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TRITERPENOID ACIDS FROM *Ziziphus jujuba*

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Ziziphus jujuba Mill. is a thorny rhamnaceous plant widely distributed in northern China. Its dried fruits have been used in traditional Chinese medicine as an immune system stimulant and antitumor [1–3]. Previous phytochemical studies revealed that *Z. jujuba* contains various constituents, such as terpenoids [4, 5], saponins [6], cyclopeptide alkaloids [7], flavonoids [8, 9], and sphingolipids [10], which have been isolated from its fruit, bark, and leaf. In the present paper, we report the isolation and identification of eight triterpenoid acids from the fruit of this plant.

The fruits of *Z. jujuba* were collected from Shandong, China, in September 2006, and authenticated by Prof. Jin-ao Duan, Nanjing University of Chinese Medicine, China. A voucher specimen (No. NJUTCM-20060910) was deposited at the Herbarium in Nanjing University of Chinese Medicine, China.

The air-dried fruits of *Z. jujuba* (30 kg) were chipped and refluxed with 80% ethanol (240 L × 2, 2 h each). The alcoholic extract was concentrated to an aqueous residue under reduced pressure, and then partitioned successively with petroleum ether (PE), EtOAc, and *n*-BuOH to afford four fractions. The PE portion (142 g) was chromatographed on a silica gel column eluting with PE–EtOAc (100:1→50:50) in a stepwise system to provide 10 fractions (I–X). Fraction II (10 g) was submitted to silica gel column chromatography, eluting with PE–EtOAc (10:1) to yield compounds **1** (100 mg) and **2** (50 mg), respectively. Fraction III (2.5 g) was subjected to silica gel column chromatography with PE–EtOAc (5:1) as eluent to afford compound **3** (25 mg). Fraction V was recrystallized by MeOH to give compound **4** (750 mg), and fraction IX was recrystallized by EtOAc to yield compound **5** (20 mg).

The EtOAc portion (259 g) was divided into ten fractions (A–J) by silica gel column chromatography, eluting with the gradient PE–EtOAc (50:1→0:100). Fraction C (11 g) was further subjected to silica chromatography, eluting with PE–EtoAc (5:1) to afford compound **6** (50 mg). From fraction E (25 g), compounds **7** (105 mg) and **8** (70 mg) were isolated by silica gel column chromatography (PE–EtOAc, 1:1).

Based on the data of PMR (500 MHz), ^{13}C NMR (125 MHz), HSQC, HMBC, NOESY, and MS spectra, eight compounds were determined as zizyberenalic acid (**1**) [11], ceanothenic acid (**2**) [12], ursonic acid (**3**) [13], betulinic acid (**4**) [14], alphitolic acid (**5**) [15], oleanolic acid (**6**) [2], ceanothic acid (**7**) [16], and epiceanothic acid (**8**) [17]. All spectral data of these compounds were in agreement with the literature. Compounds **2**, **3,** and **8** were obtained from *Z. jujuba* for the first time.

The potential antitumor activities of these eight compounds were investigated *in vitro* against MGC-803, HT-29, NCI-H460, and HepG-2 tumor cell lines by the MTT method [18]. Except for compounds **3** and **5,** the other six compounds exhibited moderate inhibitory activities against the four cell lines (Table 1). Especially, the ceanothane-type compound **1** showed a greater inhibitory effect on all four cell lines than the other five compounds. The results suggested that compound **1** may be a potential tumor inhibitor or the lead compound of antitumor drugs.

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TABLE 1. The Inhibition of Compounds **1**, **2**, **4**, **6–8** Against the Proliferation of MGC-803, HT-29, NCI-H460 and HepG-2 Tumor Cell Lines

Compound	IC_{50}, μg/mL			
	MGC-803	HT-29	NCI-H460	HepG-2
1	13.92	12.67	20.67	23.32
2	48.60	>100	96.32	67.36
4	>100	40.23	>100	>100
6	35.34	>100	34.41	>100
7	95.33	>100	>100	81.27
8	>100	>100	98.96	>100

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