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Two new 18, 19-seco Triterpenoids from *Ilex asprella* (Hook. et Arn.) Champ. ex Benth

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ABSTRACT

Two novel 18,19-seco-ursane triterpenoid saponins, ilexasprellanosides *J*–K (1–2, resp.), 3-*O*-*α*-L-Rhamnopyranosyl-(1 → 2)-*β*-D-xylopyrannosyl-19-*O*-*β*-D-glucopyranosyl-16-*β*-hydroxyl-18,19-seco-13(18)-urs-ene-21, 28-lactone (**1**), 3-*O*-*β*-D-Xylopyrannosyl-19-*O*-*α*-L-rhamnopyran osyl-(1 → 2)-*α*-L-arabinopyranoside-16, 21-epoxy-18, 19-seco-13(18)-urs-ene-28-oic acid (**2**), five known compounds (**3–7**) were isolated from the leaves of *Ilex asprella* (Hook. et Arn.) Champ. ex Benth. (Gangmeiye). The chemical structures of these compounds were elucidated through UV, IR, ESI-MS, ^{1}H NMR and ^{13}C NMR analyses. In MTT and SRB assays, compounds **1–4** presented cytotoxic activities against several human cancer cell lines, namely, the HL-60 human acute promyelocytic leukaemia, Bel 7402 liver cancer, BGC-823 gastric cancer and KB human nasopharyngeal carcinoma cell lines. Compound **1** exhibited weak cytotoxic activities against the human tumour cell lines HL-60, Bel 7402 and KB with inhibition rates of 27.97%, 21.00% and 25.60%, respectively. Compound **2** exhibited weak cytotoxic activities against the human tumour cell lines HL-60, Bel 7402 and BGC-823 with inhibition rates of 19.34%, 7.50% and 4.26%. Respectively, the compounds exerted no statistically different effects on mast cell degranulation in rats. This result indicates that the compounds do not affect mast cell degranulation

1. Introduction

Ilex asprella (Hook. et Arn.) Champ. ex Benth. is a member of the plant family *Aquifoliaceae*. The genus *Ilex* comprises 600 species and is the sole genus of the family *Aquifoliaceae* [1]. Extensive studies on the members of this genus have resulted in the identification of various compounds, such as alkaloids, flavonoids and triterpenoids. “Gangmeiye”, the leaves of *Ilex asprella*, is a well-known traditional Chinese medicine and has been used individually or in combination with other natural medicine to treat laryngopharyngitis, amygdalitis, tracheitis and pertussis [2]. This crude drug is also a key component of ‘Gan-Mao-Ling Capsules’, ‘San-Dong Herbal Tea’ and ‘Wang-Lao-Ji Herbal Tea’, which is a health beverage popular among the Chinese [3]. In China, the leaves of *Ilex asprella* (Gangmeiye) have been historically used as a traditional Chinese medicine for the common cold, headache, vertigo, throat swelling and wounds [4]. However, few studies have focused on the chemical constituents of the leaves of *Ilex asprella*. To date, most compounds that have been isolated and identified from the leaves and roots of *Ilex asprella* mainly include triterpene saponins, particularly the ursuran (ursurane) type, chlorogenic acid, flavonoids, lignans, a small number of steroids and other substances [5,6]. Pharmacological evaluation had shown that the extracts of *Ilex asprella* exhibit several bioactivities, such as anti-inflammatory, antiviral and antioxidant activities [7–9].

As part of our continuous work on *Ilex asprella* [10], we performed the bioactivity-guided fractionation of butanol extract from this plant. This effort led to the isolation of two new triterpenoid saponins and ilexasprellanosides *J*–K. This paper reports the isolation and structural elucidation of two new triterpenoid saponins, 3-*O*-*α*-L-Rhamnopyranosyl-(1 → 2)-*β*-D-xylopyrann osyl 19-*O*-*β*-D-glucopyranosyl-16-*β*-hydroxyl-18,19-seco-13(18)-urs-ene-21, 28-lactone (**1**), 3-*O*– *β*-D-Xylopyrannosyl-19-*O*-*α*-L-rhamnopyranosyl-(1 → 2)-*α*-L-arabinopyranoside-16, 21-epoxy-18, 19-seco-13(18)-urs-ene-28-oic acid (**2**), five known triterpenoid saponins (**3–7**, Fig. 1). In addition, we report the results for the evaluation of the cytotoxicity of compounds **1–4** against human cancer cell lines HL-60, Bel 7402, KB and BGC-823.

