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Xyloccensin L, a novel limonoid from *Xylocarpus granatum*

Jun Wu,[a,*] Si Zhang,[a] Qiang Xiao,[b] Qingxin Li,[a] Jianshe Huang,[a] Lijuan Long[a] and Liangmin Huang[a]

[a]*Guangdong Key Laboratory of Marine Materia Medica, South China Sea Institute of Oceanology, Chinese Academy of Sciences, 164 West Xingang Road, Guangzhou 510301, PR China*
[b]*State Bioorganic Phosphorus Chemistry Laboratory of Education Ministry, School of Sciences, Tsinghua University, Beijing 100084, PR China*

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Abstract—The isolation and structure elucidation of xyloccensin L from the stem bark of *Xylocarpus granatum* is described. Xyloccensin L is a highly oxidized heptacyclic A, B, D-*seco* limonoid with an α-8, 30-epoxy ring and a rare 1, 29 oxygen bridge.

The limonoids are modified triterpenes derived from a precursor with a 4,4,8-trimethyl-17-furanylsteroid skeleton, found to date only in plants of the order Rutales. Limonoids show a broad spectrum of biological activities. Some, like azadirachtin from the neem tree *Azadiracha indica*[1] and harrisonin from *Harrisonnia abyssinica*,[2] show marked insect antifeedant and growth regulating activities, while the rubrins from *Trichilia rubra* are potent cell adhesion inhibitory agents.[3] Past investigations on the chemical constituents of the seeds of two mangrove plants, *Xylocarpus granatum* and *Xylocarpus moluccensis*, have yielded 11 limonoids xyloccensins A-K.[4–8] In this paper, we describe the isolation and structure elucidation of a novel heptacyclic A, B, D-*seco* limonoid, xyloccensin L[9] (Fig. 1), which has an α-8, 30-epoxy ring and a rare oxygen bridge between C_1 and C_{29} from the stem bark of *X. granatum*.

The ethanolic extract of the stem bark of *X. granatum* was subjected to sequential extraction with petroleum ether and EtOAc. The resulting EtOAc extract was chromatographed on silica gel, octadecylsilyl silica gel, Sephadex LH-20 gel and followed by Prep. C_{18} HPLC to yield xyloccensin L (**1**) (Fig. 1).

The ESI-MS spectrum (positive ion mode) of **1** showed pseudo-molecular peaks at *m/z* 585 $[M+H]^+$, 607 $[M+Na]^+$ and 623 $[M+K]^+$, which suggested the molecular weight to be 584. The HRESI-MS measurements indicated a molecular formula of $C_{32}H_{40}O_{10}$, which was in agreement with the 1D NMR data.[9] Consequently, **1** had an unsaturation index of 13, which included three carbon–carbon double bonds, three ester functional groups and seven rings. The β-monosubstituted furan moiety and its position could be established

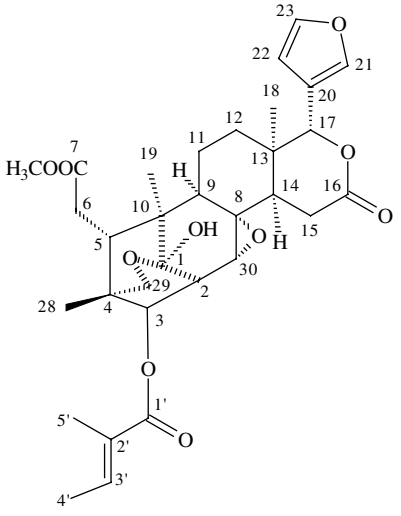

Figure 1. Structure of xyloccensin L.

Keywords: *Xylocarpus granatum*; A, B, D-*seco* limonoid; Xyloccensin L; α-8, 30-Epoxy ring; 1, 29 Oxygen bridge.
* Corresponding author. Tel.: +86-20-89023100; fax: 86-20-84451672; e-mail: wwujun2003@yahoo.com

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by the characteristic chemical shifts [δ_H 6.53(1H, dd, $J = 1.5$, 1.0 Hz), 7.57(1H, t, $J = 1.5$ Hz), 7.65(1H, dd, $J = 1.5$, 1.0 Hz); δ_C 111.1, 122.1, 142.2, 144.1] as well as the HMBC correlations from 17-H to C-20, C-21 and C-22. That C-17 was part of a δ-lactone, was shown by the HMBC correlations from 17-H to C-13, C-14 and C-16, combined with the following HMBC cross peaks (18-H_3/C-13, 18-H_3/C-14, 18-H_3/C-17, 14-H/8-C, 14-H/9-C, 14-H/13-C, 14-H/15-C, 14-H/16-C). In addition, the ^{1}H–^{1}H COSY cross signals observed (9-H/11α-H, 9-H/11β-H, 11α-H/12α-H, 11α-H/12β-H, 11β-H/12α-H, 11β-H/12β-H, 14-H/15α-H, 14-H/15β-H) established the upper right part of the structure (as drawn in Fig. 1).

