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Oxygenated pentacyclic triterpenoids from the stems and branches of *Enkianthus chinensis*

Hai-Qiang Wang [a], Shuang-Gang Ma [a], Dan Zhang [a], Yu-Huan Li [b], Jing Qu [a], Yong Li [a], Yun-Bao Liu [a], Shi-Shan Yu [a,*]

[a] State Key Laboratory of Bioactive Substance and Function of Natural Medicines, Institute of Materia Medica, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China

[b] Institute of Medicinal Biotechnology, Chinese Academy of Medical Sciences and Peking Union Medical College, Beijing 100050, People's Republic of China

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ABSTRACT

Thirty new pentacyclic triterpenoids, including five oleanane-type (**1**–**5**), twenty-three ursane-type (**9**–**23**, **26**–**33**) and two taraxerane-type (**24** and **25**), along with fourteen known triterpenoids, were isolated from the stems and branches of *Enkianthus chinensis*. Their structures were elucidated by extensive spectroscopic analyses, X-ray crystallographic data and electronic circular dichroism (ECD) techniques. Sixteen compounds (**1**–**5**, **9**–**13**, **20**, **22**, **32**, **34**–**36**) bearing a gem-hydroxymethyl group at C-4 represent rare examples of pentacyclic triterpenoids. In the *in vitro* biological activity evaluation, compounds **8**, **9**, **12**–**14**, **17**, **24**, and **44** exhibited potent hepatoprotective effects at 10 μM. Moreover, compound **25** showed latent activity against HSV-1 with an IC_{50} value of 6.4 μM.

1 Introduction

Triterpenoids, comprising of 30-carbon compounds originated from the C5 isoprene units, represent a large and structurally diverse class of natural products. Hundreds of different triterpene backbones have been found in plants, animals and microorganisms [1]. Due to a wide range of pharmacological activities, including anticancer [2], anti-inflammatory [3], antidiabetic [4], immunomodulatory [5], antiviral [6], and antimicrobial properties [7], the continuing investigation on novel plant triterpenoids is valuable and significant for discovering drug candidates.

Enkianthus chinensis Franch., a toxic shrub of the family Ericaceae, is distributed mainly in the southern and southwestern parts of the People's Republic of China. Extract of this plant has been used as a folk medicine for the treatment of phlebitis [8]. Phytochemical investigation on this plant by our group has preliminarily resulted in the isolation and identification of several hydroxylated ethacrylic acid and tiglic acid derivatives, of which some derivatives have exhibited significant anti-inflammatory activity [9]. As part of our continued study on the chemical composition and biological activities, we report herein the isolation and structural elucidation of triterpenoids from *E. chinensis*. Thirty new oxygenated pentacyclic triterpenoids were obtained (Fig. 1), including sixteen rare examples of pentacyclic triterpenoids with a gem-hydroxymethyl group at C-4. Furthermore, the hepatoprotective effects and antiviral activities of the isolated triterpenoids were evaluated *in vitro*.

2. Material and methods

2.1. Plant material

The stems and branches of *E. chinensis* grown in the county of Wuning, Jiangxi Province were collected and identified by Prof. Lin Ma (the Chinese Academy of Medical Sciences and Peking Union Medical College) in October 2017. A voucher specimen of *E. chinensis* (accession number 2017004) was deposited in the herbarium of our institute.

2.2. General experimental procedures

UV and ECD spectra were recorded on a JASCO V-650 spectrophotometer and a JASCO J-815 spectropolarimeter (JASCO, Japan), respectively. IR were performed on a Nicolet 5700 FT-IR instrument (Thermo Electron Corporation, USA). Optical rotations were detected on a Rudolph Autopol V automatic polarimeter (Rudolph Research Analytical, USA). HRESIMS data were obtained on a Thermo Scientific

* Corresponding author.
E-mail address: yushishan@imm.ac.cn (S.-S. Yu).

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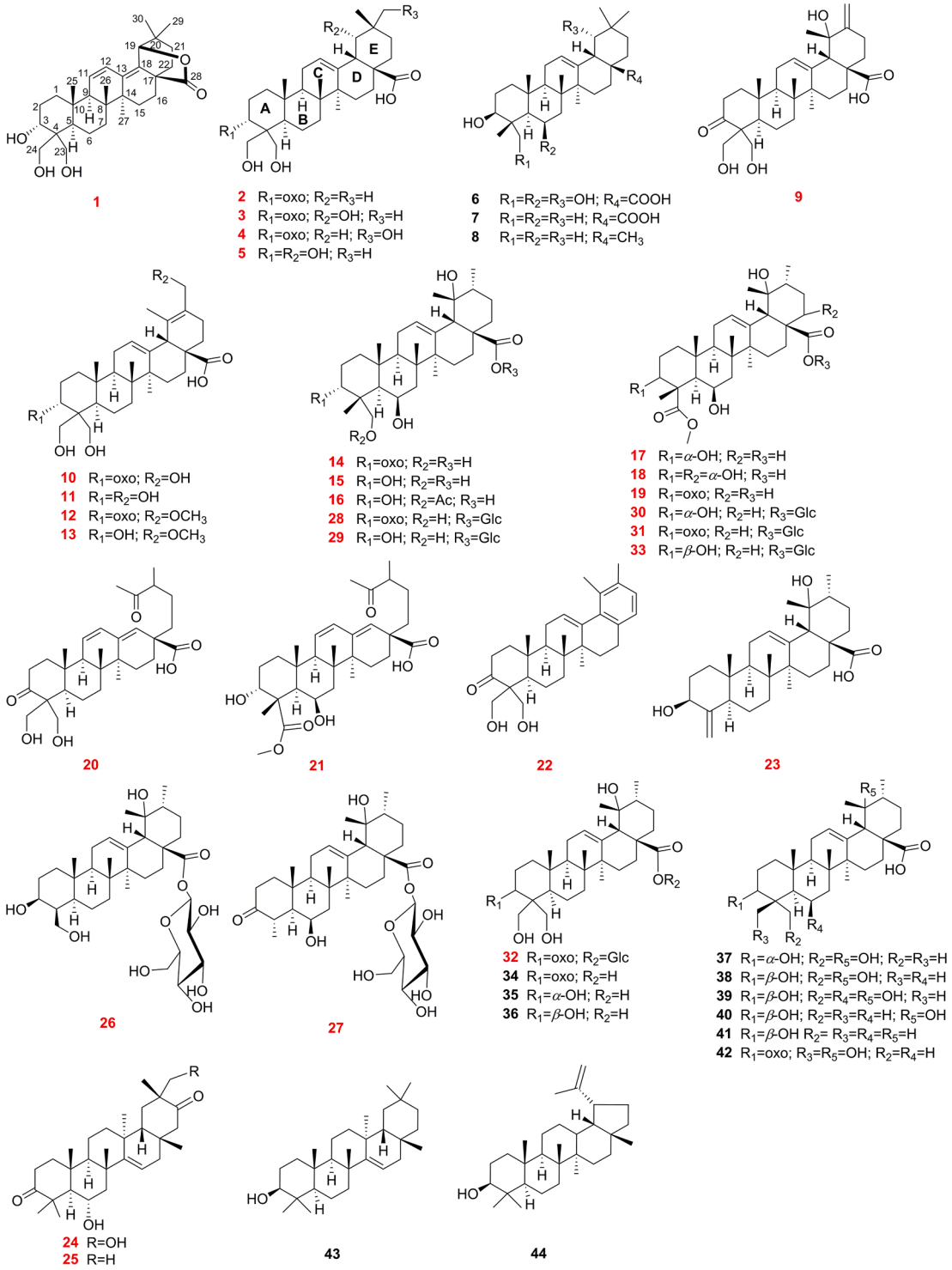

Fig. 1. Structures of compounds **1**–**44**.

Q-Exactive Focus LC/MS spectrometer (Thermo Fisher Scientific, USA). ^{1}H, ^{13}C and 2D NMR spectra were obtained on Bruker Avance III 500 and 600 MHz spectrometers (Bruker, Germany). X-ray crystallographic data were obtained using a XtaLAB Synergy R, HyPix single-crystal X-ray diffractometer (Rigaku, Japan). Semi-preparative HPLC was carried out on a Shimadzu LC-6AD apparatus with an SPD-20A detector using a SiGreen Pack C18 column (250 mm × 10 mm, 5 μm; Greenherbs Science and Technology Development Co., Ltd., P.R. China) or a YMC-Pack ODS-A column (250 × 10 mm, 5 μm; YMC Co., Ltd., Japan). Column chromatography was performed using silica gel (200–300 mesh, Qingdao Haiyang Chemical Co., Ltd., P.R. China), Sephadex LH-20 (GE Healthcare Bio-Sciences Corp., USA), ODS C18 (50 μm, Merck, Germany), macroporous resin (D101 type, Chemical Plant of Nankai University, P. R. China), and polyamide resin (30–60 mesh, Jiangsu Linjiang Chemical Reagents Factory, P.R. China).

2.3. Extraction and isolation

Dried and powdered plant material (54.0 kg) were extracted three times (each 3 h) with 95% EtOH under reflux conditions. The resulting

Table 1
. ^{1}H NMR (600 MHz) Data of compounds **1**–**5**, **9**–**15** (δ in ppm, J in Hz).

No.	1[a]	2[a]	3[b]	4[a]	5[b]	9[b]	10[b]	11[b]	12[b]	13[b]	14[a]	15[a]
1	1.65, overlap 1.46, overlap	1.92, overlap 1.43, overlap	1.77, overlap 1.48, m	1.93, overlap 1.43, overlap	1.85, overlap 1.40, overlap	1.84, m 1.54, m	1.86, overlap 1.53, m	1.86, overlap 1.47, m	1.86, overlap 1.53, m	1.86, overlap 1.48, m	1.91, overlap 1.39, overlap	1.42, overlap 1.29, overlap
2	1.96, m 1.61, overlap	2.62, m 2.32, ddd (16.6,6.1,2.5)	2.73, m 2.52, ddd (16.5,6.2,2.8)	2.60, m 2.30, m	2.08, overlap 1.85, overlap	2.72, m 2.56, ddd (16.7,5.2,2.5)	2.71, m 2.58, m	2.08, overlap 1.84, overlap	2.71, m 2.59, m	2.08, overlap 1.85, overlap	2.68, m 2.23, ddd (16.4,11.6,3.2)	1.98, m 1.44, overlap
3	4.05, dd (2.8, 2.8)				4.74, brs			4.71, brd (2.7)		4.71, brd (3.0)		3.58, brd (3.1)
5	1.76, overlap	1.95, overlap	2.44, dd (12.4, 2.6)	1.95, overlap	2.26, overlap	2.46, m	2.43, m	2.19, d (12.0)	2.44, overlap	2.20, overlap	1.91, overlap	1.75, overlap
6	1.54, overlap 1.48, overlap	1.61, overlap 1.56, overlap	1.90, m 1.77, overlap	1.59, overlap 1.59, overlap	1.85, overlap 1.66, overlap	1.91, m 1.76, overlap	1.88, overlap 1.69, overlap	1.81, overlap 1.58, m	1.86, overlap 1.69, overlap	1.82, overlap 1.58, m	4.34, brs	4.35, brs
7	1.52, overlap 1.45, overlap	1.74, overlap 1.59, overlap	1.68, m 1.41, m	1.59, overlap 1.35, m	1.73, overlap 1.41, overlap	1.76, overlap 1.47, m	1.68, overlap 1.45, m	1.73, overlap 1.43, m	1.68, overlap 1.45, m	1.73, overlap 1.43, m	1.85, m 1.57, overlap	1.84, overlap 1.50, overlap
9	2.31, brs	1.77, overlap	2.05, overlap	1.77, overlap	2.19, overlap	2.06, overlap	1.72, overlap	1.85, overlap	1.71, overlap	1.83, overlap	1.91, overlap	1.91, overlap
11	5.85, dd (10.2, 2.2)	2.00, overlap	2.05, overlap	1.99, overlap	2.14, overlap 2.07, overlap	2.09, overlap	1.98, m	2.04, overlap 1.97, overlap	1.98, overlap 2.09, overlap	2.07, overlap 1.96, overlap	2.12, overlap	2.05, m
12	6.25, dd (10.2, 3.0)	5.28, dd (3.7, 3.7)	5.59, dd (3.1, 3.1)	5.29, brs	5.60, brs	5.65, dd (2.9, 2.9)	5.74, dd (3.7, 3.7)	5.73, dd (3.7, 3.7)	5.75, dd (3.7, 3.7)	5.73, overlap	5.35, dd (3.7, 3.7)	5.34, dd (3.7, 3.7)
15	1.60, overlap 1.32, overlap	1.79, overlap 1.11, overlap	2.14, overlap 1.25, overlap	1.79, overlap 1.11, overlap	2.13, overlap 1.24, overlap	2.30, overlap 1.32, m	2.26, m 1.26, m	2.25, m 1.25, overlap	2.25, overlap 1.25, overlap	2.23, overlap 1.25, m	1.90, overlap 1.02, m	1.89, overlap 1.01, m
16	2.24, m 1.61, overlap	2.00, overlap 1.78, overlap	2.82, m 2.14, overlap	2.03, overlap 1.61, overlap	2.82, m 2.13, overlap	3.23, m 2.16, overlap	2.15, overlap 2.10, overlap	2.13, overlap 2.08, overlap	2.09, overlap	2.07, overlap 2.03, overlap	2.57, m 1.52, overlap	2.58,m 1.51, overlap
18		2.87, dd (13.9, 4.0)	3.64, brs	2.88, dd (13.6, 2.8)	3.64, brs	3.26, s	3.71, s	3.70, s	3.69, s	3.68, s	2.54, s	2.52, s
19	4.84, overlap	1.70, overlap 1.14, overlap	3.64, brs	1.81, overlap 1.10, overlap	3.62, brs							
20											1.36, overlap	1.36, overlap
21	1.52, overlap 1.45, overlap	1.36, overlap 1.21, overlap	2.14, overlap 1.17, overlap	1.49, overlap 1.15, overlap	2.17, overlap 1.16, overlap	3.17, m 2.30, overlap	2.59, m	2.59, d (8.8)	2.44, overlap 2.33, overlap	2.44, m 2.22, overlap	1.72, overlap 1.26, overlap	1.74, overlap 1.25, overlap
22	1.76, overlap 1.70, overlap	1.59, overlap 1.37, overlap	2.21, overlap 2.05, overlap	1.77, overlap 1.60, overlap	2.21, overlap 2.04, overlap	2.34, overlap 2.14, overlap	2.15, overlap 2.06, overlap	2.14, overlap 2.05, overlap	2.10, overlap 2.01, overlap	2.09, overlap 2.01, overlap	1.73, overlap 1.64, overlap	1.73, overlap 1.64, overlap
23	3.89, d (11.2) 3.72, d (11.2)	4.08, d (11.1) 3.44, d (11.1)	4.75, d (10.8) 3.98, d (10.8)	4.08, d (11.1) 3.43, d (11.1)	4.58, d (11.0) 4.37, d (11.0)	4.71, d (10.7) 4.00, d (10.7)	4.69, d (10.7) 3.99, d (10.7)	4.55, d (11.5) 4.36, d (11.5)	4.70, d (10.6) 3.99, d (10.6)	4.57, d (11.0) 4.37, d (11.0)	3.82, d (11.0) 3.43, d (11.0)	3.69, d (11.0) 3.34, d (11.0)
24	3.66, d (11.5) 3.59, d (11.5)	3.90, d (11.7) 3.57, d (11.7)	4.28, d (11.2) 4.07, d (11.2)	3.89, d (11.7) 3.57, d (11.7)	4.16, d (11.0) 4.04, d (11.0)	4.28, d (11.2) 4.09, d (11.2)	4.27, d (11.2) 4.09, d (11.2)	4.15, d (10.9) 4.02, d (10.9)	4.27, d (11.3) 4.08, d (11.3)	4.15, d (11.0) 4.02, d (11.0)	1.25, s	1.10, s
25	1.00, s	1.14, s	1.18, s	1.14, s	1.04, s	1.17, s	1.16, s	1.03, s	1.15, s	1.03, s	1.47, s	1.35, s
26	0.81, s	0.88, s	1.13, s	0.89, s	1.11, s	1.18, s	1.10, s	1.07, s	1.09, s	1.06, s	1.18, s	1.09, s
27	1.09, s	1.19, s	1.61, s	1.21, s	1.61, s	1.73, s	1.12, s	1.08, s	1.08, s	1.05, s	1.35, s	1.35, s
29	1.09, s	0.91, s	1.21, s	3.19, s	1.20, s	1.67, s	1.86, s	1.83, s	1.80, s	1.78, s	1.20, s	1.21, s
30	0.97, s	0.95, s	1.13, s	0.94, s	1.13, s	5.03, brs 4.83, brs	4.58, d (12.0) 4.37, d (12.0)	4.57, d (11.5) 4.35, d (11.5)	4.02, d (11.0) 3.98, d (11.0)	4.02, d (11.2) 3.96, d (11.2)	0.93, d (6.7)	0.94, d (6.6)
-OMe									3.31, s	3.31, s		

[a] Recorded in CD_3OD.
[b] Recorded in Pyridine-d_5.

