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## Key indicators

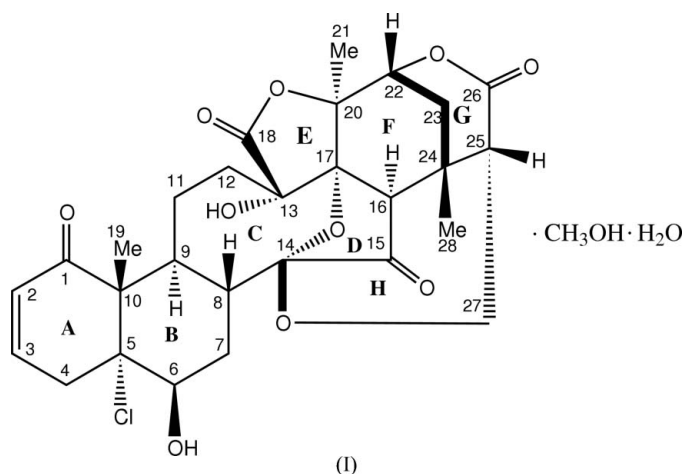
Single-crystal X-ray study  
 $T = 293\text{ K}$   
Mean  $\sigma(\text{C}-\text{C}) = 0.003\text{ \AA}$   
Disorder in solvent or counterion  
 $R$  factor = 0.035  
 $wR$  factor = 0.095  
Data-to-parameter ratio = 14.8For details of how these key indicators were  
automatically derived from the article, see  
<http://journals.iucr.org/e>.**(5*R*,6*S*,8*S*,9*R*,14*R*,15*R*,17*R*,18*S*,21*S*,24*R*,26*S*,27*R*)-  
5*α*-Chloro-16,24-cyclo-13,14-secoergost-2-ene-18,26-  
dioic acid-14:17,14:27-diepoxy-6*β*,13,20,22-tetra-  
hydroxy-1,15-dioxo- $\gamma$ -lactone  $\delta$ -lactone methanol  
solvate monohydrate**

The title compound,  $\text{C}_{28}\text{H}_{27}\text{O}_{10}\text{Cl}\cdot\text{CH}_3\text{OH}\cdot\text{H}_2\text{O}$ , was isolated from *Physalis minima*. The rigid molecule consists of eight fused rings involving three lactones. The spiro-fused  $\gamma$ -lactone rings are in half-chair and envelope conformations. The spiro-fused  $\gamma$ -lactone rings are fused to a cyclohexene ring, which is in a half-chair conformation. The outermost cyclohexene ring and  $\delta$ -lactone rings adopt half-chair and envelope conformations, respectively. Intra- and intermolecular  $\text{O}-\text{H}\cdots\text{O}$ ,  $\text{C}-\text{H}\cdots\text{Cl}$  and  $\text{C}-\text{H}\cdots\text{O}$  hydrogen bonds are observed.

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## Comment

Physalins are the steroidal lactone constituents of *Physalis* and other closely related genera, belonging to the family Solanaceae (Makino, Kawai, Kito *et al.*, 1995). Normal withanolides such as withaferin-A are C-28 steroidal compounds possessing a relatively highly oxidized ergostane-type skeleton and characterized by a six-membered lactone ring in the side chain (Kirson *et al.*, 1971; Glotter *et al.*, 1974). The physalins are biogenetically related to the withanolides and characterized by (a) oxidative C13/C14-bond cleavage yielding a nine-membered ring, (b) formation of a new six-membered carbocycle between C16 and C24, and (c) oxidation of the C13 methyl group to a carboxylic acid, which results in the formation of 18,20-lactonization (Glotter *et al.*, 1974). Physalins are commonly named as 16,24-cyclo-13,14-secoosteroids (Makino, Kawai, Kito *et al.*, 1995).



The title compound, (I), known as physalin H, is a steroidal lactone (physalin) previously isolated from *Physalis angulata* (Row *et al.*, 1978; Makino, Kawai, Ogura *et al.*, 1995). Steroidal lactones (withanolides and physalins) exhibit a number of

biological activities, including antitumour (Antoun *et al.*, 1981), immunomodulatory (Budhiraja *et al.*, 1984), antimycobacterial (Pietro *et al.*, 2000), antifungal, anti-inflammatory (Budhiraja *et al.*, 1984, 1986), insect repellent (Glatter, 1991) and immunostimulating (Bates & Eckert, 1972). Compound (I) showed moderate *in vitro* cytotoxic activity against HeLa cells (Makino, Kawai, Ogura *et al.*, 1995). As part of our ongoing research into bioactive constituents from medicinal plants, we have isolated compound (I) from *Physalis minima* for the first time. Fresh plants of *Physalis minima*, locally known as Aknaaj, were collected from Karachi (Pakistan). In the present investigation, we have established the absolute stereochemistry of (I) by single-crystal X-ray diffraction studies (Fig. 1).

