SHORT COMMUNICATION

Antibacterial sesquiterpenoids from *Solanum lyratum*

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ABSTRACT

Investigation into the chemical diversity of *Solanum lyratum* led to the discovery of one new sesquiterpenoid, solyraterpenoid A (1), and two known compounds (2 and 3). The structure incorporating absolute configuration of 1 was determined via spectroscopic data, mainly including HRESIMS and NMR, and single-crystal X-ray diffraction analysis. Compound 1 showed significant antibacterial activity against *Pseudomonas aeruginosa*, *Escherichia coli*, and *Klebsiella pneumoniae* with MIC values of 8, 8, and 4 μg/mL, respectively.

1. Introduction

The genus *Solanum* is one of the largest genera of the Solanaceae family and comprised about 1400 species widely distributed throughout the world (Hegnauer 1990). Many species of the *Solanum* genus have invoked increasing attention from a lot of chemical researchers because of their biologically active constituents, mainly including sesquiterpenoids, steroids, steroidal alkaloids, and their glycosides (Nie et al. 2014; Yuan et al. 2016; Xu et al. 2018; Li et al. 2019; Ono et al. 2020). *Solanum lyratum* Thunb. is a perennial herb and is commonly known as “Bai-Ying” in traditional Chinese medicine and “Back-Mo-Deung” in traditional Korea medicine, and has been used as an antitumor, anti-inflammatory, immunomodulatory, anti-anaphylactic, antioxidant, and antibacterial agent (Zhang et al. 2012; Chen et al. 2020). In order to discover more structurally diverse and bioactive ingredients, a phytochemical

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investigation on the whole plant of *S. lyratum* led to the isolation and characterization of three sesquiterpenoids (1–3) including one new eudesmane-type sesquiterpenoid (1) (Figure 1). The structure of 1 was undoubtedly assigned by the inspection of spectroscopic data and single-crystal X-ray diffraction analysis. The antibacterial activity assays of compounds 1–3 were undertaken against four clinical bacteria, including *Pseudomonas aeruginosa*, MRSA, *Escherichia coli*, and *Klebsiella pneumoniae*. The isolation, structure characterization, and antibacterial activity evaluation of these sesquiterpenoids were described.

2. Results and discussion

Compound 1 gave a molecular formula of C_{15}H_{24}O_{3}, indicative of four degrees of unsaturation, as assigned by a sodium adduct ion at *m/z* 275.1608 ([M + Na]^+, calcd for 275.1618) from the HRESIMS data. Analysis of the 1D and 2D NMR data (Table S1) of 1 with those of 6β-hydroxy-7α(H)-eudesm-4-en-3-one (Syah et al. 1996), indicated that both compounds were eudesmane-type sesquiterpenoids with structural resemblances, with the only diagnostic difference that a methylene in 6β-hydroxy-7α(H)-eudesm-4-en-3-one was replaced by an oxygenated methine at C-1 (δ C 75.0) in 1, as supported by the key 1H–1H COSY correlation of H-1/H2-2 and HMBC correlations of H3-14 with C-1 (δ C 75.0). The gross structure of 1 was established as shown in Figure S1.

To support the above-mentioned deduction and verify the absolute configuration of 1, a single-crystal X-ray diffraction pattern was obtained using the anomalous scattering of Cu Kα radiation (Figure S2), allowing an explicit assignment of the absolute structure as 1R,6R,7S,10R on the basis of the Flack parameter of 0.03(18). Therefore, the absolute structure of 1 was defined and named 1β,6β-dihydroxy-7α(H)-eudesm-4-en-3-one, which was given a trivial name solyraterpenoid A.

Two known compounds were identified as trichocarotin G (2) (Shi et al. 2018) and (-)-clovane-2,9-diol (3) (Heymann et al. 1994), by comparison of its NMR data and specific optical rotations with the literature.