Table 2
. ^{1}H NMR (600 MHz) Data of compounds**16** − **25** (δ in ppm, J in Hz).

No.	16[a]	17[a]	18[b]	19[b]	20[a]	21[a]	22[b]	23[a]	24[a]	25[b]
1	1.40, overlap 1.31, overlap	1.44, overlap 1.28, overlap	1.95, overlap 1.42, overlap	1.87, overlap 1.42, overlap	2.17, overlap 1.47, overlap	1.53, overlap 1.45, overlap	1.90, overlap 1.54, overlap	1.75, overlap 1.19, overlap	1.79, overlap 1.70, overlap	1.70, overlap
2	2.01, overlap 1.51, overlap	2.01, overlap 1.52, overlap	2.20, overlap 1.83, overlap	2.88, m 2.40, m	2.68, m 2.38, m	2.08, overlap 1.59, overlap	2.75, m 2.60, m	1.89, overlap 1.46, overlap	2.76, ddd (15.9,11.7,5.6) 2.23, ddd (14.4,9.8,4.6)	2.80, ddd (16.0,11.6,5.7) 2.40, ddd (15.4,9.9,4.6)
3	3.61, dd (2.9,2.9)	3.68, dd (2.9,2.9)	4.17, brs			3.67, m		3.94, dd (11.8, 5.6)		
5	1.52, overlap	2.07, overlap	2.75, brs	2.57, brs	2.01, m	2.07, overlap	2.43, overlap	1.61, overlap	1.71, overlap	1.88, d (11.0)
6	4.20, brs	4.35 brs	5.10, brs	4.42, brs	1.65, overlap 1.65, overlap	4.42, brs	1.91, overlap 1.80, overlap	1.55, overlap 1.46, overlap	3.92, ddd (11.1, 11.1, 4.2)	4.24, ddd (10.9, 10.9, 4.1)
7	1.78, overlap 1.52, overlap	1.92, overlap 1.47, overlap	2.30, overlap 1.95, overlap	2.04, overlap 1.87, overlap	1.50, overlap 1.40, overlap	1.70, overlap 1.53, overlap	1.62, overlap 1.57, overlap	1.61, overlap 1.35, overlap	2.33, dd (12.4, 4.2) 1.44, dd (12.4, 11.9)	2.62, dd (12.2, 4.1) 1.77, dd (12.4, 11.9)
9	1.91, m	1.99, overlap	2.34, overlap	2.15, overlap	2.17, overlap	2.31, overlap	1.84, overlap	1.86, overlap	1.61, overlap	1.62, m
11	2.05, overlap	2.05, overlap	2.34, overlap 2.27, overlap	2.31, overlap 2.17, overlap	5.68, dd (10.2, 2.0)	5.71, dd (10.2, 2.3)	2.15, overlap 2.05, overlap	2.12, m 2.00, m	1.79, overlap 1.66, overlap	1.70, overlap 1.55, overlap
12	5.32, dd (3.7, 3.7)	5.33, dd (3.7, 3.7)	5.70, dd (4.5, 4.5)	5.71, dd (3.6, 3.6)	6.02, dd (10.2, 3.1)	5.98, dd (10.2, 2.7)	5.53, overlap	5.31, dd (3.7, 3.7)	1.83, overlap 1.66, overlap	1.70, overlap 1.54, overlap
15	1.89, overlap 1.00, m	1.89, overlap 1.01, m	2.65, m 1.40, overlap	2.48, m 1.32, overlap	1.82, m 1.18, m	1.88, overlap 1.17, overlap	2.15, overlap 0.85, overlap	1.83, overlap 1.04, m	5.71, dd (8.2, 3.1)	5.72, dd (8.1, 3.2)
16	2.57, m 1.52, overlap	2.58, m 1.52, overlap	2.98, m 2.74, overlap	2.04, overlap 1.39, overlap	2.17, overlap 1.48, overlap	2.17, overlap 1.47, overlap	2.40, overlap	2.59, overlap 1.54, overlap	2.27, overlap 1.80, overlap	2.19, m 1.70, overlap
18	2.52, s	2.52, s	3.11, s	3.12, s	5.42, s	5.40, s		2.52, s	1.36, dd (13.6, 4.2)	1.28, dd (13.8, 4.0)
19									2.46, t (13.6) 1.40, dd (13.6, 4.2)	1.96, d (13.7) 1.47, dd (13.7, 4.0)
20	1.36, overlap	1.36, overlap	1.72, overlap	1.53, overlap	2.55, m	2.55, overlap		1.36, overlap		
21	1.73, overlap 1.25, overlap	1.73, overlap 1.25, overlap	2.46, m 1.90, overlap	2.13, overlap 1.42, overlap	1.69, overlap 1.32, overlap	1.69, overlap 1.32, overlap	7.01, d (7.4)	1.74, overlap 1.25, overlap		
22	1.73, overlap 1.63, overlap	1.75, overlap 1.63, m	4.44, dd (11.6, 4.4)	2.15, overlap	1.68, overlap 1.41, overlap	1.69, overlap 1.40, overlap	6.91, d (7.4)	1.74, overlap 1.63, overlap	2.70, d (12.9) 1.94, d (12.9)	2.77, d (13.0) 1.99, d (13.0)
23	4.09, d (10.2) 4.00, d (10.2)				4.11, d (11.1) 3.48, d (11.1)		4.70, d (10.8) 3.98, d (10.8)	5.05, d (2.0) 4.64, d (2.0)	1.32, s	1.70, s
24	1.30, s	1.54, s	2.00, s	2.13, s	3.88, d (11.6) 3.59, d (11.6)	1.51, s	4.28, d (11.3) 4.09, d (11.3)		1.34, s	1.78, s
25	1.36, s	1.38, s	1.73, s	1.73, s	1.11, s	1.34, s	1.18, s	0.77, s	0.88, s	0.94, s
26	1.08, s	1.11, s	1.78, s	1.74, s	0.79, s	1.06, s	1.03, s	0.86, s	1.19, s	1.18, s
27	1.34, s	1.39, s	1.68, s	1.75, s	0.99, s	1.00, s	0.83, s	1.38, s	1.16, s	1.10, s
28									0.83, s	0.85, s
29	1.21, s	1.21, s	1.44, s	1.49, s	2.14, s	2.14, s	2.27, s	1.21, s	3.65, dd (10.4) 3.28, dd (10.4)	1.19, s
30	0.93, d (6.6)	0.93, d (6.7)	1.18, d (6.6)	1.14, d (6.6)	1.08, d (7.0)	1.08, d (7.3)	2.22, s	0.94, d (6.7)	0.95, s	1.20, s
-OMe/ -OAc	2.06, s	3.66 s	3.61, s	3.71, s		3.67, s				

[a] Recorded in CD_3OD.
[b] Recorded in Pyridine-d_5.

extract (2.6 kg) was mixed with kieselguhr and loaded on a Soxhlet extractor, and then extracted successively with petroleum ether (PE, 10 L), CH_2Cl_2 (10 L), EtOAc (10 L), and MeOH (10 L). Six fractions (S1 − S6) were obtained from the purification of the CH_2Cl_2 fraction (150 g) by a silica gel column eluting with CH_2Cl_2-MeOH (100:1 to 1:1 v/v). Fraction S2 (21.4 g) was submitted to a silica gel column using CH_2Cl_2-acetone (20:1 to 1:1 v/v) as eluent to generate fractions S2-1 − S2-7. Subsequently, further purification of fraction S2-2 (0.7 g) yielded 13

Table 3
. ^{1}H NMR Data of compounds **26**–**33** in CD_3OD (δ in ppm, J in Hz).

No.	26[c]	27[c]	28[d]	29[c]	30[c]	31[c]	32[d]	33[c]
1	1.63, overlap 0.95, overlap	1.93, overlap 1.27, overlap	1.84, overlap 1.37, overlap	1.42, overlap 1.30, overlap	1.43, overlap 1.28, overlap	1.97, overlap 1.41, overlap	1.94, overlap 1.44, overlap	1.68, overlap 1.08, m
2	1.64, overlap 1.64, overlap	2.21, overlap 1.76, overlap	2.69, m 2.22, m	1.98, overlap 1.46, overlap	2.01, overlap 1.53, overlap	2.80, m 2.23, m	2.62, overlap 2.28, m	1.72, overlap 1.61, overlap
3	3.81, m			3.58, dd (5.3, 3.0)	3.68, m			3.90, dd (11.9,4.2)
4	2.07, overlap	2.83, m						
5	1.24, overlap	1.09, overlap	1.90, overlap	1.73, overlap	2.05, overlap	2.17, overlap	1.96, overlap	1.48, overlap
6	1.66, overlap 1.26, overlap	4.12, brs	4.33, brs	4.34, brs	4.34, brs	3.88, brs	1.57, overlap	3.83, brs
7	1.65, overlap 1.31, overlap	1.71, overlap 1.60, overlap	1.91, overlap 1.57, overlap	1.83, overlap 1.50, overlap	1.92, overlap 1.47, overlap	1.73, overlap 1.51, overlap	1.65, overlap 1.36, overlap	1.64, overlap 1.45, m
9	1.67, overlap	1.79, overlap	2.14, overlap	1.89, overlap	1.97, overlap	1.89, overlap	2.06, overlap	1.77, overlap
11	1.97, overlap	2.14, overlap	2.12, overlap	2.01, overlap	2.05, overlap	2.17, overlap 2.12, overlap	2.04, overlap	2.05, overlap
12	5.30, dd (3.7, 3.7)	5.33, dd (3.7, 3.7)	5.37, dd (3.7, 3.7)	5.35, dd (3.7, 3.7)	5.35, dd (3.7, 3.7)	5.37, dd (3.7, 3.7)	5.32, dd (3.7, 3.7)	5.34, dd (3.8, 3.8)
15	1.83, overlap 1.00, m	1.93, overlap 1.00, m	1.92, overlap 1.03, m	1.89, overlap 1.01, m	1.89, overlap 1.02, m	1.89, overlap 1.01, m	1.85, overlap 1.03, m	1.86, overlap 0.98, m
16	2.60, m 1.64, overlap	2.59, m 1.63, overlap	2.59, m 1.65, overlap	2.61, m 1.64, overlap	2.61, m 1.64, overlap	2.60, m 1.64, overlap	2.61, overlap 1.64, overlap	2.60, m 1.63, overlap
18	2.51, s	2.52, s	2.55, s	2.54, s	2.53, s	2.55, s	2.53, s	2.53, s
20	1.34, overlap	1.33, overlap	1.37, overlap	1.36, overlap	1.36, overlap	1.36, overlap	1.35, overlap	1.36, overlap
21	1.72, overlap 1.25, overlap	1.70, overlap 1.21, overlap	1.65, overlap 1.24, overlap	1.73, overlap 1.25, overlap	1.74, overlap 1.26, overlap	1.73, overlap 1.25, overlap	1.73, overlap 1.24, overlap	1.71, overlap 1.23, m
22	1.79, overlap 1.62, overlap	1.71, overlap 1.60, overlap	1.77, overlap 1.64, overlap	1.79, overlap 1.63, overlap	1.80, overlap 1.64, overlap	1.80, overlap 1.64, overlap	1.80, overlap 1.62, overlap	1.78, overlap 1.63, overlap
23		1.00, d (6.6)	3.82, d (11.4) 3.42, d (11.4)	3.69, d (11.5) 3.43, d (11.5)			4.11, d (11.1) 3.43, d (11.1)	
24	3.92,dd (10.9,9.3) 3.56,dd (10.9,2.2)		1.24, s	1.10, s	1.53, s	1.69, s	3.92, d (11.6) 3.55, d (11.6)	1.48, s
25	0.79, s	1.41, s	1.48, s	1.34, s	1.38, s	1.54, s	1.15, s	1.33, s
26	0.77, s	1.10, s	1.14, s	1.05, s	1.08, s	1.12, s	0.84, s	1.04, s
27	1.34, s	1.29, s	1.34, s	1.33, s	1.37, s	1.33, s	1.36, s	1.31, s
29	1.20, s	1.18, s	1.22, s	1.22, s	1.21, s	1.21, s	1.20, s	1.21, s
30	0.92, d (6.6)	0.90, d (6.6)	0.93, d (6.6)	0.94, d (6.7)	0.94, d (6.7)	0.93, d (6.7)	0.93, d (6.7)	0.93, d (6.7)
-OMe					3.66, s	3.69, s		3.68, s
1′	5.32, d (8.2)	5.30, d (8.2)	5.32, d (8.2)	5.31, d (8.2)	5.32, d (8.1)	5.32, d (8.1)	5.32, d (8.1)	5.30, d (8.1)
2′	3.32, overlap	3.31, overlap	3.34, overlap	3.33, overlap	3.33, overlap	3.33, overlap	3.31, overlap	3.32, overlap
3′	3.39, overlap	3.37, overlap	3.40, overlap	3.40, overlap	3.40, overlap	3.40, overlap	3.37, overlap	3.40, overlap
4′	3.35, overlap	3.34, overlap	3.37, overlap	3.37, overlap	3.36, overlap	3.37, overlap	3.37, overlap	3.36, overlap
5′	3.32, overlap	3.31, overlap	3.34, overlap	3.33, overlap	3.33, overlap	3.34, overlap	3.31, overlap	3.33, overlap
6′	3.79, dd (12.0, 2.3) 3.68, dd (12.0, 4.8)	3.77, dd (12.0, 2.3) 3.66, dd (12.0, 4.6)	3.81, dd (12.2, 2.3) 3.69, dd (12.2, 4.6)	3.81, dd (12.0, 2.3) 3.68, dd (12.0, 4.4)	3.79, dd (12.1, 2.2) 3.69, m	3.80, dd (12.0, 2.2) 3.68, m	3.80, dd (12.0, 2.2) 3.68, dd (12.0, 4.6)	3.79, dd (12.0, 2.3) 3.69, m

[c] Recorded at 600 MHz.
[d] Recorded at 500 MHz.