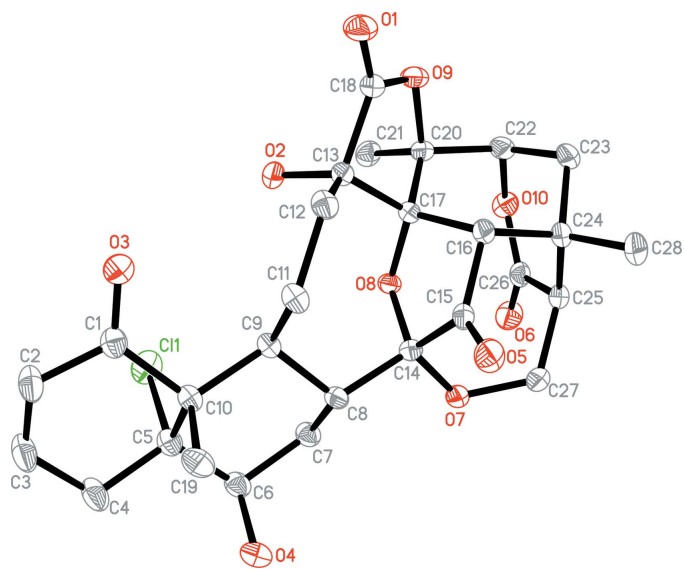
Compound (I) is a highly oxygenated steroidal lactone having eight fused rings. The six-membered ring A (C1–C5/C10) is in a half-chair conformation, with atoms C5 and C10 deviating from the C1/C2/C3/C4 plane by 0.335 (4) and  $-0.453$  (4) Å, respectively. Ring B (C5–C10) is trans-fused to ring A and adopts a chair conformation. The two spiro-fused five-membered rings D (O8/C14–C17) and E (O9/C18/C13/C17/C20) adopt half-chair and envelope conformations, respectively; in ring D, the deviations of atoms C16 and C17 from the O8/C14/C15 plane are 0.355 (4) and  $-0.226$  (4) Å, respectively, and in ring E atom C17 deviates by 0.638 (3) Å from the O9/C18/C13/C20 plane. Ring F (C16/C17/C20/C22–C24) is in a half-chair conformation, allowing the C24–C16–C17, C16–C17–C20, C17–C20–C22 and C20–C22–C23 bond angles to widen to 114.61 (14), 114.97 (14), 114.43 (14) and 114.83 (16)°, respectively, while the other internal angles remain close to the tetrahedral value. Ring G (O10/C22–C26) adopts an envelope conformation. The two epoxy seven- and eight-membered rings (O7/C14–C16/C24/C25/C27 and C8/C9/C11–C14/C17/O8) are in chair and boat–chair conformations, respectively.

The  $Csp^3-Csp^3$  bond distances lie in the range 1.508 (3)–1.566 (2) Å. The C24–C25–C26 [117.03 (15)°], C9–C11–C12 [119.48 (14)°] and C11–C12–C13 [119.98 (14)°] angles deviate significantly from ideal tetrahedral values, as reported for this class of compounds (Kawai *et al.*, 1970, 1994; Taga *et al.*, 1991). The bond angles involving the spiro atom C17 range from 102.02 (13) to 115.05 (13)°.

The water and methanol molecules of solvation participate in several hydrogen bonds. A number of O–H...O, C–H...Cl and C–H...O hydrogen bonds are observed in the molecular and crystal structures. The molecules are linked together by these interactions to form a three-dimensional molecular network (Fig. 2). Most of the intramolecular hydrogen bonds form S(5) or S(6) ring motifs (Bernstein *et al.*, 1995).