The remaining tetracyclic system was strained and not previously reported in limonoids. However, in comparison with the structurally related A, B, D-*seco* limonoids,[10] its structure was elucidated by a series of 1D NOE and 2D NMR experiments (^{1}H–^{1}H COSY, HMQC and HMBC). According to the ^{13}C NMR spectral data, C-1 (δ_C 97.8) could be an acetal or hemiacetal carbon and C-3, C-8, C-29, C-30 (δ_C 77.1, 61.4, 67.8 and 59.9, respectively) should be oxygenated. A hydroxylic proton [δ_H 4.23(1H, s)] showing HMBC correlations to C-1, C-2 and C-10 suggested a hydroxyl group attached to C-1, which therefore indicated a hemiacetal functional group. An α-8, 30-epoxy ring was suggested by the chemical shifts [δ_H 3.07(1H, d, $J = 2.0$); δ_C 59.9, 61.4], which was consistent with the published data for a structurally related compound, humilinolide F.[10] The strong NOE interactions between 30-H [δ_H 3.07 (d, $J = 2.0$ Hz)] and 17-H [δ_H 5.28(s)], 2-H [δ_H 2.89 (dd, $J = 10.0$, 2.5 Hz)], 5-H [δ_H 2.86 (dd, $J = 10.0$, 2.5 Hz)] and 15-αH [δ_H 2.82 (dd, $J = 17.0$, 6.0 Hz)] also established this α configuration (as shown in Fig. 2). Comparison of the ^{1}H and ^{13}C NMR data of **1** with those of humilinolide F[10] revealed the absence of 29-Me in **1**. However, the chemical shifts [δ_H 3.44 (1H, dd, $J = 10.0$, 2.0 Hz), 3.98 (1H, d, $J = 10.0$ Hz), δ_C 67.8] of protons of **1** and the HMBC correlation from 29-αH (δ_H 3.44) to C-1 (δ_C 97.8) suggested an oxygen bridge between C-1 and C-29. Additionally, a methyl propionate substituent at C-5 found in typical A, B, D-*seco* limonoids, was observed from the chemical shifts (δ_H 3.69; δ_C 52.1, 174.6 and 32.6) and the HMBC correlations between 5-H/C-6, 5-H/C-7, 7-OMe-H_3/C-7. Furthermore, a tiglate moiety was also established by the distinctive chemical shifts (δ_H 7.10, 1.89 and 1.93; δ_C 167.8, 128.5, 140.0, 14.6 and 12.3) as well as the HMBC correlations between 4′-H_3/C-2′, 4′-H_3/C-3′, 5′-H_3/C-1′, 5′-H_3/C-2′, 5′-H_3/C-3′. The HMBC correlation between 3-H and C-1′ indicated that the tiglate was attached to C-3. Thus the structure of **1** was elucidated as shown in Figure 1, named xyloccensin L. The relative stereochemistry of **1** was also confirmed by a series of 1D NOE experiments that were performed as shown in Figure 2. The above data are largely in agreement with those reported for other limonoids.

Xyloccensin L, having an α-8, 30-epoxy ring and an oxygen bridge between C_1 and C_{29}, is to our knowledge, the only representative of A, B, D-*seco* limonoids with such a highly oxidized carbon framework.

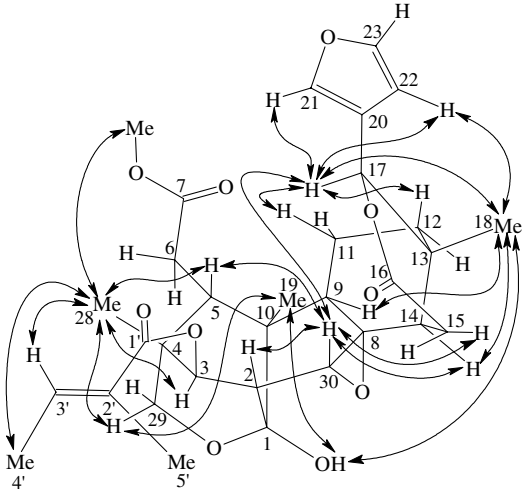

Figure 2. Significant NOE correlations in xyloccensin L.

