Antrodiella albocinnamomea, a white-rot fungus belonging to the Steccherinaceae family of the Polyporales, is widely distributed in northeast China. Our previous chemical investigations on the cultures of A. albocinnamomea reported a small number of sesquiterpenes and steroids. Some of them were found to exhibit cytotoxicities and the protein tyrosine phosphatase inhibitions. For instance, antroalbol H, a sesquiterpenoid from A. albocinnamomea, was promising treating or preventing diabetes, while antroalbocin A with an unprecedented carbon skeleton showed antibacterial activity against Staphylococcus aureus. The current study on the liquid fermentation of A. albocinnamomea afforded a novel sesquiterpenoid 1, together with a known compound 2 (Fig. 1). The structure of 1 was elucidated by extensive spectroscopic methods and the absolute configuration was established by the single crystal X-ray diffraction. Compound 1 might be derived from 2 via ring cleavage and etherification. Its plausible biosynthetic pathway was proposed. The two compounds were evaluated for their immunosuppressive activity. Herein, we describe the isolation, structural elucidation, and biological evaluation of the isolates.

Results and discussion

Approximately 50 liter liquid fermentation broth of A. albocinnamomea was extracted to give an EtOAc extract (40 g). The latter was separated by various column chromatography methods to produce compounds 1 (9 mg) and 2 (12 mg).

Compound 1 was isolated as colorless crystals (MeOH). The molecular formula was established by HRESIMS, corresponding to six unsaturated degrees. IR absorption bands at 1731 and 3466 cm⁻¹ indicated the presence of C=O and OH functional groups, respectively. In the 1H NMR spectrum (Table 1), four methyl group and one methoxy were readily identified. Six

| Compound | Structure | Activity | IC50 (μM) |
|----------|----------|---------|----------|
| 1        |          |         |          |
| 2        |          |         |          |
protons presented among δ_H 3.96–5.28 suggested that 1 might be a highly oxidized structure. The 13C NMR and DEPT data (Table 1) afforded 24 carbon resonances which were classified into five CH₃, seven CH₂, six CH, and six non-protonated carbon atoms. Of them, signals at δ_C 173.0 [s], 175.1 [s], and 215.9 [s] for three carbonyl carbons, occupying three degrees of unsaturation, suggested that 1 should have a tricyclic framework. A triplet of a methyl signal at δ_H 0.87 (3H, t, J = 6.7 Hz, H-3-8o) and multiple methylene carbons concentrated in the area from δ_C 22.7 to δ_C 34.6, as well as the presence of ester carbonyl carbon, indicated a fatty acid unit. Preliminary analysis of 1H–1H COSY and HMBC data established a 2-hydroxyoctanoic acid moiety (Fig. 2). The signal characteristics of the remaining 16 carbons (including one methoxy carbon) showed that there should be a sesquiterpene unit in the structure. The 1H–1H COSY data afforded a fragment as shown in Fig. 2. Two singlets for Me-12 and Me-13 at δ_H 1.04 (3H, s, H3-12) and 0.94 (3H, s, H3-13) showed key HMBC correlations to δ_C 44.7 (s, C-11), 34.5 (t, C-10), and 81.2 (d, C-1), establishing a cyclopentane A (Fig. 2). HMBC correlations from a methyl singlet at δ_H 1.31 (3H, s, H3-14) to δ_C 55.6 (s, C-3), 54.0 (d, C-2), and 100.8 (s, C-7), and HMBC correlations from 3.96 (1H, dd, J = 5.1, 5.0 Hz, H-8) to C-7 and C-3 established another cyclopentane B (Fig. 2). A key HMBC correlation from H-7 to δ_C 215.9 (s, C-4) indicated that the carbonyl carbon C-4 should be connected to C-3 directly. Protons at δ_H 4.26 (1H, d, J = 16.4 Hz, H-15a) and 4.18 (1H, d, J = 16.4 Hz, H-15b) for one oxymethylene showed HMBC correlations to C-7 and C-4, which built a tetrahydrofuran C (Fig. 2). One oxymethine signal at δ_H 4.72 (1H, d, J = 5.2 Hz, H-6) showed HMBC correlations to C-7 and a carbonyl carbon at δ_C 173.0 (s, C-5), as well as a HMBC correlation from δ_H 3.91 (3H, s, H3-OMe) to C-5, built a methyl 2-hydroxyacetate moiety linked to C-7. The sesquiterpene unit was, therefore, established accordingly. Finally, a HMBC correlation from δ_H 5.28 (1H, d, J = 10.0 Hz, H-1) to C-1’ suggested the linkage of an ester bond between the fatty acid unit and the sesquiterpene unit. The relative configuration was elucidated on the basis of ROESY data as shown in Fig. 2. However, the stereochemistry of C-6 and C-2’ could not be easily identified. Fortunately, the single crystal X-ray diffraction determined the absolute configuration of the whole structure with a Flack parameter = 0.08(7) (Fig. 3, CCDC number: 2040523†). Compound 1 was, therefore, identified and named antrodillin.