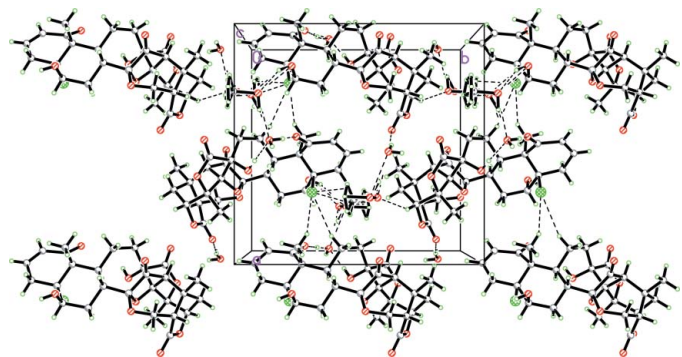
## Experimental

Air-dried and milled plant material of *Physalis minima* (25.8 kg) was extracted with methanol (120 l) over a period of 21 d at room temperature. After evaporation of the solvent, an extract (2.5 kg) was obtained, which was dissolved in distilled water (5 l) and defatted



**Figure 1**

The structure of (I), showing 50% probability displacement ellipsoids and the atom-numbering scheme. H atoms and methanol and water molecules have been omitted for clarity.



**Figure 2**

The crystal packing of (I), viewed along the *c* axis. Dashed lines indicate hydrogen bonds.

with petroleum ether (10 l). The defatted aqueous extract was further fractionated with  $CH_2Cl_2$  (35 l) and *n*-BuOH (5 l), respectively. The  $CH_2Cl_2$  extract was concentrated to a gum (350.5 g) and subjected to column chromatography. A fraction (1.4 g), obtained on elution with  $CH_2Cl_2$ –MeOH (95:5), was subjected to repeated column chromatography, which yielded sub-fractions A (120.5 mg), B (98.8 mg), C (50.5 mg), D (105.8 mg) and E (88.5 mg). Repeated column chromatography on sub-fraction B (silica gel 70–230 mesh size) using petroleum ether–acetone (80:20), afforded compound (I) (20 mg), which was recrystallized using  $CH_2Cl_2$ –MeOH (70:30) [Physalin H (I): 20 mg,  $5.7 \times 10^{-3}$ % yield, m.p. 548–551 K].

### Crystal data

$C_{28}H_{31}ClO_{10} \cdot CH_4O \cdot H_2O$   
 $M_r = 613.04$   
 Orthorhombic,  $P2_12_12_1$   
 $a = 13.0931$  (5) Å  
 $b = 13.5932$  (6) Å  
 $c = 15.6098$  (6) Å  
 $V = 2778.19$  (19) Å<sup>3</sup>  
 $Z = 4$   
 $D_x = 1.466$  Mg m<sup>−3</sup>

Mo  $K\alpha$  radiation  
 Cell parameters from 15020 reflections  
 $\theta = 2.0$ – $26.5^\circ$   
 $\mu = 0.21$  mm<sup>−1</sup>  
 $T = 293$  (2) K  
 Block, colourless  
 $0.54 \times 0.33 \times 0.21$  mm

## Data collection

Siemens SMART CCD area-detector diffractometer  
 $\omega$  scans  
 Absorption correction: multi-scan (SADABS; Sheldrick, 1996)  
 $T_{\min} = 0.897$ ,  $T_{\max} = 0.957$   
 15825 measured reflections

5745 independent reflections  
 5545 reflections with  $I > 2\sigma(I)$   
 $R_{\text{int}} = 0.017$   
 $\theta_{\text{max}} = 26.5^\circ$   
 $h = -16 \rightarrow 14$   
 $k = -17 \rightarrow 16$   
 $l = -19 \rightarrow 17$

## Refinement

Refinement on  $F^2$   
 $R[F^2 > 2\sigma(F^2)] = 0.035$   
 $wR(F^2) = 0.095$   
 $S = 0.85$   
 5745 reflections  
 389 parameters  
 H atoms treated by a mixture of independent and constrained refinement

$w = 1/[\sigma^2(F_o^2) + (0.0667P)^2 + 1.2367P]$   
 where  $P = (F_o^2 + 2F_c^2)/3$   
 $(\Delta/\sigma)_{\text{max}} = 0.002$   
 $\Delta\rho_{\text{max}} = 0.25 \text{ e } \text{\AA}^{-3}$   
 $\Delta\rho_{\text{min}} = -0.25 \text{ e } \text{\AA}^{-3}$   
 Absolute structure: Flack (1983), with 2520 Friedel pairs  
 Flack parameter: 0.02 (6)

Table 1

Hydrogen-bond geometry ( $\text{\AA}$ ,  $^\circ$ ).

