc., Perkin I*, 2700 (1980).
12. M. Sahai, H. E. Gottlieb, A. B. Ray, A. Ali, E. Glotter and I. Kirson, *J. Chem. Res. (Synop.)*, 346 (1982).
13. N. D. Abdullaev, V. A. Maslennikova, R. N. Tursunova, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 197 (1984).
14. D. Lavie, I. Kirson, E. Glotter, *Israel J. Chem.*, 6, 671 (1968).
15. a) A. Yardin and D. Lavie, *J. Chem. Soc.*, 2925 (1962), b) D. Lavie, E. Glotter, and Y. Shvo, *J. Chem. Soc.*, 7517 (1965).
16. I. Kirson, E. Glotter, A. Abraham, and D. Lavie, *Tetrahedron*, 26, 2209 (1970).
17. I. Kirson, D. Lavie, and E. Glotter, *Phytochemistry*, 14, 189 (1975).
18. I. Kirson, and H. E. Gottlieb, *J. Chem. Res. (Synop.)*, 338; (M) 4275 (1980).
19. H. E. Gottlieb and I. Kirson, *J. Org. Magn. Reson.*, 16, 20 (1981).
20. M. Sahai, P. Neogi, and A. B. Ray, *Heterocycles*, 19, 37 (1982).
21. M. D. Antoun, D. Abramson, R. L. Tyson, Ching Jer Chang, J. L. McLaughlin, G. Peck, and J. M. Cassidy, *J. Natural Prod.*, 44, 579 (1981).
22. R. N. Tursunova, V. A. Maslennikova, N. K. Abubakirov, *Khim. Prir. Soedin.*, 147 (1977).
23. E. Glotter, I. Kirson, A. Abraham, P. D. Sethi, and S. S. Subramanian, *J. Chem. Soc., Perkin I*, 1370 (1975).
24. K. K. Purushothaman and S. Vasanth, 1st International Conference on the Chemistry and Biotechnology of Biologically Active Natural Products, (Proceedings) (ed. B. Atanasova), Bulgarian Academy of Sciences, Sofia, Vol. 3 (1), (1981), pp. 267-271.
25. N. S. Bhacca and D. H. Williams, *Applications of NMR Spectroscopy in Organic Chemistry*, Holden-Day, San Francisco (1964).
26. V. N. Vekhov, I. A. Gubanov, and G. F. Lebedeva, *Cultivated Plants of the USSR [in Russian]*, Moscow (1978), pp. 283-284.
27. S. M. Aslanov, Sh. E. Gorcheva, and V. Kh. Khalikova, *Izv. Akad. Nauk AzSSR, Seriya, Biol. Nauk*, No. 6, 32 (1976).
28. R. R. Alluri, R. J. Miller, W. H. Shelver, S. K. W. Khalil, *Lloydia*, 39, 405 (1976).
29. K. Mohana, R. Uma, and K. K. Purushothaman, *Indian J. Exp. Biol.*, 17, 690 (1979).
30. G. L. R. Das, P. D. Sethi, K. B. Sharma, and S. S. Subramanian, *Indian J. Pharm.*, 32, 70 (1970).
31. M. Yoshida, A. Hoshi, K. Kuretani, M. Ishiguro, and N. Ikekawa, *J. Pharm. Dyn.*, 2, 92 (1979).
32. A. G. Gonzales, V. Darias, H. D. A. Martin, and M. C. Soares, *Fitoterapia*, 53, 85 (1982); *Chem. Abstr.*, 98, 191295f (1983).
33. M. Suffness and J. Douros, *J. Natural Prod.*, 45, 1 (1982).
34. N. B. Mulchandani, S. S. Iyer, and L. P. Badheka, Government of India Atomic Energy Commission (Report), No. 764 (1974), p. 11.
35. B. P. Khare, S. B. Gupta, and S. Chandra, *Indian J. Agric. Res.*, 8, 243 (1974); *Chem. Abstr.*, 84, 26828k (1976).
36. K. R. S. Asher, N. E. Nening, M. Eliyahu, I. Kirson, A. Abraham, and E. Glotter, *Experientia*, 36, 998 (1980).
37. S. M. Kupchan, W. K. Anderson, P. Bollinger, R. W. Duskotch, R. M. Smith, J. A. S. Renault, H. K. Shnoes, A. L. Burlingame, and D. H. Smith, *J. Org. Chem.*, 34, 3858 (1969).
38. a) D. Lavie, I. Kirson, E. Glotter, D. Rabinovich, and Z. Shakked, *J. Chem. Soc. Chem. Commun.*, 877 (1972). b) E. Glotter, I. Kirson, A. Abraham, and D. Lavie, *Tetrahedron*, 29, 1353 (1973). c) E. Glotter, A. Abraham, G. Gunzberg, and I. Kirson, *J. Chem. Soc., Perkin I*, 341 (1977).
39. V. A. Maslennikova, R. N. Tursunova, K. L. Seitanidi, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 214 (1980).
40. K. Sakurai, H. Ishii, Sh. Kobayashi, and T. Iwao, *Chem. Pharm. Bull.*, 24, 1403 (1976).
41. R. N. Tursunova, V. A. Maslennikova, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 187 (1981).
42. T. K. Bhattacharya, T. N. C. Vedantham, S. S. Subramanian, and I. Kirson, *Indian J. Pharm. Sci.*, 177, (1978).
43. A. B. Ray, M. Sahai, and B. C. Das, *J. Indian Chem. Soc.*, 55, 1175 (1978).
44. L. R. Row and K. Sambhi Reddy, K. Dhavaji, and T. Matsuura, *Phytochemistry*, 23, 427 (1984).
45. A. B. Ray, A. Ali, M. Sahai, P. L. Schiff, J. E. Knapp, and D. J. Slatkin, *Chem. Ind. (London)*, 62 (1981).
46. V. A. Maslennikova, R. N. Tursunova, and N. K. Abubakirov, *Khim. Prir. Soedin.*, 531 (1977).