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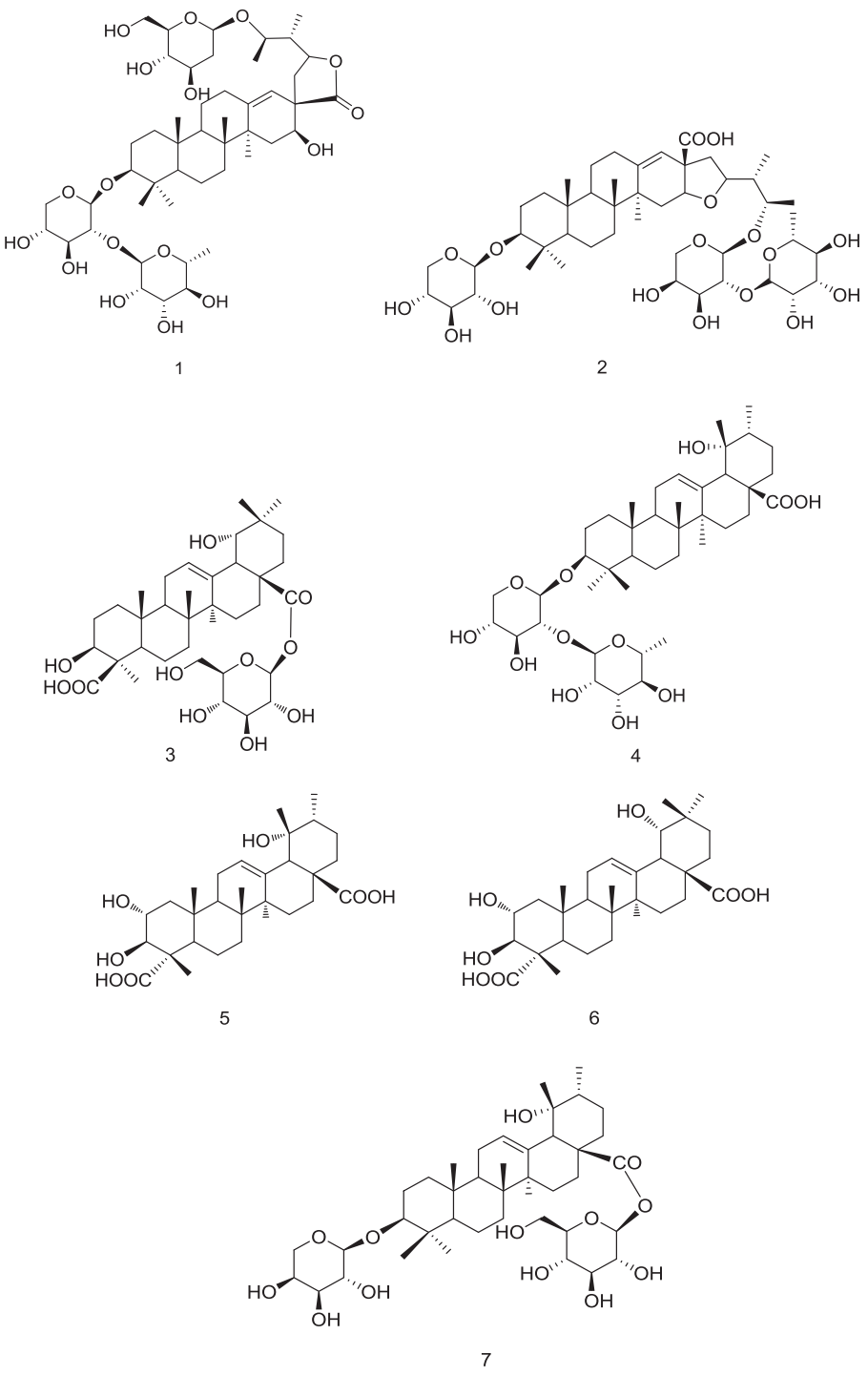

Fig. 1. Structures of compounds 1–7.

2. Experimental

2.1. General procedures

Column chromatography with silica gel H (200–300 mesh, 100–200 mesh), thin layer chromatography with silica gel GF_{254} (Qingdao Marine Chemical Plant, Qingdao, China), reverse-phase silica gel C_{18} (Merck, Germany) and Sephadex LH-20 (Pharmacia, United States) were used. All the solvents were of analytical grade and were purchased from Beijing Chemical Company Ltd. A semipreparative chromatographic column (Waters, C_{18} 300 mm × 7.8 mm, 5 μm) was used to isolate the compounds. NMR was performed with a Bruker Avance DRX-500, Varian INOVA-500 and Avance UNITY-500 Nuclear Magnetic Resonance Instrument. ESI-MS high-resolution mass spectrometry analysis was performed on a Bruker APEX-II FT-ICR-MS mass spectrometer (San Jose, CA, USA) and a Waters 2996 HPLC (Palo Alto, CA, USA) with an Alltech evaporative light-scattering detector.

2.2. Plant material

Ilex asprella roots were collected in August 2006 from GuangDong Province, People's Republic of China. The plant was identified by