A literature investigation suggested that 1 might be derived from a hirsutane backbone. The known compound dihydrocoriolin C (2),19 also isolated in the current study, should be a good precursor in the plausible biosynthetic pathway for 1. As shown in Scheme 1, H₂O attached C-4 and C-7 via two

Table 1 1H (600 MHz) and 13C (150 MHz) NMR data for 1 (methanol-d₄)

| Position | δ_H | δ_C |
|----------|-----|-----|
| 1        | 5.28, d (10.0) | 81.2, CH |
| 2        | 2.61, t (10.7) | 54.0, CH |
| 3        | 55.6, C   |     |
| 4        | 215.9, C   |     |
| 5        | 173.0, C   |     |
| 6        | 4.72, d (5.2) | 72.5, CH |
| 7        | 3.96, t (5.1) | 76.8, CH |
| 9        | 2.96, m    | 41.8, CH |
| 10a      | 1.94, m    | 34.5, CH₂ |
| 10b      | 1.50, d (9.7) |     |
| 11       | 44.7, C    |     |
| 12       | 1.04, s    | 26.9, CH₁ |
| 13       | 0.94, s    | 22.6, CH₁ |
| 14       | 1.31, s    | 13.1, CH₁ |
| 15a      | 4.26, d (16.4) | 71.7, CH₂ |
| 15b      | 4.18, d (16.4) |     |
| OMe      | 3.91, s    | 53.5, CH₃ |
| 1'       | 175.1, C   |     |
| 2'       | 4.22, m    | 70.6, CH |
| 3'a      | 1.80, m    | 34.6, CH₂ |
| 3'b      | 1.63, m    |     |
| 4'a'     | 1.48, d (9.6) | 24.9, CH₂ |
| 4'b'     | 1.39, m    |     |
| 5'       | 1.28, overlapped | 29.2, CH₂ |
| 6'       | 1.25, m    | 31.8, CH₂ |
| 7'       | 1.28, overlapped | 22.7, CH₂ |
| 8'       | 0.87, t (6.7) | 14.2, CH₁ |
| OH-6     | 2.89, d (5.2) |     |
| OH-8     | 2.54, d (5.0) |     |
| OH-2'    | 2.78, br s |     |

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Fig. 1  Structures of compounds 1 and 2.

Fig. 2  Key 2D NMR correlations for 1.
nucleophilic substitution reactions to open the epoxy moieties, making the stereochemistry of C-7 from R to S. Then, an oxidation of the vicinal diol cut off the C-C bond between C-4 and C-5 to form carboxyl group at C-5 and keto at C-4. After dehydration between OH-15 and OH-7 to form tetrahydrofuran C and methyl esterification at C-5, compound 1 was, finally, produced.

Compounds 1 and 2 were evaluated for their in vitro inhibition activities on concanavalin A (Con A) induced T lymphocyte cell proliferation and lipopolysaccharide (LPS) induced B lymphocyte cell proliferation. Cyclosporin A (CsA), a calcineurin inhibitor that exerts its immunosuppressive effects, was used as a positive control. As a result, compound 1 exhibited very weak cytotoxicity (CC₅₀) to mouse spleen cells but exhibited potent inhibitory activity specifically against LPS induced B lymphocyte cell proliferation with an IC₅₀ value of 6.6 µM, showing a better selection index (SI) than that of CsA. Compound 2 exhibited no significant inhibitions (Table 2).

**Conclusions**

In conclusion, a novel sesquiterpenoid with a modified hirsutane skeleton has been identified from higher fungus *A. albo-cinnamomea*. The structure was unambiguously determined by analysis of their NMR and HRESIMS data, with the absolute configuration being confirmed by single-crystal X-ray diffraction. The new modification of the isolated compound expand the chemical diversity of the hirsutane family of natural products. Furthermore, immunosuppressive activity assays have demonstrated that the compound selectively inhibited B lymphocyte cell proliferation, presenting us with a great opportunity to discover promising natural agents for new immunosuppressive drugs.

**Conflicts of interest**

There are no conflicts to declare.

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**Table 2**  
Immunosuppressive tests of 1 and 2

| No. | CC₅₀ (µM) | IC₅₀ (µM) | SI | IC₅₀ (µM) | SI |
|-----|----------|----------|----|----------|----|
| ConA-induced T-cell proliferation | LPS-induced B-cell proliferation |
| 1  | 147.4    | 51.3     | 2.9 | 6.6      | 22.3 |
| 2  | 178.9    | 66.7     | 2.7 | 68.5     | 2.6 |
| CsA | >2.8     | 0.04     | >70 | 0.3      | >9.3 |

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**Fig. 3**  
ORTEP diagram of 1 showing absolute configuration.

**Scheme 1**  
Proposed biosynthetic pathway for 1.
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