fractions (S2-2–1 − S2-2–13) by ODS-MPLC eluting with MeOH-H_2O gradient system (60%, 70%, 80%, 90%, and 100%). The main fraction S2-2–6 (50 mg) was separated on a semi-preparative RP-HPLC column with 80% MeOH as mobile phase (2 mL/min) to give compounds **23** (3.1 mg, t_R 32 min) and **40** (2.0 mg, t_R 44 min). Compounds **7** (12.0 mg, t_R 36 min) and **41** (16.0 mg, t_R 38 min) were isolated from fraction S2-2–9 (50 mg) via semi-preparative RP-HPLC with 90% MeOH at 2 mL/min. Fraction S2-3 (1 g) was loaded onto a Sephadex LH-20 column eluting with PE-CH_2Cl_2-MeOH (5:5:1 v/v/v) to generate six fractions (S2-3–1 − S2-3–6). Fraction S2-3–4 (170 mg) was subjected to an ODS-MPLC eluting with MeOH-H_2O gradient system (30%, 50%, 70%, 90%, and 100%). Then, compounds **19** (3.1 mg, t_R 30 min) and **24** (17.3 mg, t_R 36 min) were purified from 70% MeOH fraction by semi-preparative RP-HPLC with 70% MeOH as mobile phase. Fraction S2-6 (5.7 g) was separated on an ODS-MPLC (eluted successively with 50%, 60%, 70%, 80%, 90%, 95%, and 100% MeOH-H_2O) to give 14 fractions (S2-6-1-S2-6-14). Fraction S2-6–6 was further purified by a Sephadex LH-20 column and separated chromatographically via semi-preparative RP-HPLC with MeOH-H_2O-TFA (73:27:0.01, 2 mL/min) to afford compounds **16** (6.5 mg, t_R 55 min), **37** (3.3 mg, t_R 69 min), and **42** (1.5 mg, t_R 67 min). Fractions S3 (5.6 g) and S4 (10 g) obtained above were subjected to a Sephadex LH-20 column with PE-CH_2Cl_2-MeOH (5:5:1 v/v/v) as eluent to produce seven fractions (S3-1-S3-7) and five fractions (S4-1-S4-5), respectively. Fractions S3-6-1-S3-6-6 were obtained from the purification of the fraction S3-6 (1.3 g) using an OSD-MPLC with a gradient elution of MeOH-H_2O system (30%, 40%, 50%, 60%, 70%, and 100%). Fraction S3-6–5 (45 mg) was then separated by semi-preparative RP-HPLC with 65% MeOH-H_2O to give compounds **9** (3.2 mg, t_R 34 min) and **14** (1.2 mg, t_R 55 min). Eight fractions (S4-4-1-S4-4-8) was obtained from fraction S4-4 (3 g) using a silica gel column with a gradient elution of CH_2Cl_2-MeOH (100:1 to 1:1 v/v). Then, fraction S4-4–5 yielded compounds **20** (2.3 mg, t_R 45 min) and **3** (2.8 mg, t_R 48 min) as well as **10** (1.6 mg, t_R 51 min) using semi-preparative HPLC with MeOH-H_2O-TFA (67:33:0.01, 2 mL/min).

The EtOAc-soluble extract (85.0 g) obtained above was applied to a polyamide resin column using a successive elution of H_2O, 30% EtOH, 60% EtOH, and 95% EtOH. The 30% EtOH fraction extract (13 g) was loaded on a Sephadex LH-20 column to produce fractions (E1−E9) using 90% MeOH as eluent. The 60% EtOH fraction (18 g) was chromatographed over a silica gel column eluting with CH_2Cl_2-MeOH (100:1 to 1:1 v/v) to afford 11 fractions (F1-F11). Fractions E5 (2.9 g) and E7 (0.5 g) were subjected to silica gel columns to obtain six fractions (E5-1-E5-6)

Table 4
. ^{13}C NMR (150 MHz) Data of compounds **1**–**5**, **9**–**18** (δ in ppm).

No.	1[a]	2[a]	3[b]	4[a]	5[b]	9[b]	10[b]	11[b]	12[b]	13[b]	14[a]	15[a]	16[a]	17[a]	18[b]
1	34.3, CH_2	39.5, CH_2	38.7, CH_2	39.5, CH_2	33.9, CH_2	38.9, CH_2	39.1, CH_2	34.5, CH_2	39.2, CH_2	34.6, CH_2	41.2, CH_2	36.4, CH_2	36.3, CH_2	35.6, CH_2	35.3, CH_2
2	26.5, CH_2	37.2, CH_2	37.1, CH_2	37.2, CH_2	26.7, CH_2	37.2, CH_2	37.3, CH_2	26.9, CH_2	37.3, CH_2	26.9, CH_2	36.3, CH_2	26.8, CH_2	26.0, CH_2	26.1, CH_2	26.5, CH_2
3	71.1, CH	217.2, C	215.7, C	217.2, C	70.2, CH	216.0, C	216.1, C	70.1, CH	216.1, C	70.1, CH	219.2, C	78.6, CH	73.0, CH	75.7, CH	75.0, CH
4	46.6, C	59.7, C	59.5, C	59.7, C	46.4, C	59.4, C	59.3, C	46.5, C	59.3, C	46.5, C	54.9, C	41.9, C	41.9, C	53.4, C	53.5, C
5	45.2, CH	49.9, CH	49.8, CH	49.9, CH	45.6, CH	49.8, CH	49.6, CH	45.6, CH	49.6, CH	45.6, CH	49.7, CH	44.9, CH	48.1, CH	46.1, CH	46.0, CH
6	19.6, CH_2	20.5, CH_2	20.4, CH_2	20.5, CH_2	19.6, CH_2	20.4, CH_2	20.2, CH_2	19.4, CH_2	20.2, CH_2	19.4, CH_2	69.3, CH	69.4, CH	69.3, CH	71.6, CH	70.7, CH
7	34.5, CH_2	33.8, CH_2	33.4, CH_2	33.8, CH_2	34.0, CH_2	33.9, CH_2	34.4, CH_2	34.9, CH_2	34.4, CH_2	34.9, CH_2	41.6, CH_2	41.6, CH_2	41.8, CH_2	41.5, CH_2	41.5, CH_2
8	42.4, C	40.7, C	40.3, C	40.7, C	40.5, C	40.5, C	40.0, C	40.1, C	40.0, C	40.1, C	40.5, C	40.4, C	40.2, C	40.9, C	40.9, C
9	54.5, CH	48.2, CH	47.8, CH	48.2, CH	48.9, CH	47.0, CH	47.4, CH	48.7, CH	47.4, CH	48.7, CH	48.0, CH	48.8, CH	48.7, CH	48.9, CH	48.7, CH
10	37.9, C	37.6, C	36.1, C	37.6, C	37.8, C	37.0, C	36.8, C	37.5, C	36.8, C	37.5, C	37.1, C	37.7, C	37.8, C	37.6, C	37.5, C
11	131.1, CH	25.0, CH_2	24.8, CH_2	25.0, CH_2	24.7, CH_2	24.8, CH_2	24.5, CH_2	24.3, CH_2	24.5, CH_2	24.4, CH_2	25.0, CH_2	24.7, CH_2	24.6, CH_2	24.7, CH_2	24.4, CH_2
12	124.3, CH	123.6, CH	123.7, CH	123.7, CH	124.2, CH	128.5, CH	127.8, CH	127.9, CH	128.1, CH	128.1, CH	129.8, CH	129.9, CH	129.8, CH	129.9, CH	128.7, CH
13	136.7, C	145.5, C	145.3, C	145.4, C	145.2, C	140.1, C	138.7, C	138.5, C	138.5, C	138.4, C	139.7, C	139.4, C	139.4, C	139.6, C	139.7, C
14	41.9, C	43.2, C	42.6, C	43.2, C	42.5, C	42.7, C	44.3, C	44.2, C	44.3, C	44.2, C	43.6, C	43.3, C	43.2, C	43.5, C	43.7, C
15	26.8, CH_2	29.0, CH_2	29.5, CH_2	29.0, CH_2	29.6, CH_2	29.6, CH_2	29.0, CH_2	29.0, CH_2	29.0, CH_2	28.9, CH_2	29.7, CH_2	29.7, CH_2	29.7, CH_2	29.7, CH_2	29.2, CH_2
16	25.5, CH_2	24.2, CH_2	28.7, CH_2	24.2, CH_2	28.7, CH_2	27.2, CH_2	24.3, CH_2	24.2, CH_2	24.4, CH_2	24.2, CH_2	26.8, CH_2	26.8, CH_2	26.8, CH_2	26.8, CH_2	19.7, CH_2
17	45.5, C	47.8, C	46.4, C	48.1, C	46.4, C	48.7, C	47.3, C	47.2, C	47.2, C	47.2, C	49.2, C	49.1, C	49.1, C	49.2, C	54.9, C
18	133.8, C	42.9, CH	45.2, CH	42.2, CH	45.2, CH	55.7, CH	51.5, CH	51.4, CH	51.4, CH	51.4, CH	55.4, CH	55.3, CH	55.2, CH	55.4, CH	55.9, CH
19	86.7, CH	47.4, CH_2	81.5, C	41.5, CH_2	81.6, C	73.3, C	132.0, C	132.1, C	134.8, C	135.0, C	73.7, C	73.8, C	73.8, C	73.8, C	72.9, C
20	36.9, C	31.8, C	36.1, C	37.0, C	36.1, C	156.9, C	130.1, C	130.0, C	126.6, C	126.6, C	43.2, CH	43.3, CH	43.3, CH	43.3, CH	41.0, CH
21	33.9, CH_2	35.0, CH_2	29.5, CH_2	29.4, CH_2	29.5, CH_2	29.3, CH_2	25.0, CH_2	25.0, CH_2	25.3, CH_2	25.3, CH_2	27.4, CH_2	27.5, CH_2	27.5, CH_2	27.5, CH_2	36.3, CH_2
22	35.7, CH_2	33.9, CH_2	34.0, CH_2	33.2, CH_2	34.0, CH_2	39.8, CH_2	33.9, CH_2	34.0, CH_2	33.7, CH_2	33.7, CH_2	39.1, CH_2	39.2, CH_2	39.2, CH_2	39.2, CH_2	75.4, CH
23	68.8, CH_2	64.3, CH_2	64.7, CH_2	64.2, CH_2	69.5, CH_2	65.0, CH_2	65.1, CH_2	69.5, CH_2	65.1, CH_2	69.5, CH_2	66.9, CH_2	72.1, CH_2	73.0, CH_2	179.1, C	178.0, C
24	64.6, CH_2	63.6, CH_2	63.5, CH_2	63.6, CH_2	64.9, CH_2	63.6, CH_2	63.6, CH_2	65.0, CH_2	63.6, CH_2	65.0, CH_2	20.5, CH_3	20.1, CH_3	19.9, CH_3	20.1, CH_3	20.4, CH_3
25	18.7, CH_3	15.9, CH_3	15.6, CH_3	15.9, CH_3	15.9, CH_3	15.9, CH_3	16.4, CH_3	16.5, CH_3	16.4, CH_3	16.5, CH_3	17.3, CH_3	17.6, CH_3	17.5, CH_3	17.4, CH_3	17.5, CH_3
26	17.5, CH_3	17.9, CH_3	17.8, CH_3	17.9, CH_3	17.8, CH_3	17.7, CH_3	18.4, CH_3	18.3, CH_3	18.4, CH_3	18.3, CH_3	19.1, CH_3	18.6, CH_3	18.5, CH_3	18.9, CH_3	18.8, CH_3
27	19.7, CH_3	26.5, CH_3	25.1, CH_3	26.5, CH_3	25.1, CH_3	24.3, CH_3	22.5, CH_3	22.6, CH_3	22.4, CH_3	22.5, CH_3	25.0, CH_3	25.1, CH_3	25.0, CH_3	25.2, CH_3	25.4, CH_3
28	180.4, C	181.9, C	181.3, C	181.8, C	181.3, C	180.5, C	180.2, C	180.2, C	180.1, C	180.1, C	182.4, C	182.5, C	182.5, C	182.4, C	180.2, C
29	28.2, CH_3	33.7, CH_3	29.2, CH_3	74.6, CH_2	29.2, CH_3	27.9, CH_3	17.3, CH_3	17.3, CH_3	17.5, CH_3	17.5, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3
30	23.6, CH_3	24.1, CH_3	25.2, CH_3	19.7, CH_3	25.2, CH_3	105.7, CH_2	63.5, CH_2	63.5, CH_2	73.8, CH_2	73.8, CH_2	16.7, CH_3	16.8, CH_3	16.8, CH_3	16.7, CH_3	17.0, CH_3
-OMe/-OAc									57.9, CH_3	57.9, CH_3			173.7, C 21.1, CH_3	52.2, CH_3	51.7, CH_3

[a] Recorded in CD_3OD.
[b] Recorded in Pyridine-d_5.

and 10 fractions (E7-1-E7-10), respectively. Fraction E7-9 was further purified by semi-preparative RP-HPLC eluting with MeOH-H_2O-TFA (63:37:0.02) to generate compound **15** (2.7 mg, t_R 43 min). Separation of fractions E5-6 (0.5 g) and E5-2 (0.2 g) via an ODS column (eluted with 40%, 50%, 60%, 70%, 80%, and 100% MeOH-H_2O) produced eight fractions (E5-6-1-E5-6-8) and 10 fractions (E5-2-1-E5-2-10), respectively. Compounds **12** (65% MeOH-0.0.5% TFA, 1.5 mg, t_R 45 min) and **25** (75% MeCN-0.0.5% TFA, 2.8 mg, t_R 28 min) were isolated, respectively, from fractions E5-2-5 (43 mg) and E5-2-9 (18 mg) via semi-preparative RP-HPLC. Compounds **32** (58% MeOH-0.0.2% TFA, 13 mg, t_R 42 min) and **28** (40% MeOH-0.0.2% TFA, 3.2 mg, t_R 69 min) were obtained from fractions E5-6-4 (98 mg) and E5-6–5 (56 mg) using a semi-preparative RP-HPLC, respectively. Fraction E6 (2 g) was chromatographed on an ODS column to obtain eight major fractions (E6-1-E6-8). Subsequently, compound **18** (2.0 mg, t_R 28 min) was isolated from fraction E6-4 (20 mg) by semi-preparative RP-HPLC (MeOH-H_2O-TFA, 65:35:0.02). Purification of fraction E6-6 (70 mg) using semi-preparative RP-HPLC with MeOH-H_2O-TFA (62:38:0.05) as mobile phase led to the isolation of compounds **34** (5.3 mg, t_R 43 min) and **11** (20.0 mg, t_R 50 min). Fraction E6-7 (200 mg) was applied to a silica gel

column with a gradient elution of CH_2Cl_2-MeOH (50:1 to 1:1 v/v) to afford one terpenoid-containing fraction, which was then separated by semi-preparative RP-HPLC to obtain compounds **5** (2.7 mg, t_R 26 min), **35** (6.1 mg, t_R 28 min), and **13** (4.0 mg, t_R 28 min). Subsequent separation of fraction F2 (50 mg) afforded compounds **44** (3 mg, t_R 38 min), **43** (2 mg, t_R 43 min), and **8** (4.5 mg, t_R 45 min) by semi-preparative RP-HPLC (MeOH-H_2O-TFA, 99:1:0.02). Fractions F3 (0.25 g), F5 (0.4 g) and F9 (0.5 g) were subjected to silica gel columns to obtain 10 fractions (F3-1 − F3-10), 11 fractions (F5-1-F5-11), and seven fractions (F9-1-F9-7), respectively. Fraction F3-8 (30 mg) was chromatographed by semi-preparative RP-HPLC (MeOH-H_2O-TFA, 90:10:0.05) to furnish compound **22** (6 mg, t_R 35 min). Purification of fractions F5-4 (30 mg) and F5-6 (30 mg) resulted in the isolation of compounds **2** (85% MeOH-0.02% TFA, 18 mg, t_R 22 min) and **38** (65% MeOH-0.02% TFA, 3.4 mg, t_R 40 min) by semi-preparative RP-HPLC. Compounds **39** (3.4 mg, t_R 42 min) and **6** (1.3 mg, t_R 44 min) were acquired from fraction F9-7 using semi-preparative RP-HPLC (MeOH-H_2O-TFA, 70:30:0.02).

