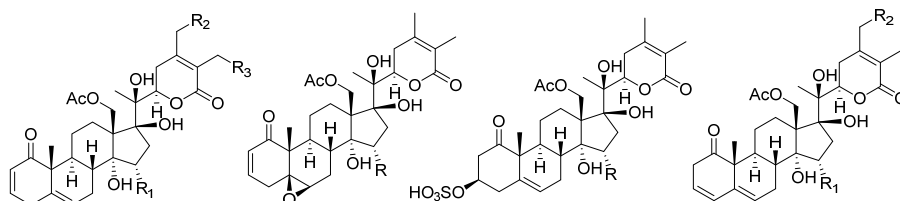


Withanolides from Aeroponically Grown *Physalis crassifolia* (Yellow Nightshade Ground Cherry) and Their Potent and Selective Cytotoxicity for Prostate Cancer Cells

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When cultivated under aeroponic growth conditions, *Physalis crassifolia* produced eleven new withanolides and seven known withanolides including those obtained from the wild-crafted plant. The structures of new withanolides, 15 α -hydroxyphysachenolide D (**1**), 27-hydroxyphysachenolide D (**2**), 15 α -acetoxy-27-hydroxyphysachenolide D (**3**), 15 α -acetoxy-27-O- β -D-glucopyranosyl-physachenolide D (**4**), 15 α -acetoxy-28-O- β -D-glucopyranosylphysachenolide D (**5**), 15 α -acetoxyphysachenolide C (**6**), 15 α -acetoxy-2,3-dihydrophysachenolide D-3 β -O-sulfate (**7**), 15 α ,18-diacetoxy-28-hydroxy-17-*epi*-withanolide K (**8**), 23 β -hydroxyphysacoztolide E (**9**), 14 α -hydroxywithanolide A (**10**), and 16-oxo-17(20)-dehydrohyoscyamilactol (**11**), were elucidated by the application of spectroscopic techniques and the known withanolides, physachenolide D (**12**), 15 α -acetoxyphysachenolide D (**13**), 15 α -acetoxy-28-hydroxyphysachenolide D (**14**), physachenolide C (**15**), 2,3-dihydrophysachenolide D-3 β -O-sulfate (**16**), 18-acetoxy-17-*epi*-withanolide K (**17**), and physacoztolide E (**18**), were identified by comparison of their spectroscopic data with those reported. Withanolides **1–11** and **16** were evaluated for their potential anticancer activity using five tumor cell lines. Of these, 17 β -hydroxy-18-acetoxywithanolides **1**, **2**, **6**, **7**, and **16** showed potent anti-proliferative activity, some with selectivity for prostate adenocarcinoma (LNCaP and PC-3M) compared to breast adenocarcinoma (MCF-7), non-small cell lung cancer (NCI-H460), and CNS glioma (SF-268) cell lines. Cytotoxicity data for **12–15**, **17**, and **19** suggested existence of additional structure-activity relationships (SARs) for 17 β -hydroxy-18-acetoxywithanolides.



- 1** R₁ = OH, R₂ = R₃ = H
2 R₁ = R₂ = H, R₃ = OH
3 R₁ = OAc, R₂ = H, R₃ = OH
4 R₁ = OAc, R₂ = H, R₃ = O- β -glc
5 R₁ = OAc, R₂ = O- β -glc, R₃ = H
12 R₁ = R₂ = R₃ = H
13 R₁ = OAc, R₂ = R₃ = H
14 R₁ = OAc, R₂ = OH, R₃ = H
6 R = OAc
15 R = H
7 R = OAc
16 R = H
8 R₁ = OAc, R₂ = OH
17 R₁ = R₂ = H
19 R₁ = OAc, R₂ = H