47. M. Sahai, A. Ali, A. B. Ray, D. Slatkin, and I. Kirson, *J. Chem. Res. Synop.*, 152 (1983).
48. K. P. Balitskii and A. L. Vorontsova, *Medicinal Plants and Cancer [in Russian]*, Kiev (1982), p. 271.
49. I. Kirson, A. Cohen, M. Greenberg, and A. Abraham, *J. Chem. Res. (M)*, 1178 (1979).
50. I. Kirson, H. E. Gottlieb, and E. Glotter, *J. Chem. Res. (M)*, 2134 (1980).
51. M. Kawai and T. Matsuura, *Tetrahedron*, 26, 1743 (1970).
52. T. Matsuura, M. Kawai, R. Nakashima, and Y. Butsugan, *J. Chem. Soc. (C)*, 664 (1970).
53. T. Matsuura, and M. Kawai, *Tetrahedron Lett.*, 1765 (1969).
54. L. R. Row and K. S. Reddy, N. S. Sarma, T. Matsuura, and R. Nakashima, *Phytochemistry*, 19, 1175 (1980).
55. K. K. Purushothaman and S. Vasanth, and R. Nakashima, *Indian J. Chem. Soc., Sect. B*, 20B (1981).
56. L. R. Row, N. S. Sarma, T. Matsuura, and R. Nakashima, *Phytochemistry*, 17, 1647 (1978).
57. L. R. Row, N. S. Sarma, K. S. Reddy, T. Matsuura, and R. Nakashima, *Phytochemistry*, 17, 1647 (1978).\*
58. B. D. Benjamin and N. B. Mulchandani, *Planta Med.*, 37, 88 (1979).
59. N. B. Mulchandani, S. S. Iyer, and L. P. Badheka, *Planta Med.*, 37, 268 (1979).
60. I. Kirson, E. Glotter, A. B. Ray, A. Ali, H. E. Gottlieb, and M. Sahai, *J. Chem. Res. (Synop.)*, 120 (1983).
61. A. Bagchi, P. Neogi, M. Sahai, A. B. Ray, Y. Oshima, and H. Hikino, *Phytochemistry*, 23, 853 (1984).

\*As in Russian Original.

#### LIPIDS OF THE SEEDS OF *Securinega suffruticosa*

S. G. Yunusova, S. D. Gusakova,  
and A. I. Glushenkova

UDC 547.915:665:33

The lipid composition of the seeds of *Securinega suffruticosa* (*Euphorbiaceae*) has been studied, and eight classes of lipids have been identified with a predominance of triacylglycerols; the fatty acid compositions and structures of the triacylglycerols have been determined. Among the hydroxy acids of the hydroxyacylglycerols 13 components belonging to saturated, monoenic, and dienic acids of the C<sub>17</sub>, C<sub>18</sub>, and C<sub>20</sub> series have been identified; 12-hydroxyheptadecanoic and 12-hydroxyeicosanoic acids are new.

The family Euphorbiaceae include 280 genera and 8000 species, the genera *Euphorbia*, *Croton*, and *Phyllanthus* being the most widespread. Some indices of the total lipids and of the fatty acids have been determined for the seeds of more than 58 species of *Euphorbiaceae* [1]. There is no information in the literature on *Securinega suffruticosa* (Pall.) Rend., but it is known [2] that this plant contains alkaloids which serve as a basis for the creation of medicinal preparations used in hypotension, afflictions of the nervous system, and chronic alcoholism [2].

We have investigated the seed lipids of the Far Eastern species *S. suffruticosa* introduced into the Tashkent Botanical Garden. The total lipids were separated by column chromatography on silica gel into individual classes of compounds. The lipids were identified by their chromatographic mobilities in TLC in comparison with model samples, from the results of chemical transformations, and from their IR, UV, and mass spectra. The lipid composition is given below (% by weight): hydrocarbons 0.2; triacylglycerols (TAGs) 95.0; free fatty acids (FFAs) 1.0; sterols 0.6; total diacyl- and hydroxyacyldiacylglycerols (DAGs and HAGs) 2.6; monoacylglycerols (MAGs) 0.1; polar lipids (PLs) 0.5. Thus, the seed lipids of *S. suffruticosa* consist of a total of eight classes with a predominance of TAGs.

---

Institute of the Chemistry of Plant Substances, Academy of Sciences of the Uzbek SSR, Tashkent. Translated from *Khimiya Prirodnykh Soedinenii*, No. 3, pp. 277-281, May-June, 1986. Original article submitted October 23, 1985.