The MeOH-soluble extract (2.7 kg) was directly subjected to separation over a polyamide resin column eluting successively with H_2O, 30% EtOH, and 60% EtOH. The 30% EtOH fraction (112 g) was fractionated on a D101 macroporous resin column eluting successively with 30% EtOH, 50% EtOH, 70% EtOH, and 95% EtOH. The 70% EtOH fraction (10 g) obtained was then resolved on an MCI gel column (eluted with 30%, 50%, 60%, 70%, and 100% MeOH-H_2O) to furnish 10 fractions (M1-M10). Fractions M4 and M5 were further purified using semi-preparative RP-HPLC (MeOH-H_2O, 60:40) to obtain compounds **4** (2.7 mg, t_R 45 min) and **33** (6.1 mg, t_R 39 min), respectively. Fraction M6 was submitted to an MCI gel column and further purified with MeOH-H_2O-TFA (60:40:0.01) as mobile phase to afford compounds **29** (6.4 mg, t_R 53 min) and **30** (2.3 mg, t_R 63 min). Similar to fraction M6, fraction M7 was fractionated by an MCI gel column and purified to yield compounds **31** (65% MeOH-0.01% TFA, 3.6 mg, t_R 37 min), **27** (65% MeOH-0.01% TFA, 6.8 mg, t_R 32 min), and **26** (62% MeOH, 2.4 mg, t_R 32 min). The 95% EtOH fraction (5 g) obtained above was subjected to a silica gel column with CH_2Cl_2-MeOH (50:1 to 1:1 v/v) as eluent to produce nine fractions (N1 − N9). Fraction N4 (0.6 g) was submitted to an ODS column with MeOH-H_2O gradient system (60%, 70%, 80%, 90%, and 100%) to give four fractions (N4-1-N4-4). Compounds **17** (15.6 mg, t_R 44 min) and **21** (2.0 mg, t_R 41 min) were obtained from fraction N4-1 by semi-preparative HPLC (MeOH-H_2O-TFA, 69: 31:0.01). Compound **1** (1.3 mg, t_R 36 min) was purified from fraction N4-4 with MeOH-H_2O-TFA (68:32:0.01) as mobile phase.

*2.3.1. 3α,23,24-Trihydroxyolean-11,13(18)-dien-28,19β-olide (**1**)*

white powder; $[\alpha]^{20}_D$ + 34.8 (c 0.07, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.40), 252 (3.74) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 229 (-8), 255 (-5) nm; IR (KBr) 3587, 3304, 2938, 1784, 1683, 1452, 1389, 1373, 1310, 1208, 1138, 1084, 1027, 935 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 507.3082 $[M + Na]^+$ (calcd for $C_{30}H_{44}O_5Na$, 507.3081).

*2.3.2. 23,24-Dihydroxy-3-oxo-olean-12-en-28-oic acid (**2**)*

white powder; $[\alpha]^{20}_D$ + 47.4 (c 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.74) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 223 (−2.3), 308 (−0.2) nm; IR (KBr) ν_{max} 3462, 2941, 2565, 1694, 1461, 1382, 1210, 1179, 1034, 978 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 485.3277 $[M-H]^-$ (calcd for $C_{30}H_{45}O_5$, 485.3262).

*2.3.3. 19α,23,24-trihydroxy-3-oxo-olean-12-en-28-oic acid (**3**)*

white powder; $[\alpha]^{20}_D$ + 10.1 (c 0.56, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.51) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 219 (-5.83), 303 (-0.43) nm; IR (KBr) ν_{max} 3488, 2941, 1687, 1455, 1384, 1234, 1206, 1045 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 501.3216 $[M-H]^-$ (calcd for $C_{30}H_{45}O_6$, 501.3211).

*2.3.4. 23,24,29-trihydroxy-3-oxo-olean-12-en-28-oic acid (**4**)*

white powder; $[\alpha]^{20}_D$ + 55.3 (c 0.21, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.81) nm; IR (KBr) ν_{max} 3459, 2920, 1695, 1459, 1383, 1272, 1232, 1203, 1181, 1046, 1009 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 501.3225 $[M-H]^-$ (calcd for $C_{30}H_{45}O_6$, 501.3211).

*2.3.5. 3α,19α,23,24-tetrahydroxyolean-12-en-28-oic acid (**5**)*

white powder; $[\alpha]^{20}_D$ + 12.7 (c 0.43, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.84) nm; IR (KBr) ν_{max} 3459, 3382, 2930, 1704, 1451, 1382, 1197, 1078, 1046, 990 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 503.3372 $[M-H]^-$ (calcd for $C_{30}H_{47}O_6$, 503.3367).

*2.3.6. 19α,23,24-trihydroxyurs-12,20(30)-dien-3-one-28-oic acid (**9**)*

white powder; mp 201–202 °C; $[\alpha]^{20}_D$ + 54.4 (c 0.38, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.75) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 231 (-0.5), 264 (1.1) nm; IR (KBr) ν_{max} 3504, 2940, 1701, 1455, 1378, 1205, 1038, 907 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 499.3050 $[M-H]^-$ (calcd for $C_{30}H_{43}O_6$, 499.3054).

*2.3.7. 23,24,30-trihydroxyurs-12,19-dien-3-one-28-oic acid (**10**)*

white powder; $[\alpha]^{20}_D$ + 16.4 (c 0.17, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.51) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 212 (–22.6) nm; IR (KBr) ν_{max} 3417, 2939, 1700, 1452, 1378, 1200, 1036, 804 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 499.3064 $[M-H]^-$ (calcd for $C_{30}H_{43}O_6$, 499.3054).

*2.3.8. 3α,23,24,30-tetrahydroxyurs-12,19-dien-28-oic acid (**11**)*

white powder; $[\alpha]^{20}_D$ −1.4 (c 0.15, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.79) nm; IR (KBr) ν_{max} 3381, 2939, 1701, 1448, 1381, 1207, 1033, 991 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 501.3224 $[M-H]^-$ (calcd for $C_{30}H_{45}O_6$, 501.3211).

*2.3.9. 23,24-dihydroxyurs-12,19-dien-3-one-28-oic acid 30-methyl ether (**12**)*

white powder; $[\alpha]^{20}_D$ + 0.9 (c 0.22, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.72) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 211 (−26) nm; IR (KBr) ν_{max} 3448, 2926, 1716, 1691, 1450, 1378, 1217, 1196, 1083, 1041, 803 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 513.3224 $[M-H]^-$ (calcd for $C_{31}H_{45}O_6$, 513.3211).

*2.3.10. 3α,23,24-trihydroxyurs-12,19-dien-28-oic acid 30-methyl ether (**13**)*

white powder; $[\alpha]^{20}_D$ −3.4 (c 0.18, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.47) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 212 (-8) nm; IR (KBr) ν_{max} 3454, 2939, 1702, 1451, 1378, 1261, 1211, 1070, 1025, 898 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 515.3372 $[M-H]^-$ (calcd for $C_{31}H_{47}O_6$, 515.3367).

*2.3.11. 6β,19α,23-trihydroxyurs-12-en-3-one-28-oic acid (**14**)*

white powder; $[\alpha]^{20}_D$ + 2.9 (c 0.07, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.05) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 219 (-1.6), 297 (-0.2) nm; IR (KBr) ν_{max} 3575, 3509, 2921, 1733, 1639, 1464, 1379, 1262, 1102, 1041, 803 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 501.3219 $[M-H]^-$ (calcd for $C_{30}H_{45}O_6$, 501.3211).

*2.3.12. 3α,6β,19α,23-tetrahydroxyurs-12-en-28-oic acid (**15**)*

white powder; $[\alpha]^{20}_D$ + 8.7 (c 0.07, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.66) nm; IR (KBr) ν_{max} 3435, 2930, 1693, 1448, 1377, 1206, 1148, 1044, 929 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 1 and 4; HRESIMS *m/z* 503.3384 $[M-H]^-$ (calcd for $C_{30}H_{47}O_6$, 503.3378).

*2.3.13. 23-acetoxy-3α,6β,19α-trihydroxyurs-12-en-28-oic acid (**16**)*

white powder; $[\alpha]^{20}_D$ −7.9 (c 0.58, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.72) nm; IR (KBr) ν_{max} 3503, 2931, 1717, 1456, 1376, 1256, 1156, 1034, 932 cm^{-1}; ^1H and ^{13}C NMR data, see Tables 2 and 4; HRESIMS *m/z* 545.3486 $[M-H]^-$ (calcd for $C_{32}H_{49}O_7$, 545.3473).

Table 5
. ^{13}C NMR Data of compounds **19**–**33** (δ in ppm).

No.	19[b,c]	20[a,c]	21[a,c]	22[b,c]	23[a,c]	24[a,c]	25[b,c]	26[a,c]	27[a,c]	28[a,d]	29[a,c]	30[a,c]	31[a,c]	32[a,d]	33[a,c]
1	41.2, CH_2	39.2, CH_2	34.9, CH_2	38.9, CH_2	40.3, CH_2	38.8, CH_2	38.1, CH_2	39.9, CH_2	43.3, CH_2	41.3, CH_2	36.5, CH_2	35.6, CH_2	42.0, CH_2	39.4, CH_2	41.9, CH_2
2	35.2, CH_2	37.0, CH_2	25.9, CH_2	36.9, CH_2	33.3, CH_2	34.1, CH_2	33.6, CH_2	27.6, CH_2	38.4, CH_2	36.3, CH_2	26.7, CH_2	26.1, CH_2	35.5, CH_2	36.9, CH_2	27.7, CH_2
3	211.3, C	216.7, C	75.7, CH	215.9, C	74.0, CH	222.8, C	218.8, C	75.3, CH	217.4, C	219.1, C	78.6, CH	75.7, CH	213.5, C	217.2, C	77.4, CH
4	64.3, C	59.9, C	53.3, C	59.5, C	154.6, C	40.1, C	39.1, C	50.2, CH	43.8, CH	54.9, C	41.9, C	53.4, C	64.8, C	59.8, C	56.4, C
5	53.3, CH	49.3, CH	46.2, CH	49.5, CH	51.7, CH	60.0, CH	59.3, CH	49.6, CH	56.7, CH	48.9, CH	44.9, CH	46.1, CH	53.9, CH	49.8, CH	54.1, CH
6	70.9, CH	20.5, CH_2	71.0, CH	19.8, CH_2	22.6, CH_2	68.3, CH	67.1, CH	25.5, CH_2	68.8, CH	69.4, CH	69.4, CH	71.6, CH	71.8, CH	20.6, CH_2	72.0, CH
7	41.7, CH_2	33.0, CH_2	40.4, CH_2	34.0, CH_2	32.9, CH_2	51.7, CH_2	51.8, CH_2	33.9, CH_2	39.6, CH_2	41.5, CH_2	41.5, CH_2	41.5, CH_2	41.7, CH_2	34.0, CH_2	42.0, CH_2
8	40.6, C	41.7, C	41.3, C	40.3, C	41.3, C	41.1, C	40.4, C	41.9, C	40.4, C	40.7, C	40.6, C	41.1, C	41.1, C	41.2, C	41.0, C
9	48.2, CH	55.0, CH	56.0, CH	47.1, CH	46.3, CH	48.7, CH	47.9, CH	47.7, CH	46.3, CH	48.1, CH	48.8, CH	49.0, CH	48.7, CH	47.9, CH	49.4, CH
10	36.5, C	37.4, C	37.6, C	36.6, C	39.9, C	40.1, C	38.0, C	37.2, C	37.2, C	37.1, C	37.7, C	37.6, C	36.9, C	37.5, C	37.3, C
11	24.5, CH_2	128.0, CH	128.4, CH	24.1, CH_2	25.7, CH_2	18.3, CH_2	17.7, CH_2	25.1, CH_2	25.3, CH_2	25.0, CH_2	24.8, CH_2	24.7, CH_2	24.9, CH_2	25.2, CH_2	24.8, CH_2
12	128.3, CH	131.4, CH	131.0, CH	125.6, CH	129.8, CH	34.8, CH_2	34.0, CH_2	129.7, CH	129.9, CH	130.1, CH	130.2, CH	130.1, CH	129.8, CH	129.6, CH	129.9, CH
13	139.9, C	144.0, C	144.2, C	139.2, C	140.3, C	39.2, C	38.1, C	139.8, C	139.4, C	139.3, C	139.0, C	139.2, C	139.2, C	139.9, C	139.1, C
14	43.2, C	42.5, C	43.1, C	44.5, C	43.0, C	159.8, C	158.8, C	42.9, C	43.5, C	43.6, C	43.3, C	43.6, C	43.5, C	42.9, C	43.3, C
15	29.6, CH_2	27.3, CH_2	27.2, CH_2	32.6, CH_2	29.7, CH_2	117.9, CH	117.0, CH	29.8, CH_2	29.8, CH_2	29.8, CH_2	29.8, CH_2	29.8, CH_2	29.8, CH_2	29.8, CH_2	29.8, CH_2
16	26.7, CH_2	28.0, CH_2	28.0, CH_2	31.4, CH_2	26.8, CH_2	38.8, CH_2	38.1, CH_2	26.7, CH_2	26.7, CH_2	26.7, CH_2	26.8, CH_2	26.7, CH_2	26.7, CH_2	26.7, CH_2	26.7, CH_2
17	48.7, C	48.2, C	48.2, C	138.8, C	49.1, C	38.4, C	38.0, C	49.6, C	49.6, C	49.7, C	49.6, C	49.6, C	49.7, C	49.5, C	49.6, C
18	55.1, CH	128.9, CH	128.6, CH	139.5, C	55.4, CH	50.1, CH	49.8, CH	55.2, CH	55.2, CH	55.3, CH	55.1, CH	55.2, CH	55.2, CH	55.2, CH	55.1, CH
19	73.0, C	215.3, C	215.3, C	133.9, C	73.7, C	32.5, CH_2	37.9, CH_2	73.8, C	73.8, C	73.7, C	73.8, C	73.8, C	73.7, C	73.7, C	73.8, C
20	42.7, CH	48.4, CH	48.4, CH	135.4, C	43.2, CH	50.3, C	43.6, C	43.1, CH	43.1, CH	43.1, CH	43.1, CH	43.1, CH	43.1, CH	43.7, CH	43.1, CH
21	27.3, CH_2	28.8, CH_2	28.9, CH_2	128.0, CH	27.4, CH_2	221.4, C	218.1, C	27.4, CH_2	27.4, CH_2	27.4, CH_2	27.4, CH_2	27.4, CH_2	27.3, CH_2	27.4, CH_2	27.4, CH_2
22	38.8, CH_2	39.5, CH	39.4, CH	123.5, CH	39.1, CH_2	55.6, CH_2	52.1, CH_2	38.4, CH_2	38.4, CH_2	38.4, CH	38.4, CH	38.4, CH	38.3, CH	38.4, CH	38.4, CH
23	175.1, C	64.0, CH_2	178.9, C	64.5, CH_2	103.0, CH_2	32.4, CH_3	32.3, CH_3		11.6, CH_3	66.9, CH_2	72.1, CH_2	179.1, C	176.1, C	64.4, CH_2	180.4, C
24	19.8, CH_3	63.2, CH_2	19.7, CH_3	63.3, CH_2		20.5, CH_3	20.9, CH_3	61.2, CH_2		20.5, CH_3	20.1, CH_3	20.1, CH_3	19.7, CH_3	63.6, CH_2	12.8, CH_3
25	16.5, CH_3	17.9, CH_3	19.8, CH_3	16.2, CH_3	14.1, CH_3	16.8, CH_3	16.7, CH_3	15.7, CH_3	15.8, CH_3	17.4, CH_3	17.6, CH_3	17.5, CH_3	16.7, CH_3	16.0, CH_3	17.6, CH_3
26	18.9, CH_3	17.0, CH_3	17.9, CH_3	17.0, CH_3	17.6, CH_3	26.4, CH_3	26.3, CH_3	17.7, CH_3	19.2, CH_3	19.3, CH_3	18.9, CH_3	19.2, CH_3	19.1, CH_3	17.8, CH_3	18.8, CH_3
27	25.1, CH_3	20.4, CH_3	20.5, CH_3	27.5, CH_3	25.0, CH_3	20.9, CH_3	20.9, CH_3	24.8, CH_3	24.9, CH_3	24.9, CH_3	24.9, CH_3	25.1, CH_3	24.9, CH_3	24.8, CH_3	24.8, CH_3
28	181.0, C	179.2, C	179.3, C		182.4, C	33.6, CH_3	33.2, CH_3	178.7, C	178.6, C	178.6, C	178.7, C	178.7, C	178.6, C	178.7, C	178.6, C
29	27.4, CH_3	28.5, CH_3	28.5, CH_3	17.1, CH_3	27.2, CH_3	71.4, CH_2	28.6, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3	27.2, CH_3
30	17.1, CH_3	16.7, CH_3	16.7, CH_3	21.0, CH_3	16.7, CH_3	19.4, CH_3	23.7, CH_3	16.7, CH_3	16.7, CH_3	16.7, CH_3	16.8, CH_3	16.7, CH_3	16.7, CH_3	16.8, CH_3	16.7, CH_3
OMe	52.6, CH_3		52.2, CH_3									52.2, CH_3	52.9, CH_3		52.5, CH_3
1′								95.9, CH	96.0, CH	96.0, CH	96.0, CH	96.0, CH	96.0, CH	95.9, CH	96.0, CH
2′								74.0, CH	74.1, CH	74.0, CH	74.1, CH	74.0, CH	74.0, CH	74.0, CH	74.0, CH
3′								78.5, CH	78.4, CH	78.4, CH	78.4, CH	78.4, CH	78.4, CH	78.5, CH	78.4, CH
4′								71.3, CH	71.4, CH	71.3, CH	71.4, CH	71.4, CH	71.3, CH	71.2, CH	71.3, CH
5′								78.7, CH	78.7, CH	78.7, CH	78.7, CH	78.7, CH	78.7, CH	78.8, CH	78.7, CH
6′								62.6, CH_2	62.6, CH_2	62.5, CH_2	62.6, CH_2	62.6, CH_2	62.5, CH_2	62.5, CH_2	62.6, CH_2