D—H...A	D—H	H...A	D...A	D—H...A
O11A—H11O...O1W <sup>i</sup>	0.96 (4)	1.84 (4)	2.780 (5)	163 (4)
O1W—H1W1...O3 <sup>ii</sup>	0.84	2.08	2.775 (2)	139
O2—H1O2...O1W <sup>ii</sup>	0.82	1.98	2.786 (2)	170
O4—H1O4...O11A <sup>ii</sup>	0.82	1.97	2.718 (5)	152
O1W—H2W1...O6 <sup>iii</sup>	0.82	2.03	2.832 (2)	170
C4—H4B...O4 <sup>ii</sup>	0.97	2.54	2.898 (3)	102
C7—H7A...Cl1 <sup>ii</sup>	0.97	2.72	3.1140 (19)	105
C7—H7B...O7 <sup>ii</sup>	0.97	2.31	2.696 (2)	102
C9—H9...Cl1 <sup>ii</sup>	0.98	2.75	3.1814 (17)	107
C9—H9...O2	0.98	2.27	3.065 (2)	138
C11—H11A...O5 <sup>ii</sup>	0.97	2.41	3.191 (2)	137
C11—H11B...O3 <sup>ii</sup>	0.97	2.38	2.894 (2)	112
C19—H19B...Cl1 <sup>iv</sup>	0.96	2.71	3.578 (2)	150
C19—H19C...O4 <sup>ii</sup>	0.96	2.38	3.012 (3)	123
C21—H21B...O2 <sup>ii</sup>	0.96	2.28	2.871 (2)	119
C21—H21C...O8 <sup>ii</sup>	0.96	2.51	2.871 (2)	102
C22—H22...O11A <sup>iii</sup>	0.98	2.54	3.404 (6)	146

Symmetry codes: (i)  $x + \frac{1}{2}, -y + \frac{1}{2}, -z + 1$ ; (ii)  $x, y, z$ ; (iii)  $-x + \frac{3}{2}, -y, z + \frac{1}{2}$ ; (iv)  $x - \frac{1}{2}, -y + \frac{1}{2}, -z + 1$ .

The O atom of the methanol molecule is disordered over two positions with occupancies of 0.602 (6) and 0.398 (6). During the refinement, the  $U^{\text{ij}}$  components of the disordered atoms were restrained to be equal. Atom H11O was located in a difference map and refined isotropically. The water H atoms were located in a difference map and allowed to ride on their parent atom with  $U_{\text{iso}}(\text{H}) = 1.5U_{\text{eq}}(\text{O})$  (O—H = 0.82 and 0.84  $\text{\AA}$ ). All other H atoms

were placed in calculated positions (O—H = 0.82  $\text{\AA}$  and C—H = 0.93–0.98  $\text{\AA}$ ), with  $U_{\text{iso}}$  values constrained to be  $1.5U_{\text{eq}}$  of the carrier atom for the methyl and hydroxyl H atoms, and  $1.2U_{\text{eq}}(\text{C})$  for the others.

Data collection: SMART (Siemens, 1996); cell refinement: SAINT (Siemens, 1996); data reduction: SAINT; program(s) used to solve structure: SHELXTL (Sheldrick, 1997); program(s) used to refine structure: SHELXTL; molecular graphics: SHELXTL; software used to prepare material for publication: SHELXTL and PLATON (Spek, 2003).

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**(5*R*,6*S*,8*S*,9*R*,14*R*,15*R*,17*R*,18*S*,21*S*,24*R*,26*S*,27*R*)-  
5*α*-Chloro-16,24-cyclo-13,14-secoergost-2-ene-18,26-  
dioic acid-14:17,14:27-diepoxy-6*β*,13,20,22-tetra-  
hydroxy-1,15-dioxo- $\gamma$ -lactone  $\delta$ -lactone methanol  
solvate monohydrate. Corrigendum**

Some errors in the paper by Choudhary, Yousuf, Atta-ur-Rahman, Anjum, Fun & Ali [*Acta Cryst.* (2005), **E61**, o3523–o3525] are corrected. In the *Abstract*, the text ‘The rigid molecule consists of eight fused rings involving three lactones. The spiro-fused  $\gamma$ -lactone rings are in half-chair and envelope conformations. The spiro-fused  $\gamma$ -lactone rings are fused to a cyclohexene ring, which is in a half-chair conformation.’ is corrected to ‘The rigid molecule consists of eight fused rings involving two lactones. The spiro-fused rings *D* and *E* are in half-chair and envelope conformations. The spiro-fused  $\gamma$ -lactone rings are fused to a cyclohexene ring *F*, which is in a half-chair conformation.’ In line 11 of the *Comment*, an atom label is corrected so that the text reads ‘(*c*) oxidation of the C18 methyl group’.

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