Compounds 1–3 were evaluated for the antibacterial activity against *Pseudomonas aeruginosa*, methicillin-resistant *Staphylococcus aureus* (MRSA), *Escherichia coli*, and *Klebsiella pneumoniae*. As a result (Table S2), compound 1 showed remarkable antibacterial activity against *P. aeruginosa*, MRSA, *E. coli*, and *K. pneumoniae* with MIC values of 8, 32, 8, and 4 μg/mL, respectively, while compound 2 showed weak antibacterial activity against *P. aeruginosa* and MRSA with MIC values of 32 and 64 μg/mL,
respectively, and compound 3 showed weak antibacterial activity against MRSA with a MIC value of 32 μg/mL.

3. Experimental

3.1. General experimental procedures

UV data were collected on a Shimadzu UV2401PC spectrophotometer. Optical rotations (in MeOH) were collected using a JASCO P-1020 digital polarimeter. IR spectra were measured on a Tenor 27 FT-IR spectrometer with KBr pellets. NMR data were obtained on a Bruker DRX-600 NMR spectrometer at 600 MHz for 1H NMR and 150 MHz for 13C NMR. The 1H and 13C NMR chemical shifts were referenced to the solvent peaks for CDCl3 (δH 7.26/δC 77.2). HRESIMS data were acquired on an API QSTAR Pulsar 1 spectrometer in the positive ion mode. Compounds were purified by an Agilent 1100 liquid chromatography using an RP-C18 column (5 μm, 9.4 × 250 mm, Welch Ultimate XB-C18). Silica gel (200–300 mesh, Qingdao Marine Chemical Inc., China), Sephadex LH-20 (GE Healthcare Bio-Sciences AB, Sweden), and ODS (50 μm, YMC Co. Ltd., Japan) were applied for the column chromatography (CC). Fractions were monitored by TLC and spots were visualized by spraying heated silica gel plates with 10% H2SO4 in EtOH.

3.2. Plant material

The whole plant S. lyratum was collected from the Wudang Mountain area of Hubei Province of China in September 2020. The voucher specimen (20200902) was deposited in Hubei University of Medicine (Shiyan, China).

3.3. Extraction and isolation

The air-dried whole plant S. lyratum (2.5 kg) was powdered and extracted with 75% aqueous ethanol by maceration (3 × 5 L) at room temperature. The solvent was dried under reduced pressure to yield a crude extract, which was then suspended in water and sequentially partitioned with EtOAc. The EtOAc extract (55 g) was then subjected to a silica gel column using a step-wise gradient elution of CHCl3–MeOH (1:0, 20:1, 10:1, 5:1, 2:1, 0:1, v/v) to afford five main fractions (A–E).

Fraction B (9 g) was subjected to an RP-C18 silica gel column eluted with MeOH–H2O (20:80, 40:60, 60:40, 80:20, 100:0, v/v) to afford six main fractions, C1–C6. Fraction C3 (1.5 g) was purified using silica gel CC eluted with petroleum ether–EtOAc (8:1, 4:1, 2:1, 1:1, v/v) to afford six fractions, C3a–C3f. Fraction C3d (110.2 mg) was subjected to Sephadex LH-20 (CH2Cl2–CH3OH, 1:1, v/v) and further purified by semipreparative HPLC (MeCN–H2O, 50:50, 2.5 mL/min) to afford compound 1 (4.6 mg, tR 32 min) and 3 (3.2 mg tR 35 min). Fractions C3e (160.8 mg) was subjected to Sephadex LH-20 (CH2Cl2–CH3OH, 1:1, v/v) and further purified by semipreparative HPLC (MeCN–H2O, 50:50, 2.5 mL/min) to afford compound 2 (4.2 mg, tR 20 min).
3.4. Solyraterpenoid A (1)

Colorless crystals; C_{15}H_{24}O_{3}; [x]^{22}_D: -5.4 (c 0.1, MeOH); UV (MeOH) \lambda_{max} (log e): 245 (4.05) nm; IR (\mu_{max}): 3429, 2943, 2871, 1651, 1456, 1412, 1384, 1324, 1176, 1128, 1073, 1026, 578 cm\(^{-1}\); For \(^1\)H and \(^{13}\)C NMR data, see Table S1; HRESIMS at m/z 275.1608 ([M + Na]\(^+\), calcd for 275.1618).