[a] Recorded in CD_3OD.
[b] Recorded in Pyridine-d_5.
[c] Recorded 150 MH.

[d] Recorded at 125 MHz.

*2.3.14. 3α,6β,19α-trihydroxyurs-12-en-28-oic acid-23-carboxylic acid methyl ester (**17**)*

white powder; $[\alpha]^{20}_{D}$ −17.7 (c 0.81, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.91) nm; IR (KBr) ν_{max} 3462, 2933, 1709, 1451, 1377, 1236, 1154, 1044, 1033, 930 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 4; HRESIMS *m/z* 531.3328 $[M-H]^{-}$ (calcd for $C_{31}H_{47}O_7$, 531.3316).

*2.3.15. 3α,6β,19α,22α-tetrahydroxyurs-12-en-28-oic acid-23-carboxylic acid methyl ester (**18**)*

white powder; $[\alpha]^{20}_{D}$ −5.9 (c 0.29, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.34) nm; IR (KBr) ν_{max} 3448, 2940, 1685, 1453, 1378, 1206, 1144, 1055, 1028, 932 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 4; HRESIMS *m/z* 547.3281 $[M-H]^{-}$ (calcd for $C_{31}H_{47}O_8$, 547.3265).

*2.3.16. 6β,19α-dihydroxyurs-12-en-3-one-28-oic acid-23-carboxylic acid methyl ester (**19**)*

white powder; $[\alpha]^{20}_{D}$ −6.4 (c 0.11, MeOH); UV (MeOH) λ_{max} (log ε) 206 (3.13) nm; IR (KBr) ν_{max} 3573, 2929, 1720, 1688, 1451, 1378, 1261, 1210, 1144, 1104, 1075, 802 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 529.3176 $[M-H]^{-}$ (calcd for $C_{31}H_{45}O_7$, 529.3160).

*2.3.17. 23,24-dihydroxy-3,19-dioxo-18,19-seco-11,13(18)-urs-diene-28-oic acid (**20**)*

white powder; $[\alpha]^{20}_{D}$ −15.5 (c 0.1, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.14), 241 (4.18), 281 (3.36) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 243.5 (-7.6), 300 (-0.4) nm; IR (KBr) ν_{max} 3358, 2921, 1702, 1660, 1633, 1468, 1423, 1413, 1201, 1136, 1051, 721 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 523.3029 $[M + Na]^{+}$ (calcd for $C_{30}H_{44}O_6Na$, 523.3030).

*2.3.18. 3α,6β-dihydroxy-19-oxo-18,19-seco-11,13(18)-urs-dien-28-oic acid-23-carboxylic acid methyl ester (**21**)*

white powder; $[\alpha]^{20}_{D}$ −75.4 (c 0.11, MeOH); UV (MeOH) λ_{max} (log ε) 203 (4.02), 241 (4.25) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 244 (-1.9) nm; IR (KBr) ν_{max} 3487, 2936, 1702, 1453, 1378, 1265, 1204, 1186, 1154, 1097, 1072, 1045, 1017, 981, 858 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 553.3136 $[M + Na]^{+}$ (calcd for $C_{31}H_{46}O_7Na$, 553.3136).

*2.3.19. 23,24-dihydroxy-28-norursane-3-one-12,17,19,21-tetraene (**22**)*

white powder; $[\alpha]^{20}_{D}$ + 13.2 (c 0.17, MeOH); UV (MeOH) λ_{max} (log ε) 213 (4.16), 244 (3.76) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 219 (-3.5), 245 (14.5) nm; IR (KBr) ν_{max} 3392, 2950, 1687, 1453, 1374, 1203, 1177, 1050 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 437.3044 $[M + H]^{+}$ (calcd for $C_{29}H_{41}O_3$, 437.3050).

*2.3.20. 3β,19α-dihydroxy-24-norurs-4(23),12-dien-28-oic acid (**23**)*

white powder; $[\alpha]^{20}_{D}$ + 50.3 (c 0.33, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.66) nm; ECD (MeOH) λ_{max} ($\Delta\varepsilon$) 224 (-0.2), 276 (-0.5) nm; IR (KBr) ν_{max} 3401, 2938, 1691, 1451, 1383, 1262, 1206, 1142, 1051, 1019, 802 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 455.3152 $[M - H]^{-}$ (calcd for $C_{29}H_{43}O_4$, 455.3156).

*2.3.21. 6α,29-dihydroxy-3,21-dioxo-taraxer-14-ene (**24**)*

white powder; mp 239–240 °C; $[\alpha]^{20}_{D}$ + 155.7 (c 0.42, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.80) nm; ECD (MeOH)λ_{max} ($\Delta\varepsilon$) 218 (−0.9), 294 (17.3) nm; IR (KBr) ν_{max} 3473, 3402, 2946, 1698, 1683, 1462, 1417, 1376, 1257, 1202, 1173, 1145, 1045, 1005, 980 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 471.3469 $[M+H]^{+}$ (calcd for $C_{30}H_{47}O_4$, 471.3469).

*2.3.22. 6α-hydroxy-3,21-dioxo-taraxer-14-ene (**25**)*

white powder; $[\alpha]^{20}_{D}$ + 152.7 (c 0.20, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.73) nm; ECD (MeOH)λ_{max} ($\Delta\varepsilon$) 223 (-0.36), 242 (0.51), 273 (0.29), 316 (-0.12) nm; IR (KBr) ν_{max} 3457, 2960, 1702, 1468, 1423, 1382, 1261, 1210, 1170, 1147, 1110, 1044, 1006, 980 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 2 and 5; HRESIMS *m/z* 455.3512 $[M+H]^{+}$ (calcd for $C_{30}H_{47}O_3$, 455.3520).

*2.3.23. 3β,19α,24-trihydroxy-23-norurs-12-en-28-O-β-D-glucopyranosyl ester (**26**)*

white powder; $[\alpha]^{20}_{D}$ + 29.9 (c 0.11, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.76) nm; IR (KBr) ν_{max} 3379, 2921, 2855, 1735, 1676, 1577, 1456, 1379, 1320, 1261, 1173, 1075, 1031, 803 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 659.37659 $[M + Na]^{+}$ (calcd for $C_{35}H_{56}O_{10}Na$, 659.37657).

*2.3.24. 6β,19α-dihydroxy-24-norurs-12-en-3-one-28-O-β-D-glucopyranosyl ester (**27**)*

white powder; $[\alpha]^{20}_{D}$ + 12.0 (c 0.13, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.72) nm; IR (KBr) ν_{max} 3392, 2919, 1731, 1693, 1596, 1456, 1427, 1378, 1262, 1204, 1181, 1074, 930, 804 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 657.3611 $[M+Na]^{+}$ (calcd for $C_{35}H_{54}O_{10}Na$, 657.3609).

*2.3.25. 6β,19α,23-trihydroxyurs-12-en-3-one-28-O-β-D-glucopyranosyl ester (**28**)*

white powder; $[\alpha]^{20}_{D}$ −1.1 (c 0.28, MeOH); UV (MeOH) λ_{max} (log ε) 207 (3.66) nm; IR (KBr) ν_{max} 3413, 2934, 1733, 1691, 1457, 1379, 1265, 1227, 1204, 1175, 1140, 1070, 934 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 709.3814 $[M + HCOO]^{-}$ (calcd for $C_{37}H_{57}O_{13}$, 709.3749).

*2.3.26. 3α,6β,19α,23-tetrahydroxyurs-12-en-28-O-β-D-glucopyranosyl ester (**29**)*

white powder; $[\alpha]^{20}_{D}$ −2.9 (c 0.31, MeOH); UV (MeOH) λ_{max} (log ε) 207 (4.15) nm; IR (KBr) ν_{max} 3402, 2933, 1731, 1672, 1452, 1376, 1320, 1264, 1227, 1205, 1074, 1033, 930 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 689.3873 $[M + Na]^{+}$ (calcd for $C_{36}H_{58}O_{11}Na$, 689.3871).

*2.3.27. 3α,6β,19α-trihydroxyurs-12-en-23,28-dioic acid 23-methyl ester 28-O-β-D-glucopyranosyl ester (**30**)*

white powder; $[\alpha]^{20}_{D}$ –23.0 (c 0.19, MeOH); UV (MeOH) λ_{max} (log ε) 203 (3.91) nm; IR (KBr) ν_{max} 3448, 2932, 1723, 1453, 1377, 1262, 1238, 1205, 1178, 1072, 1031, 929 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 717.3815 $[M + Na]^{+}$ (calcd for $C_{37}H_{58}O_{12}Na$, 717.3820).

*2.3.28. 6β,19α-dihydroxyurs-12-en-3-one-23,28-dioic acid 23-methyl ester 28-O-β-D-glucopyranosyl ester (**31**)*

white powder; $[\alpha]^{20}_{D}$ −7.1 (c 0.38, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.65) nm; IR (KBr) ν_{max} 3436, 2932, 1729, 1702, 1455, 1375, 1260, 1177, 1075, 1031, 929, 803 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 715.3666 $[M + Na]^{+}$ (calcd for $C_{37}H_{56}O_{12}Na$, 715.3664).

*2.3.29. 19α,23,24-trihydroxyurs-12-en-3-one-28-O-β-D-glucopyranosyl ester (**32**)*

white powder; $[\alpha]^{20}_{D}$ + 17.1 (c 0.28, MeOH); UV (MeOH) λ_{max} (log ε) 204 (3.87) nm; IR (KBr) ν_{max} 3415, 2931, 1732, 1686, 1454, 1380, 1261, 1203, 1177, 1138, 1074 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 665.3887 $[M + H]^{+}$ (calcd for $C_{36}H_{57}O_{11}$, 665.3895).

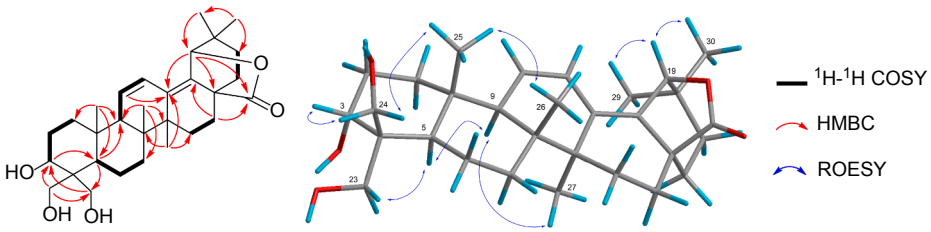

Fig. 2. Key ^{1}H–^{1}H COSY, HMBC, and ROESY correlations of **1**.

*2.3.30. 3β,6β,19α-trihydroxyurs-12-en-23,28-dioic acid 23-methyl ester 28-O-β-D-glucopyranosyl ester (**33**)*

white powder; $[\alpha]^{20}_{D}$ + 14.9 (c 0.3, MeOH); UV (MeOH) λ_{max} (log ε) 205 (3.87) nm; IR (KBr) ν_{max} 3386, 2935, 1714, 1452, 1372, 1261, 1187, 1142, 1071, 929 cm^{-1}; ^{1}H and ^{13}C NMR data, see Tables 3 and 5; HRESIMS *m/z* 717.3819 [M + Na]$^+$ (calcd for $C_{37}H_{58}O_{12}Na$, 717.3820).

2.4. X-ray crystallographic analysis

Single crystals of **9** and **24** were cultured from isopropanol–MeOH (5:1) and MeOH solutions, respectively. Their X-ray crystallographic structures were acquired by anomalous scattering of Cu K*a* radiation. Crystallographic data for **9** and **24** were deposited at the Cambridge Crystallographic Data Centre (CCDC 2050806 and 2050807).

*2.4.1. Crystallographic data of **9***

$C_{33}H_{52}O_7$, M = 560.74, a = 7.97913(13) Å, b = 11.6325(2) Å, c = 31.5927(5) Å, α = 90°, β = 90°, γ = 90°, V = 2932.34(8) Å^3, T = 100 K, orthorhombic, space group $P2_12_12_1$ (no. 19), Z = 4, μ(Cu Kα) = 0.700 mm^{-1}, 20445 reflections measured (8.1° ≤ 2θ ≤ 144.214°), 5672 unique (R_{int} = 0.0399, R_{sigma} = 0.0346) which were used in all calculations. The final R_1 was 349 (I > 2σ(I)) and wR_2 was 0.0893 (all data). The goodness of fit on F^2 was 1.030. Flack parameter = −0.08(7).