Acknowledgements

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9. Xyloccensin L (**1**) was obtained as colorless amorphous solid, mp 110–112 °C; $[\alpha]_D^{25}$ −56 (*c* 0.6, acetone); UV (acetone) $\lambda_{max}(\varepsilon)$: No maxima above 214 nm; IR ν_{max} (KBr) cm^{-1}: 3446, 3141, 2951, 2873, 1733, 1652, 1646,

1635, 1558, 1506, 1457, 1436, 1383, 1265, 1159, 1125, 1079, 1026, 875, 769, 737, 603; HR-ESIMS m/z: 607.2521 $[M+Na]^+$ ($C_{32}H_{40}O_{10}Na$ requires 607.2519); ^1H NMR (500 MHz, acetone-d_6) (δ, ppm) 2.89 (dd, 1H, $J = 10.0$, 2.5 Hz, H-2), 5.10 (d, 1H, $J = 10.0$ Hz, H-3), 2.86 (dd, 1H, $J = 10.0$, 2.5 Hz, H-5), 2.48 (d, 1H, $J = 10.0$ Hz, H-6a), 2.45 (d, 1H, $J = 2.5$ Hz, H-6b), 2.09 (overlapped, 1H, H-9), 1.72–1.76 (m, 1H, H-11α), 1.89 (overlapped, 1H, H-11β), 1.37 (dt, 1H, $J = 14.5$, 4.5 Hz, H-12α), 2.06 (overlapped, 1H, H-12β), 1.57 (dd, 1H, $J = 13.0$, 6.0 Hz, H-14), 2.82 (dd, 1H, $J = 17.0$, 6.0 Hz, H-15α), 3.14 (dd, 1H, $J = 17.5$, 12.5 Hz, H-15β), 5.28 (s, 1H, H-17), 0.99 (s, 3H, H_3-18), 1.04 (s, 3H, H_3-19), 7.65 (dd, 1H, $J = 1.5$, 1.0 Hz, H-21), 6.53 (dd, 1H, $J = 1.5$, 1.0 Hz, H-22), 7.57 (t, 1H, $J = 1.5$ Hz, H-23), 0.68 (s, 3H, H_3-28), 3.44 (dd, 1H, $J = 10.0$, 2.0 Hz, H-29α), 3.98 (d, 1H, $J = 10.0$ Hz, 29β), 3.07 (d, 1H, $J = 2.0$ Hz, H-30), 3.69 (s, 3H, 7-OMe), 4.23 (s, 1H, 1-OH), 7.10 (qq, 1H, $J = 7.0$, 1.5 Hz, H-3′, Tiglate), 1.89 (d, 3H, $J = 7.0$ Hz, H_3-4, Tiglate), 1.93 (s, 3H, H_3-5′, Tiglate); ^{13}C NMR (125 MHz, acetone-d_6) (δ, ppm) 97.8 (s, C-1), 43.1 (d, C-2), 77.1 (d, C-3), 37.8 (s, C-4), 36.0 (d, C-5), 32.6 (t, C-6), 174.6 (s, C-7), 61.4 (s, C-8), 47.8 (d, C-9), 42.1 (s, C-10), 19.2 (t, C-11), 34.2 (t, C-12), 36.2 (s, C-13), 46.1 (d, C-14), 33.8 (t, C-15), 171.5 (s, C-16), 80.0 (d, C-17), 27.0 (q, C-18), 14.7 (q, C-19), 122.1 (s, C-20), 142.2 (d, C-21), 111.1 (d, C-22), 144.1 (d, C-23), 15.4 (q, C-28), 67.8 (t, C-29), 59.9 (d, C-30), 52.1 (q, 7-OMe), 167.8 (s, C-1′, Tiglate), 128.5 (s, C-2′, Tiglate), 10.0 (d, C-3′, Tiglate), 14.6 (q, C-4′, Tiglate), 12.3 (q, C-5′, Tiglate).

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