3.5. Single-crystal X-ray diffraction analysis

Suitable crystals of compound 1 were obtained in CH\(_3\)OH. The intensity data for 1 were recorded on a Bruker APEX DUO diffractometer equipped with an APEX II CCD using Cu K\(\alpha\) radiation at 100 K. Cell refinement and data reduction were carried out using Bruker SAINT. The structures were solved by direct methods using SHELXS-97. Refinements were performed with SHELXL-97 using full-matrix least-squares, with anisotropic displacement parameters used for all non-hydrogen atoms. The hydrogen atoms were attached at calculated positions and refined with a riding model. Molecular graphics were computed with PLATON. Crystallographic data for the reported structures (excluding structure factor tables) have been deposited in the Cambridge Crystallographic Data Center as supplementary publication no. CCDC 1554097 for 1. Copies of the data can be obtained free of charge from the CCDC, 12 Union Road, Cambridge CB 1EZ, UK [fax: Int. +44(0) (1223) 336 033]; e-mail: deposit@ccdc.cam.ac.uk.

Crystallographic data for compound 1: \(C_{15}H_{24}O_{3}\), \(M = 252.34\), orthorhombic, \(a = 7.0686(10)\) Å, \(b = 10.4801(2)\) Å, \(c = 18.9502(4)\) Å, \(\alpha = 90^\circ\), \(\beta = 90^\circ\), \(\gamma = 90^\circ\), \(V = 1403.82(4)\) Å\(^3\), \(T = 100(2)\) K, space group \(P2_1\), \(Z = 4\), \(\mu(Cu K\alpha) = 0.649\) mm\(^{-1}\), 9137 reflections measured, 2406 independent reflections (\(R_{int} = 0.0455\)). The final \(R_1\) values were 0.0342 (\(I > 2\sigma(I)\)). The final w\(R(F^2)\) values were 0.0903 (\(I > 2\sigma(I)\)). The final \(R_1\) values were 0.0343 (all data). The final w\(R(F^2)\) values were 0.0906 (all data). The goodness of fit on \(F^2\) was 1.049. Flack parameter = 0.03(18).

3.6. Antibacterial activity assay

The strains \(Pseudomonas aeruginosa\) ATCC 15442, methicillin-resistant \(Staphylococcus aureus\) (MRSA) ATCC BAA-1720, \(Escherichia coli\) ATCC 35131, and \(Klebsiella pneumoniae\) ATCC 31488 used in the antibacterial activity assay were obtained from the ATCC. The reference compounds [ceftriaxone (Sigma, cat # 1098184); vancomycin (Sigma, cat # 861987); amikacin (Sigma, cat # 1019508); meropenem (Sigma, cat # M2574)] were recommended by the National Committee for Clinical Laboratory Standards. The investigated compounds were \(\geq95\%\) pure (HPLC, wavelength = 210 nm). All the test compounds were dissolved in DMSO as 20 mg/mL stock solutions. Determinations of the MICs were performed according to the previously reported broth microdilution strategy (Gao et al. 2019).

4. Conclusions

In conclusion, a new eudesmane-type sesquiterpenoid, solyraterpenoid A (1), together with two known compounds (2 and 3), were isolated and characterized from the
whole plant *S. lyratum*. The absolute configuration of 1 was elucidated by single-crystal X-ray diffraction analysis. Compound 1 showed significant antibacterial activity against *P. aeruginosa*, *E. coli*, and *K. pneumoniae* with MIC values of 8, 8, and 4 μg/mL, respectively. Our current work greatly expands the chemical and pharmacological knowledge on the plants of *Solanum* genus.

**Disclosure statement**

No potential conflict of interest was reported by the authors.

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