*2.4.2. Crystallographic data of **24***

$C_{30}H_{46}O_4$, M = 470.67, a = 8.88371(14) Å, b = 11.82467(19) Å, c = 25.3311(4) Å, α = 90°, β = 90°, γ = 90°, V = 2660.95(7) Å^3, T = 108.55 (10) K, orthorhombic, space group $P2_12_12_1$ (no. 19), Z = 4, μ(Cu Kα) = 0.593 mm^{-1}, 9202 reflections measured (8.252° ≤ 2θ ≤ 142.154°), 5027 unique (R_{int} = 0.0256, R_{sigma} = 0.0369) which were used in all calculations. The final R_1 was 0.0396 (I > 2σ(I)) and wR_2 was 0.1022 (all data). The goodness of fit on F^2 was 1.030. Flack parameter = 0.02 (10).

2.5. Acid hydrolysis and determination of the absolute configurations of the sugar units of compounds **26**–**33**

Compounds **26**–**33** (each 1.0 mg) were dissolved in MeOH and treated with 2 M HCl (1.0 mL). After heating at 90 °C for 10 h, each solution was diluted with H_2O (2.0 mL) and extracted with EtOAc three times. The H_2O-soluble layer was then concentrated and dried in vacuo to give the sugar residue. The residue was dissolved in anhydrous pyridine (1.0 mL), and L-cysteine methyl ester hydrochloride (1.0 mg) was added. The mixture was kept at 60 °C for 2 h. Then, *N*-trimethylsilylimidazole (0.2 mL) was added and stirred at 60 °C for 2 h. The reaction was quenched by the addition of 1.0 mL of water. After extraction with *n*-hexane three times, the *n*-hexane layer was detected by gas chromatography under the following conditions: SE-54 column (30 m × 0.25 mm), FID detector (280 °C), and N_2 as the carrier gas. The initial oven temperature of 200 °C was raised to 280 °C at a rate of 10 °C/min, and held for 35 min. Finally, D-glucose was defined by comparing the retention time of its derivative with that of the standard D-glucose derivative.

2.6. Hepatoprotective assay

As previously described, the MTT assay method was used to test the hepatoprotective effects of the isolated compounds (**3**, **5**, **7**–**9**, **12**–**14**, **16**–**19**, **22**, 24, **25**, **32**, **34**–**41**, and **44**) [10]. The detailed process is described in the Supporting Information.

2.7. In vitro anti-HSV-1 and anti-CVB3 activity assays

Anti-HSV-1 and anti-CVB3 activities of the isolated compounds were tested by the Reed-Muench method [11], as described in the Supporting Information.

3. Results and discussion

Compound **1** was obtained as a white powder. Its molecular formula

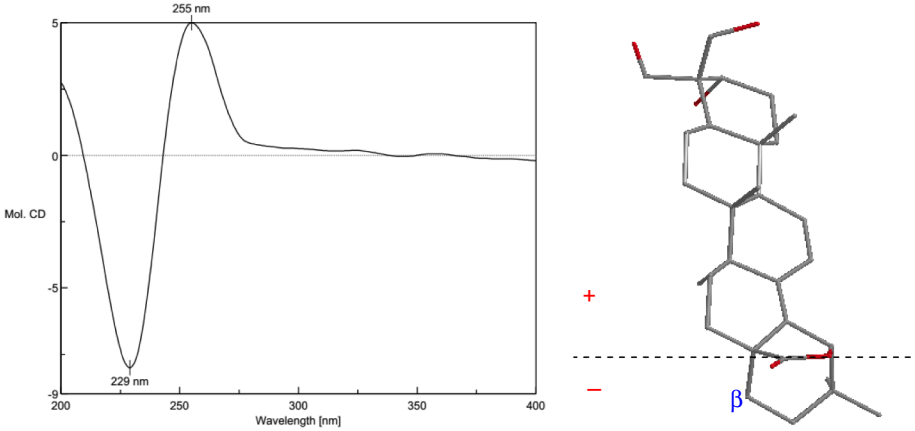

Fig. 3. Experimental ECD spectrum of **1** (left) and the Beecham's rules for the bridged-ring lactone of **1** (right).

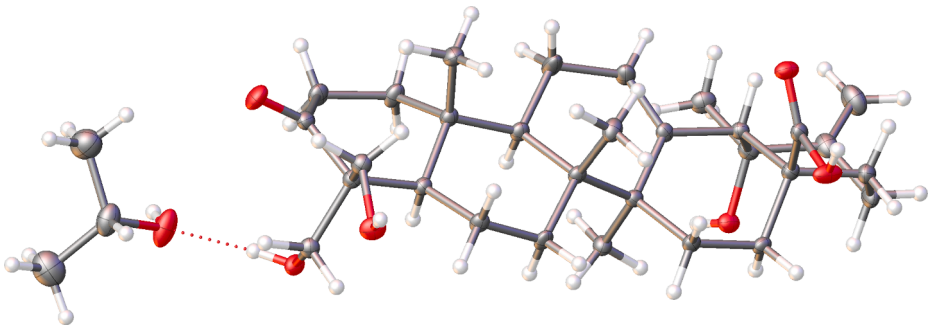

Fig. 4. ORTEP diagram of **9**.

was determined as $C_{30}H_{44}O_5$ based on HRESIMS analysis (507.3082 [M + Na]$^+$, calcd for $C_{30}H_{44}O_5Na$, 507.3081) and ^{13}C NMR data, indicating nine degrees of unsaturation. The IR spectrum showed absorption bands for hydroxy (3587, 3304 cm^{-1}) and carbonyl (1784 cm^{-1}) groups. The ^1H NMR data (Table 1) clearly displayed five methyl groups (δ_H 1.09, 1.09, 1.00, 0.97, and 0.81), two olefinic protons [δ_H 6.25 (1H, dd, J = 10.2, 3.0 Hz), 5.85 (1H, dd, J = 10.2, 2.2 Hz)], two oxygenated methylenes [δ_H 3.89 (1H, d, J = 11.2 Hz), 3.72 (1H, d, J = 11.2 Hz), δ_H 3.66 (1H, d, J = 11.5 Hz), and 3.59 (1H, d, J = 11.5 Hz)], and two oxygenated methines [δ_H 4.84 (overlap), 4.05 (1H, dd, J = 2.8, 2.8 Hz)]. The ^{13}C NMR data (Table 4) revealed 30 carbon signals attributed to five methyls, 10 methylenes (including two oxygenated), six methines (including two olefinic and two oxygenated), and nine quaternary carbons (including one carbonyl and two olefinic). These characteristics of **1** were consistent with those of oleanane-type triterpenoids. The HMBC correlation (Fig. 2) of H-19 (δ_H 4.84)/C-28 (δ_C 180.4) indicated that **1** possessed a bridged-ring lactone unit between C-28 and C-19. The above data of **1** were similar to those of 2α,3β,23-trihydroxyolean-11,13(18)-dien-28,19β-olide [12], except for the disappearance of the 2α-OH and the presence of an additional hydroxy group at C-24, which was confirmed by the HMBC cross-peaks from H_2-23 (δ_H 3.89, 3.72) to C-24 (δ_C 64.6), and from H_2-24 (δ_H 3.66, 3.59) to C-3 (δ_C 71.1), along with the coupling system [–CH_2(1)–CH_2(2)–CH(3)-] in the ^1H–^1H COSY spectrum. The 3β-H configuration was established by the small coupling constant (J = 2.8, 2.8 Hz) between H-3 and H_2-2. This assignment was further supported by a ROESY correlation of H-3 (δ_H 4.05)/H-24 (δ_H 3.66) (Fig. 2). Additional ROESY correlations of H_2-24/H_3-25 (δ_H 1.00), H_3-25/H_3-26 (δ_H 0.81), H_2-23/H-5 (δ_H 1.76), H-5/H-9 (δ_H 2.31), and H-9/H_3-27 (δ_H 1.09) indicated that H_2-24, H_3-25 and H_3-26 are β-oriented, while H-5, H-9, H_2-23, and H_3-27 are α-oriented.

To determine its absolute configuration, the ECD spectrum (Fig. 3) of **1** was measured in MeOH solution, and strong Cotton effects (CEs) were observed at 229 and 255 nm for the $n - \pi^*$ transition of a bridged-ring lactone moiety and for the $\pi - \pi^*$ transition of a conjugated diene moiety, respectively. According to Beecham's rules [13–15], the sign of the $n - \pi^*$ CE of the bridged-ring lactone mainly depends upon the location of C-β relative to the lactone ring plane. Based on this rule, the (–)-CE at 229 nm implied that the C-β of the lactone ring was below the C-CO—O—C lactone plane, suggesting a 19*S* configuration (Fig. 3). Additionally, the sign of the $\pi - \pi^*$ transition (255 nm) was deduced by the diene helicity rule [16], which allowed for elucidation of the configurations 8*R*,9*R*,14*S*,17*R*. In combination with the observed ROESY correlations, the absolute configurations of the remaining chiral carbons were determined to be 3*R*,5*R*,10*S*. Therefore, the structure of **1** was identified as 3α,23,24-trihydroxyolean-11,13(18)-dien-28,19β-olide.

Compound **2** displayed an [M − H]$^-$ ion at *m/z* 485.3277 (calcd for $C_{30}H_{45}O_5$, 485.3262), which corresponded to a molecular formula of $C_{30}H_{46}O_5$ by HRESIMS analysis. The ^1H and ^{13}C NMR data (Tables 1 and 4) of **2** were structurally similar to those of 24-hydroxy-3-oxo-olean-12-en-28-oic acid [17], except for the presence of an additional hydroxymethyl group (δ_H 4.08, 3.44; δ_C 64.3) in **2**. The key HMBC correlations from δ_H 4.08 and 3.44 (H_2-23) to C-3 (δ_C 217.2), C-4 (δ_C 59.7), C-5 (δ_C 49.9) and C-24 (δ_C 63.6) suggested that the hydroxy group is located at C-23. The relative configuration of **2** was also similar to that of 24-hydroxy-3-oxo-olean-12-en-28-oic acid according to their similar ROESY correlations. In the ECD spectrum of **2** (Fig. S24), a weak (–)-CE at 307.5 nm for the n–π^* transition of the C-3 carbonyl group suggested a (5*R*,8*R*,9*R*,10*R*,14*S*,17*S*,18*S*) configuration based on the cyclohexanone octant rule [18]. Thus, the structure of **2** was considered as 23,24-dihydroxy-3-oxo-olean-12-en-28-oic acid.

Compounds **3** and **4** showed the same molecular formula of $C_{30}H_{46}O_6$ by HRESIMS analysis (calcd for $C_{30}H_{45}O_6$, 501.3211). Their 1D NMR data (Tables 1 and 4) were similar to those of **2**, except that compounds **3** and **4** each possessed an additional hydroxy group. In the ^1H–^1H COSY spectrum of **3**, the fragment [−CH(18) − CH(19) −] was evidence of the hydroxy group attached at C-19. The 19α-OH configuration of **3** was determined by the H-19 broad singlet at δ_H 3.64. This assignment was also supported via a ROESY correlation of H-19/H_3-30 (δ_H 1.13). The ECD spectrum of **3** (Fig. S35) exhibited a weak negative sign at 303.5 nm due to the n–π^* transition of the C-3 carbonyl group, which indicated the absolute configuration of **3** to be 5*R*,8*R*,9*R*,10*R*,14*S*,17*R*,18*S*,19*S* using the cyclohexanone octant rule and the observed ROESY correlations. In the HMBC spectrum of **4**, the long-range correlations of the hydroxymethyl group (δ_H 3.19) with C-19 (δ_C 41.5), C-20 (δ_C 37.0) and C-21 (δ_C 29.4), together with the ROESY correlation of H-18 (δ_H 2.88)/H_3-30 (δ_H 0.94), indicated that the hydroxy group is attached to C-29 in **4**. According to the above evidence, the structures of **3** and **4** were considered as 19α,23,24-trihydroxy-3-oxo-olean-12-en-28-oic acid and 23,24,29-trihydroxy-3-oxo-olean-12-en-28-oic acid, respectively.

Compound **5** exhibited an [M – H]$^-$ ion at *m/z* 503.3372 (calcd for $C_{30}H_{47}O_6$, 503.3367), and its molecular formula, $C_{30}H_{48}O_6$, was established by HRESIMS analysis. The ^1H and ^{13}C NMR data (Tables 1 and 4) of **5** displayed a resemblance to those of **1** for the AB rings, while the CDE rings were the same as **3**. This deduction was confirmed by the 2D NMR data (Figs. S51-S54). The ROESY spectrum of **5** showed the correlations of H-3 (δ_H 4.74)/H-24 (δ_H 4.16) and H-24/H_3-25 (δ_H 1.04), suggesting that the relative configuration of H-3 is β-oriented. The 19α-OH configuration was undoubtedly confirmed by the broad singlet of H-19 in the ^1H NMR spectrum. Thus, the structure of **5** was identified as 3α,19α,23,24-tetrahydroxyolean-12-en-28-oic acid.

The molecular formula of **9** was determined to be $C_{30}H_{44}O_6$ by HRESIMS analysis (*m/z* 499.3050 [M – H]$^-$, calcd for $C_{30}H_{43}O_6$, 499.3054). In the 1D NMR spectroscopic data (Tables 1 and 4) of **9**, there were clearly observed signals from four methyls (δ_H 1.73, 1.67, 1.18, 1.17; δ_C 27.9, 24.3, 17.7, 15.9), one *exo*-olefin (δ_H 5.03, 4.83; δ_C 156.9, 105.7), one trisubstituted double bond (δ_H 5.65; δ_C 140.1, 128.5), two hydroxymethyl groups (δ_H 4.71, 4.00, 4.28, 4.09; δ_C 65.0, 63.6), and one carbonyl carbon (δ_C 216.0). The above data were very similar to those of the known compound 19α,23,24-trihydroxyurs-3-oxo-12-en-28-oic acid (**34**), except for the presence of an *exo*-olefin on the E ring in **9** instead of a methyl group in **34**. According to the key HMBC

correlations of H_2-30 (δ_H 5.03, 4.83) with C-19 (δ_C 73.3) and C-21 (δ_C 29.3), this *exo*-olefin was determined to be located at $\triangle^{20(30)}$. In the ECD data of **9** (Fig. S66), a (–)-CE at 309 nm attributed to $n-\pi^*$ transition of C-3 carbonyl group was observed. From the cyclohexanone octant rule and observed ROESY data, the absolute configuration of **9** was assigned as 5*R*,8*R*,9*R*,10*R*,14*S*,17*S*,18*S*,19*S*, which was corroborated by the X-ray crystallographic data [Flack parameter of − 0.08(7)] (Fig. 4). Based on this evidence, the structure of **9** was unambiguously established as 19α,23,24-trihydroxyurs-12,20(30)-dien-3-one-28-oic acid.

Compound **10** had the same molecular formula ($C_{30}H_{44}O_6$) as that of **9** based on HRESIMS analysis (*m/z* 499.3064[M − H]$^-$, calcd for $C_{30}H_{43}O_6$, 499.3054). The 1D NMR spectroscopic data (Tables 1 and 4) of **10** displayed high similarity to those of **9**, except for the E ring signals. The E ring of **10** possessed a hydroxy group at C-30 and a double bond between C-19 and C-20, which was determined by the HMBC correlations from H_3-29 (δ_H 1.86) to C-18 (δ_C 51.5), C-19 (δ_C 132.0), and C-20 (δ_C 130.1) and from H_2-30 (δ_H 4.58, 4.37) to C-19, C-20, and C-21 (δ_C 25.0). Consequently, the structure of **10** was defined as 23,24,30-trihydroxyurs-12,19-dien-3-one-28-oic acid.

