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Cytotoxic effect of triterpenoids from the root bark of Hibiscus syriacus

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- 36 6439576)
- β-sitosterol (PubChem CID: 222284) 37
- $\beta\text{-sitosterol-3-O-}\beta\text{-D-glucoside}$ (PubChem 38
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Abbreviations: El, electron impact; NMR, nuclear magnetic resonance; MS, mass spectrometry; HR El MS, high-resolution electron impact-mass spectrometry; MTT, 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide; FBS, fetal bovine serum; PCR, polymerase chain reaction; HPLC, high performance liquid chromatography; HMBC, heteronuclear multiple bond correlations; NOESY, nuclear Overhauser enhancement spectroscopy; NOE, nuclear Overhauser effect; COSY, correlation spectroscopy; HSQC, heteronuclear single quantum coherence.

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ABSTRACT

In this study, 4 new triterpenoids -3β - acetoxy-olean-11-en, 28, 13 β -olide (1), 3 β - acetoxy- 17 11α , 12α -epoxy-olean-28, 13β -olide (2), 19α -epi-betulin (3), and 20, 28-epoxy- 17β , 19β -lupan- 18 3β -ol (4)—and 12 known compounds, were isolated from the root bark of *Hibiscus syriacus* L, by 19 using acetone extraction. Their structures were characterized by extensive spectroscopic analysis. 20 To investigate cytotoxicity, A549 human lung cancer cells were exposed to the extract and 21 the compounds identified from it. Significantly reduced cell viability was observed with 22 betulin-3-caffeate (12) (IC_{50} , 4.3 μ M). The results of this study indicate that betulin-3-caffeate 23 (12) identified from H. syriacus L. may warrant further investigation for potential as anticancer 24 therapies. 25

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51 **1. Introduction**

52Hibiscus syriacus L. (Malvaceae) is a widely cultivated ornamental shrub, found throughout eastern and southern 53 Asia. The root bark of H. syriacus L. has been used in 54Asian folk medicine as a fungicide, antipyretic, and anthel-55mintic in the treatment of dysentery, eczema, tinea, and 56scabies [1,2]. Several triterpenoids [3,4], cyclic peptides 57 [5,6], feruloyltyramines, isoflavonoids [7], lignans [7,8], 58naphthalenes [9], sesquiterpenoids [10], and coumarins [8] 59have previously been identified in this plant. Crude extracts 60 of H. syriacus and compounds isolated thereof have been 61 reported to inhibit monoamine oxidase [8] and neutrophil 62elastase [10]; they also inhibit lipid peroxidation [4,9] and 63 oxidation [7,8] and have cytotoxic effects [4,9,11]. 64

The acetone extract of the *H. syriacus* root bark has a strong dose-dependent antiproliferative effect on human nonsmall cell lung cancer cells and induced apoptosis in human A549 lung cancer cells by suppressing the expression of p53 and apoptosis-induced factor [11]. To investigate the potential antitumor agents present in this Chinese herb, we prepared an acetone extract of *H. syriacus* in order to isolate and characterize its constituents. This led to the isolation and characterization 72 of 4 new compounds— 3β -acetoxy-olean-11-en-28,13 β -olide 73 (1), 3β -acetoxy-11 α ,12 α -epoxy-olean-28,13 β -olide (2), 19 α - 74 *epi*-betulin (3), and 20,28-epoxy-17 β ,19 β -lupan-3 β -ol (4) 75 (Fig. 1)—and 12 known compounds. Here, we have reported 76 the isolation procedures and structural identification of com-77 pounds **1–4** and the cytotoxic activities of these and other 78 compounds present in *H. syriacus* on the human lung cancer 79 cell line A549. 80

2. Material and methods

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2.1. General experimental procedures

Proton NMR spectra were recorded on Bruker Avance 83 500 (500 MHz) and AVIII 800 (800 MHz) spectrometers. The 84 chemical shifts (ppm) were measured using tetramethylsilane 85 (TMS) as an internal standard and deuterated chloroform as 86 the solvent. Mass spectrometry was performed in the EI mode 87 on a FINNIGAN MAT 95S spectrometer. Optical rotation was 88 recorded using a JASCO DIP 370 polarimeter. Merck silica gel 60 89



Fig. 1. Chemical structures of compounds 1-4.

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