The molecular formula of **11** was determined to be $C_{30}H_{46}O_6$ by HRESIMS analysis. The 1D NMR spectroscopic data (Tables 1 and 4) were highly similar to those of **10**, except that the carbonyl signal for C-3 was replaced by an oxygen-bearing methine (δ_H 4.71, δ_C 70.1). This speculation was confirmed by the [−CH_2(1) − CH_2(2) − CH(3) −] fragment in the ^{1}H–^{1}H COSY data in combination with the HMBC correlations from H_2-23 (δ_H 4.55, 4.36) and H_2-24 (δ_H 4.15, 4.02) to C-3 (δ_C 70.1). Finally, the NOE correlation of H-3 (δ_H 4.71)/H-24 (δ_H 4.15) and the splitting pattern of H-3 (4.71, brd, J = 2.7 Hz) revealed that H-3 is β-oriented. Thus, the structure of **11** was identified as 3α,23,24,30-tetrahydroxyurs-12,19-dien-28-oic acid.

The HRESIMS ion of **12** at *m/z* 513.3224 [M − H]$^-$ revealed a molecular formula of $C_{31}H_{46}O_6$. Detailed analysis of the 1D NMR spectroscopic data (Tables 1 and 4) indicated that **12** were extremely similar to **10**. The only difference was the presence of an additional oxygen-bearing methoxyl group (δ_H 3.31, δ_C 57.9) in **12**. In the HMBC spectrum, a key correlation from the oxygen-bearing methoxyl group to C-30 (δ_C 73.8) suggested that this group was attached to the C-30 position. Thus, the structure of **12** was identified as 23,24-dihydroxyurs-12,19-dien-3-one-28-oic acid 30-methyl ether.

Compound **13** possessed an HRESIMS ion at *m/z* 515.3372 [M − H]$^-$, which revealed a molecular formula of $C_{31}H_{48}O_6$. The ^{1}H and ^{13}C NMR data (Tables 1 and 4) closely resembled those of **12**, except for the presence of an oxygenated methine signal (δ_H 4.71, δ_C 70.1) in **13** instead of the carbonyl group at C-3 in **12**. This signal assignable to C-3 was deduced by the fragment [−CH_2(1) − CH_2(2) − CH(3) −] in the ^{1}H–^{1}H COSY spectrum. The 3α-OH configuration was assigned by a NOE signal of H-3 (δ_H 4.71)/H-24 (δ_H 4.15), which was further supported by the splitting pattern of H-3 (4.71, brd, J = 3.0 Hz). Therefore, the structure of **13** was elucidated as 3α,23,24-trihydroxyurs-12,19-dien-28-oic acid 30-methyl ether.

The HRESIMS spectrum of **14** displayed an [M − H]$^-$ ion at *m/z* 501.3219 (calcd for $C_{30}H_{45}O_6$, 501.3211), which corresponded to a molecular formula of $C_{30}H_{46}O_6$. The 1D NMR data (Tables 1 and 4) of **14** was almost identical to those of the known compound silphanolic acid B [19]. The only difference was the presence of a hydroxy group at C-19, as confirmed by the HMBC correlations from H_3-29 (δ_H 1.20) and H_3-30 (δ_H 0.93) to δ_C C-19 (73.7). Furthermore, the ROESY correlation of H-18 (δ_H 2.54)/H_3-29 indicated 19-OH to be α-oriented. NOE correlations of H-23 (δ_H 3.43)/H-6 (δ_H 4.34), and H_3-24 (δ_H 1.25)/H_3-25 (δ_H 1.47) suggested that the 6-OH is β-oriented. Thus, the structure of **14** was identified as 6β,19α,23-trihydroxyurs-12-en-3-one-28-oic acid.

Compound **15** exhibited a molecular formula of $C_{30}H_{48}O_6$ by HRESIMS analysis (*m/z* 503.3384 [M - H]$^-$, calcd for $C_{30}H_{47}O_6$, 503.3378). The ^{1}H and ^{13}C NMR data (Tables 1 and 4) of **15** were found to be closely comparable to those of **14**, except for the appearance of an oxygenated methine signal (δ_H 3.58, δ_C 78.6) in **15** instead of the carbonyl group at C-3 in **14**. In the HMBC spectrum of **15**, the long-range correlations from H_2-23 (δ_H 3.69, 3.34) and H_3-24 (δ_H 1.10) to C-3 (δ_C 78.6) indicated that the oxygenated methine is attached to C-3. In the NOESY experiment, the key correlations of H-3 (δ_H 3.58)/H_3-24, H_3-24/H_3-25 (δ_H 1.35), and H-6 (δ_H 4.35) /H-23 (δ_H 3.34) suggested that H-3 was assigned to be β-oriented, whereas H-6 was assigned to be α-oriented. Therefore, the structure of **15** was determined as 3α,6β,19α,23-tetrahydroxyurs-12-en-28-oic acid.

Compound **16** had a molecular formula of $C_{32}H_{50}O_7$ based on HRESIMS analysis (*m/z* 545.3486 [M - H]$^-$, calcd for $C_{32}H_{49}O_7$, 545.3473). The 1D NMR data (Tables 2 and 4) of **16** were structurally similar to those of **15**, except for an additional acetoxy group (δ_H 2.06, δ_C 173.7, 21.1) at C-23 in **16**. This assignment was unambiguously confirmed by the HMBC correlations from H_2-23 (δ_H 4.09, 4.00) to C-1′ (δ_C 173.7). Furthermore, the 3α-OH and 6β-OH configurations were deduced from the NOE signals of H-3 (δ_H 3.61)/H_3-24 (δ_H 1.30), H_3-24/H_3-25 (δ_H 1.36), and H-6 (δ_H 4.20)/H-23 (δ_H 4.09). Hence, the structure of **16** was determined as 23-acetoxy-3α,6β,19α-trihydroxyurs-12-en-28-oic acid.

Compound **17** possessed a molecular formula of $C_{31}H_{48}O_7$ by HRESIMS analysis (*m/z* 531.3328 [M - H]$^-$, calcd for $C_{31}H_{47}O_7$, 531.3316) and ^{13}C NMR data. The ^{1}H and ^{13}C NMR data (Tables 2 and 4) of **17** were highly similar to those of the reported compound elatumic acid [20], except for the broad singlet of H-6 in **17**, which was assigned to be the 6α-H configuration. Furthermore, the NOE correction of H-3 (δ_H 3.68) with H_3-24 (δ_H 1.54) revealed that H-3 is β-oriented. Finally, the structure of **17** was elucidated as 3α,6β,19α-trihydroxyurs-12-en-28-oic acid-23-carboxylic acid methyl ester.

The HRESIMS spectrum of **18** showed an [M - H]$^-$ ion at *m/z* 547.3281 (calcd for $C_{31}H_{47}O_8$, 547.3265), which gave a molecular formula of $C_{31}H_{48}O_8$. The 1D NMR spectroscopic data (Tables 2 and 4) of **18** displayed similarity to those of **17** except for an additional oxymethine at C-22 (δ_H 4.44, δ_C 75.4). This assumption was established based on the HMBC correlation of H-22 (δ_H 4.44)/C-28 (δ_C 180.2) along with the fragment [−CH(20) − CH_2(21) − CH(22) −] in the ^{1}H–^{1}H COSY spectrum. Moreover, the 22α-OH configuration was determined by the splitting pattern of H-22 (J = 11.6, 4.4 Hz), which was also supported by the ROESY correlations of H-22 with H-18 (δ_H 3.11) and H_3-29 (δ_H 1.44). Therefore, the structure of **18** was assigned as 3α,6β,19α,22α-tetrahydroxyurs-12-en-28-oic acid-23-carboxylic acid methyl ester.

The molecular formula of **19** was determined to be $C_{31}H_{46}O_7$ based on the HRESIMS ion at *m/z* 529.3176 [M - H]$^-$ (calcd for $C_{31}H_{45}O_7$, 529.3160). The 1D NMR spectroscopic data (Tables 2 and 5) of **19** were almost similar to those of **17** except for an additional carbonyl group (δ_C 211.3) at C-3 in **19** instead of the oxymethine in **17**, which was confirmed by the HMBC correlations from H_3-24 (δ_H 2.13) and H-1 (δ_H 1.87) to C-3. Thus, the structure of **19** was elucidated as 6β,19α-dihydroxyurs-12-en-3-one-28-oic acid-23-carboxylic acid methyl ester.

Compound **20** possessed a molecular formula of $C_{30}H_{44}O_6$ as determined by an [M + Na]$^+$ ion at *m/z* 523.3029 (calcd for $C_{30}H_{44}O_6Na$, 523.3030) in the HRESIMS spectrum. The 1D NMR data (Tables 2 and 5) of **20** resembled to those of the known compound 3β-hydroxy-19-oxo-18,19-seco-11,13(18)-ursa- diene-28-oic acid [21]. Significant differences included the presence of a keto carbonyl group (δ_C 216.7, C-3) instead of an oxygenated methine and the presence of two additional hydroxy groups at C-23 and C-24, as confirmed by the HMBC correlations from H_2-23 (δ_H 4.11, 3.48) to C-3 (δ_C 216.7) and C-5 (δ_C 49.3), and from H_2-24 (δ_H 3.88, 3.59) to C-3 and C-5. The relative configuration of **20** was determined to be the same as that of **9** by ROESY spectrum analysis. In the experimental ECD data of **20**, a strong (–)-CE at 243.5 nm (Fig. S181) for the $\pi-\pi^*$ transition of the cyclic conjugated diene unit, which revealed the absolute configuration of **20** to be 5*R*,8*R*,9*R*,10*S*,14*S*,17*S* [22]. Thus, the structure of **20** was determined as 23,24-dihydroxy-3,19-dioxo-18,19-seco-11,13(18)-urs-diene-28-oic

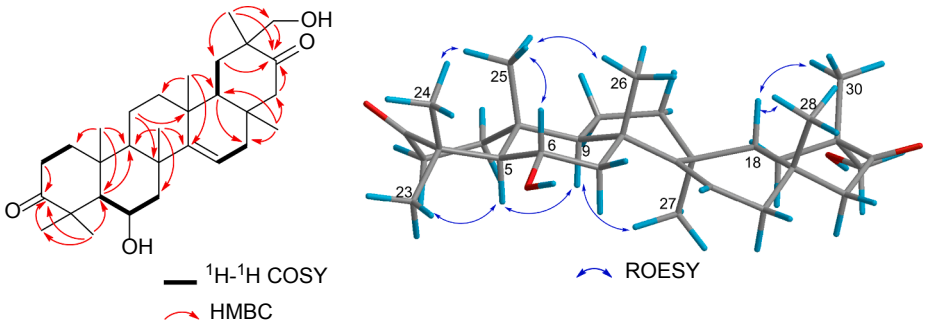

Fig. 5. Key ^{1}H–^{1}H COSY, HMBC, and ROESY correlations of **24**.

acid.

Compound **21** exhibited an $[M + Na]^+$ ion at *m/z* 553.3136 (calcd for $C_{31}H_{46}O_7Na$, 553.3136) in the HRESIMS spectrum, which revealed a molecular formula of $C_{31}H_{46}O_7$. The 1D NMR data (Tables 2 and 5) of **21** were highly similar to those of **17** for the AB rings, while the remaining resonances were the identical to those of **20**. This deduction was further corroborated by the 2D NMR data. The ECD spectrum of **21** exhibited a close resemblance to that of **20** (Fig. S192), suggesting a (3*R*,4*S*,5*R*,6*R*,8*R*,9*R*,10*R*,14*S*,17*S*) configuration [22]. Therefore, the structure of **21** was determined as 3*α*,6*β*-dihydroxy-19-oxo-18,19-seco-11,13(18)-urs-dien-28-oic acid-23-carboxylic acid methyl ester.

The HRESIMS spectrum of **22** exhibited an $[M + H]^+$ ion at *m/z* 437.3044 (calcd for $C_{29}H_{41}O_3$, 437.3050), which corresponded to a molecular formula of $C_{29}H_{40}O_3$. The 1D NMR data (Tables 2 and 5) of **22** closely resembled those of (3*R*)-3,23,24-trihydroxy-28-norursane-12,17,19,21-tetraene, a 28-nortriterpenoid previously isolated from *Rhododendron latoucheae* by our group [23], except for the presence of a keto carbonyl group (δ_C 215.9) at C-3 in **22** instead of an oxygenated methine. This assignment was further confirmed by the HMBC correlations from H_2-23 (δ_H 4.70, 3.98), H_2-24 (δ_H 4.28, 4.09), and H-1(δ_H 1.90) to C-3 (δ_C 215.9). The experimental ECD spectrum of **22** showed an intense (+) CE at 244 nm (Fig. S203) due to the $\pi - \pi^*$ electronic transition of the conjugated chromophores. This result revealed that the absolute configuration of **22** was 5*R*,8*R*,9*R*,10*R*,14*S* [23]. Therefore, the structure of **22** was elucidated as 23,24-dihydroxy-28-norurs-3-one-12,17,19,21-tetraene.

Compound **23** gave a molecular formula of $C_{29}H_{44}O_4$ based on the HRESIMS ion at *m/z* 455.3152 $[M - H]^-$ (calcd for $C_{29}H_{43}O_4$, 455.3156). The ^{1}H NMR data (Table 2) of **23** showed five methyl groups (δ_H 1.38, 1.21, 0.94, 0.86, and 0.77), three olefinic protons [δ_H 5.31 (1H, dd, J = 3.7, 3.7 Hz), 5.05 (1H, d, J = 2.0 Hz), and 4.64 (1H, d, J = 2.0 Hz)], and one oxygen-bearing methine [δ_H 3.94 (1H, dd, J = 11.8, 5.6 Hz)]. The ^{13}C NMR data (Table 5) revealed 29 carbon signals, including five methyl carbons, ten methylenes (one olefinic), six methines (one oxygen-bearing and one olefinic), and eight quaternary carbons (one oxygenated, two olefinic and one carboxyl). The above data closely resembled that of 2*α*,3*α*,19*α*-trihydroxy-24-norurs-4(23),12-dien-28-oic acid, a 24-nortriterpenoid isolated from *Rumex japonicas* [24]. These compounds differed by the absence of the hydroxy group at C-2 in **23**, which was elucidated by the fragment [–CH_2(1)–CH_2(2)–CH(3)-] in the ^{1}H–^{1}H COSY spectrum. The NOE correlation of H-3 (δ_H 3.94)/H-5 (δ_H 1.61) revealed a 3*α*-H configuration. Consequently, the structure of **23** was defined as 3*β*,19*α*-dihydroxy-24-norurs-4(23),12-dien-28-oic acid.

Compound **24** was obtained as a white powder with a molecular formula of $C_{30}H_{46}O_4$ based on the $[M + H]^+$ ion at *m/z* 471.3469 (calcd for $C_{30}H_{47}O_4$, 471.3469) in its HRESIMS spectrum. Its ^{1}H NMR data (Table 2) clearly exhibited seven singlet methyl groups (δ_H 1.34, 1.32, 1.19, 1.16, 0.95, 0.88, and 0.83), one hydroxymethyl group [δ_H 3.65 (1H, d, J = 10.4 Hz), 3.28 (1H, d, J = 10.4 Hz)], one oxygenated methine [δ_H 3.92, (1H, ddd, J = 11.1, 11.1, 4.2 Hz)] and one olefinic proton [δ_H 5.71, (1H, dd, J = 8.2, 3.1 Hz)]. A total of 30 carbon signals, including seven methyl carbons, nine methylenes (one oxygen-bearing), five methines (one oxygen-bearing and one olefinic), and nine quaternary carbons (one olefinic and two carbonyl), were recognized in its ^{13}C NMR data (Table 5). The above data suggested that **24** belongs to the Δ^{14}-taraxerene-type triterpene skeleton. The key HMBC correlations (Fig. 4) from H_2-2 (δ_H 2.76, 2.23), H_3-23 (δ_H 1.32) and H_3-24 (δ_H 1.34) to C-3 (δ_C 222.8) and from H_2-29 (δ_H 3.65, 3.28), H_3-30 (δ_H 0.95) and H_2-22 (δ_H 2.70, 1.94) to C-21 (δ_C 221.4) indicated the presence of two carbonyl groups at C-3 and C-21 and the presence of a hydroxy group at C-29. In addition, the [−CH(5) − CH(6) − CH_2(7) −] fragment in the ^{1}H–^{1}H COSY spectrum suggested that the other hydroxy group was attached to C-6. The observed ROESY cross-peaks (Fig. 5) of H-6 (δ_H 3.92)/H_3-25 (δ_H 0.88) indicated that the 6-OH was assigned as *α*-oriented. In the ECD

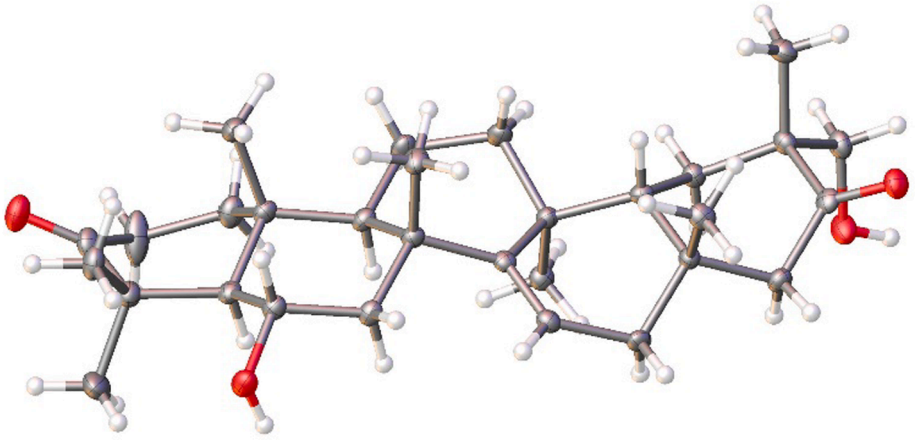

Fig. 6. ORTEP diagram of **24**.

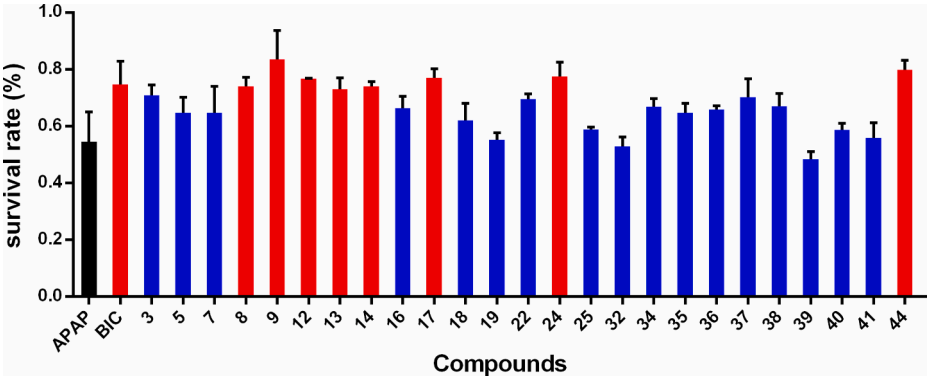

Fig. 7. Effects of the isolated compounds on the survival rates of APAP-treated HepG2 cells. Data are presented as the mean ± SD (n = 3). BIC was used as the positive control.

data of **24** (Fig. S225), a strong (+)-CE at 294 nm mainly due to $n-\pi^*$ transition of C-21 carbonyl group was observed, indicating a 20*R* configuration according to the cyclohexanone octant rule. Finally, The absolute configuration of **24** was unambiguously determined to be 5*R*,6*S*,8*R*,9*R*,13*S*,17*S*,18*R*,20*R* on the basis of the X-ray crystallographic data [Flack parameter: 0.02(10)] (Fig. 6). Hence, the structure of **24** was determined as 6*α*,29-dihydroxy-3,21-dioxo-taraxer-14-ene.

Compound **25** gave a molecular formula of $C_{30}H_{46}O_3$ (*m/z* 455.3512 $[M+H]^+$, calcd for $C_{30}H_{47}O_3$, 455.3520) using HRESIMS analysis and ^{13}C NMR data. Comparing the 1D NMR data (Tables 2 and 5) and the molecular formula of **25** with those of **24** implied the presence of an additional methyl group (δ_H 1.19; δ_C 28.6) at C-29 in **25** instead of the hydroxymethyl group in **24**. This deduction was further supported by the key HMBC correlations of H_3-29 (δ_H 1.19) with C-19 (δ_C 37.9), C-20 (δ_C 43.6) and C-21 (δ_C 218.1) and of H_3-30 (δ_H 1.20) with C-19, C-20, and C-21. Finally, the structure of **25** was determined as 6*α*-hydroxy-3,21-dioxo-taraxer-14-ene.

The HRESIMS analysis of **26** showed a molecular formula of $C_{35}H_{56}O_{10}$ based on a deprotonated molecular ion at *m/z* 659.37659 $[M+Na]^+$ (calcd for $C_{35}H_{56}O_{10}Na$, 659.37657). The 1D NMR data (Tables 3 and 5) of **26** closely resembled those of 3*β*,19*α*,24-trihydroxy-23-norurs-12-en-28-oic acid [25]. In the ROESY spectrum, a key correlation of H_2-24 (δ_H 3.92, 3.56) with H_3-25 (δ_H 0.79) indicated a 24*β*-OH configuration, which supported **26** to be a 23-nortriterpenoid saponin. Additionally, the ROESY correlations of H-3 (δ_H 3.81) with H-5 and H-18 (δ_H 2.51) with H_3-29 (δ_H 1.20) indicated 3*β*-OH and 19*α*-OH configurations. The 1D NMR spectra of **26** also displayed characteristic resonances assignable to a sugar unit [δ_H 5.32 (1H, d, J = 8.2 Hz, H-1′), 3.32–3.39 (4H, overlap, H-2′ to H-5′, 3.79 (1H, dd, J = 12.0, 2.3 Hz, H-6′a), 3.68 (1H, dd, J = 12.0, 4.8 Hz, H-6′b); δ_C 95.9, 74.0, 78.5, 71.3, 78.7, 62.6]. Furthermore, the sugar unit was determined to be linked at C-28 by the HMBC correlation of the anomeric proton H-1′ with the carbonyl carbon C-28 (δ_C 178.7). A large coupling constant of the anomeric proton (J = 8.2 Hz) indicated the sugar moiety to be *β*-configuration. An acid hydrolysis assay of **26** revealed that the sugar unit is D-configuration. Thus, the structure of **26** was identified as 3*β*,19*α*,24-trihydroxy-23-norurs-12-en-28-*O*-*β*-D-glucopyranosyl ester.

Compound **27** showed an $[M+Na]^+$ ion at *m/z* 657.3611 (calcd for $C_{35}H_{54}O_{10}Na$, 657.3609) in the HRESIMS, which revealed a molecular formula of $C_{35}H_{54}O_{10}$. The 1D NMR data (Tables 3 and 5) of **27** closely resembled those of ilexpuson B, a 24-nortriterpenoid saponin from *Ilex pubescens* [26], except for an additional hydroxy group at C-6. This assignment was further supported by the fragment [−CH(5) − CH(6) − CH_2(7) −] in the ^1H–^1H COSY spectrum. The ROESY corrections of H-6 (δ_H 4.12)/H_3-23 (δ_H 1.00) and H-4 (δ_H 2.83)/H_3-25 (δ_H 1.41) indicated that H-6 is *α*-oriented. Additionally, the presence of *β*-D-glucopyranose was confirmed based on the large coupling constant of the anomeric proton and the acid hydrolysis assay. According to the above evidence, the structure of **27** was identified as 6*β*,19*α*-dihydroxy-24-norurs-12-en-3-one-28-*O*-*β*-D-glucopyranosyl ester.

Compounds **28**–**32** possessed the molecular formulas of $C_{36}H_{56}O_{11}$, $C_{36}H_{58}O_{11}$, $C_{37}H_{58}O_{12}$, $C_{37}H_{56}O_{12}$ and $C_{36}H_{56}O_{11}$, respectively, on the basis of their respective HRESIMS and ^{13}C NMR data. Detailed analyses of their 1D and 2D NMR data (Tables 3 and 5) indicated that compounds **28**–**32** were glycosides of **14**, **15**, **17**, **19**, and **34**, respectively. In the HMBC spectra, the long-range correlations observed from the anomeric proton to carbonyl carbon C-28 indicated that the sugar units are linked to C-28 in each molecule. The large coupling constants (J = 8.1 ~ 8.2 Hz) of anomeric protons revealed that the relative configurations of the glucopyranoses were all determined as *β*-oriented. Additionally, the acid hydrolysis assays of **28**–**32** indicated each sugar unit to be D-configuration. Thus, the structures of compounds **28**–**32** were identified as 6*β*,19*α*,23-trihydroxyurs-12-en-3-one-28-*O*-*β*-D-glucopyranosyl ester, 3*α*,6*β*,19*α*,23-tetrahydroxyurs-12-en-28-*O*-*β*-D-glucopyranosyl ester, 3*α*,6*β*,19*α*-trihydroxyurs-12-en-23,28-dioic acid 23-methyl ester 28-*O*-*β*-D-glucopyranosyl ester, 6*β*,19*α*-dihydroxyurs-12-en-3-one-23,28-dioic acid 23-methyl ester 28-*O*-*β*-D-glucopyranosyl ester, and 19*α*,23,24-trihydroxyurs-12-en-3-one-28-*O*-*β*-D-glucopyranosyl ester, respectively.

Compound **33** had the same molecular formula ($C_{37}H_{58}O_{12}$) as **30**, which was deduced from the HRESIMS ion at *m/z* 717.3819 $[M+Na]^+$ (calcd for $C_{37}H_{58}O_{12}Na$, 717.3820). The ^1H and ^{13}C NMR data (Tables 3 and 5) of **33** displayed high similarities with those of **30**, especially for the resonances assigned to the BCDE ring and one glucopyranose unit, while the A ring was different. The major difference was the large coupling constant (J = 11.9, 4.2 Hz) between H-3 and H_2-2 in **33**, suggesting that 3-OH is *β*-oriented. The ROESY correlation of H-3 (δ_H 3.90) with H-5 (δ_H 1.48) also supported the 3*β*-OH configuration. In addition, *β*-D-glucopyranose was determined to be present by the large coupling constant of the anomeric proton and the acid hydrolysis method. Finally, the structure of **33** was refined as 3*β*,6*β*,19*α*-trihydroxyurs-12-en-23,28-dioic acid 23-methyl ester 28-*O*-*β*-D-glucopyranosyl ester.

In addition, fourteen known compounds were isolated from *E. chinensis*. Their structures were identified as 3*β*,6*β*,19*α*,23-tetrahydroxyolean-12-en-28-oic acid (**6**) [27], oleanolic acid (**7**) [28], *β*-amyrin (**8**) [29], 19*α*,23,24-trihydroxyurs-12-en-3-one-28-oic acid (**34**) [30], clethric acid (**35**) [31], 3*β*,19*α*,23,24-tetrahydroxyurs-12-en-28-oic acid (**36**) [32], 4-*epi*-barbinervic acid (**37**) [33], rotundic acid (**38**) [34], 3*β*,6*β*,19*α*,23-tetrahydroxyurs-12-en-28-oic acid (**39**) [27], pomolic acid (**40**) [35], ursolic acid (**41**) [36], 19*α*,24-dihydroxyurs-12-en-3-one-28-oic acid (**42**) [37], taraxerol (**43**) [38], and lupeol (**44**) by comparison of their obtained NMR spectra with the reported data [39].

The hepatoprotective effects of compounds **3**, **5**, **7**–**9**, **12**–**14**, **16**–**19**, **22**, **24**, **25**, **32**, **34**–**41**, and **44** were evaluated in an acetaminophen (APAP)-induced damage model of HepG2 cells at 10 μM. The results are shown in Fig. 7, and compounds **8**, **9**, **12**–**14**, **17**, **24**, and **44** significantly improved the survival rates of HepG2 cells from 54.6% to 73.1%

Table 6
Antiviral activities of **7**, **24**, **25**, and **37**[a] against HSV-1 in Vero cells.

Compound	TC_{50} [b] (μM)	IC_{50} (μM)	SI
7	33.3	11.1	3.0
24	57.7	14.3	4.0
25	57.7	6.4	9.0
37	>100	25.9	>3.9
Acyclovir[c]	>100	0.3	>370.4

[a] Compounds **3**, **5**, **8**–**9**, **12**–**14**, **16**–**19**, **22**, **32**, **34**–**36**, **38**–**41**, and **44** were inactive at their maximal nontoxic concentration.
[b] Cytotoxic concentration required to inhibit Vero cell growth by 50%.
[c] Positive control.

Table 7
. Antiviral activity of **24**[a] against CVB3 in Vero cells.

Compound	TC_{50} [b] (μM)	IC_{50} (μM)	SI
24	57.7	23.1	2.5
Pleconaril[c]	15.41	0.0007	22014.3
Ribavirin[c]	2000	168.85	11.8

[a] Compounds **3**, **5**, **7**–**9**, **12**–**14**, **16**–**19**, **22**, **25**, **32**, **34**–**41**, and **44** were inactive at their maximal nontoxic concentration.
[b] Cytotoxic concentration required to inhibit Vero cell growth by 50%.
[c] Positive control.

– 83.5%, while the positive control bicyclol (BIC), a clinically used hepatoprotective agent, increased the cell survival rate to 74.4%. In addition, these compounds were tested for their antiviral (HSV-1 and Coxsackie B3) activities (Tables 6 and 7). Compound **25** showed potent activity against HSV-1 with an IC_{50} value of 6.4 μM, while compounds **7**, **24**, and **37** exhibited moderate activity with IC_{50} values ranging from 11.1 to 25.9 μM. Moreover, compound **24** displayed moderate activity against CVB3 with an IC_{50} value of 23.1 μM.

4. Conclusion

In summary, a phytochemical investigation of the stems and branches of *E. chinensis* led to the isolation and identification of forty-four triterpenoids, including thirty new triterpenoids (**1**–**5**, **9**–**33**) using modern column chromatography separation techniques and extensive spectroscopic methods. Structurally, sixteen triterpenoids with a gem-hydroxymethyl group at C-4 are unusual examples in natural products. In the evaluation of the hepatoprotective effects, compounds **8**, **9**, **12**–**14**, **17**, **24**, and **44** significantly improved the survival rates of APAP-treated HepG2 cells at 10 μM. In addition, compound **25** showed latent activity against HSV-1 with an IC_{50} value of 6.4 μM.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bioorg.2021.104866.

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