

Supporting Information for

Discovery of Wedelolactone from *Eclipta Prostrata* (L.) Linn. as a Natural PDE4 Inhibitor with Potent anti-Psoriasis Effects

Lingyu Wu^{a1}, Yingying Wu^{a1}, Shangding Yang^{a1}, Siyu Jin^{a1}, Zhongbin Cheng^a, Qing Zhang^a, Chaohui Wu^a, Yiming Hao^a, Ling Sun^a, Wenwen Liu^a, Donglei Shi^a, Jian Li^{a b c}, Yi-You Huang^{a*}, Baoli Li^{a*}, and Hai-Bin Luo^{a d*}

^aKey Laboratory of Tropical Biological Resources of Ministry of Education and Hainan Engineering Research Center for Drug Screening and Evaluation, School of Pharmaceutical Sciences, Hainan University, Haikou 570228, China

^bState Key Laboratory of Bioreactor Engineering, Shanghai Frontiers Science Center of Optogenetic Techniques for Cell Metabolism, Frontiers Science Center for Materiobiology and Dynamic Chemistry, Shanghai Key Laboratory of New Drug Design, School of Pharmacy, East China University of Science and Technology, Shanghai 200237, China

^cKey Laboratory of Xinjiang Phytomedicine Resource and Utilization, Ministry of Education, School of Pharmacy, Shihezi University, Shihezi 832003, China

^dSong Li' Academician Workstation of Hainan University (School of Pharmaceutical Sciences), Yazhou Bay, Sanya, 572000, China.

Table of Contents

S1. ¹ H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compounds 1	S2
S2. ¹ H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compounds 2	S3
S3. ¹ H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compounds 3	S4
S4. Serum Levels of AST and UREA in Mice from the Subacute Toxicity Assay.	S5

* Corresponding authors.

E-mail addresses: hyyou@hainanu.edu.cn (Y.-Y. Huang), baolili@hainanu.edu.cn (B. Li), hbluo@hainanu.edu.cn (H.-B. Luo).

¹ These authors contributed equally to this work.

S1. ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 1

^1H NMR (400 MHz, $\text{DMSO}-d_6$) δ 10.90 (s, 1H), 9.40 (s, 2H), 7.20 (d, $J = 30.8$ Hz, 2H), 6.62 (s, 1H), 6.46 (s, 1H), 3.82 (s, 3H). HRMS (ESI) m/z calcd for $\text{C}_{16}\text{H}_9\text{O}_7$ $[\text{M}-\text{H}]^+$: 313.0354, found 313.0355.

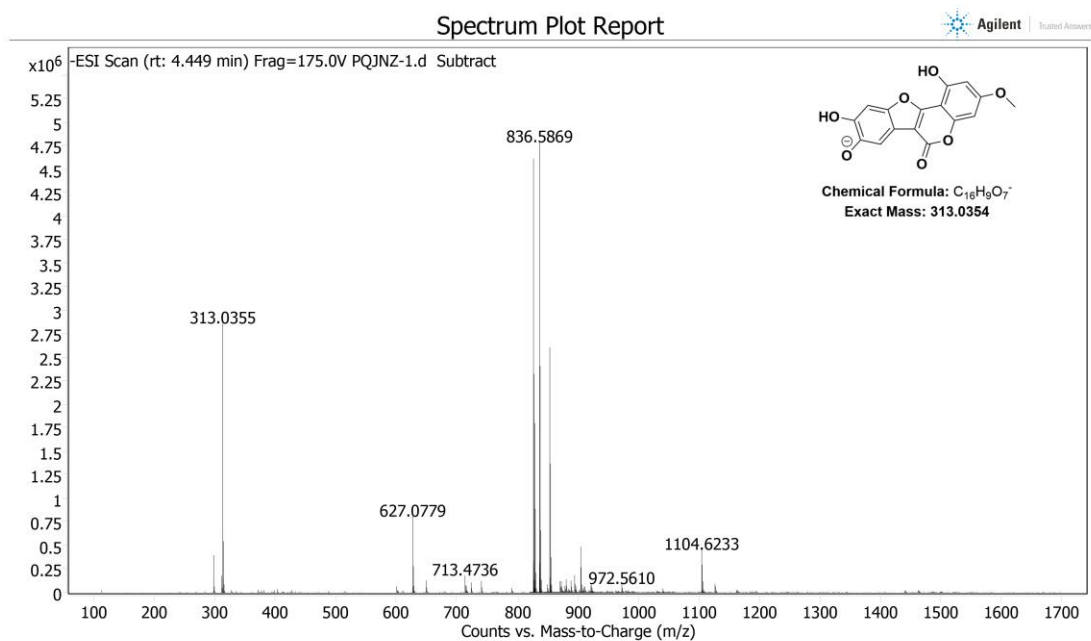
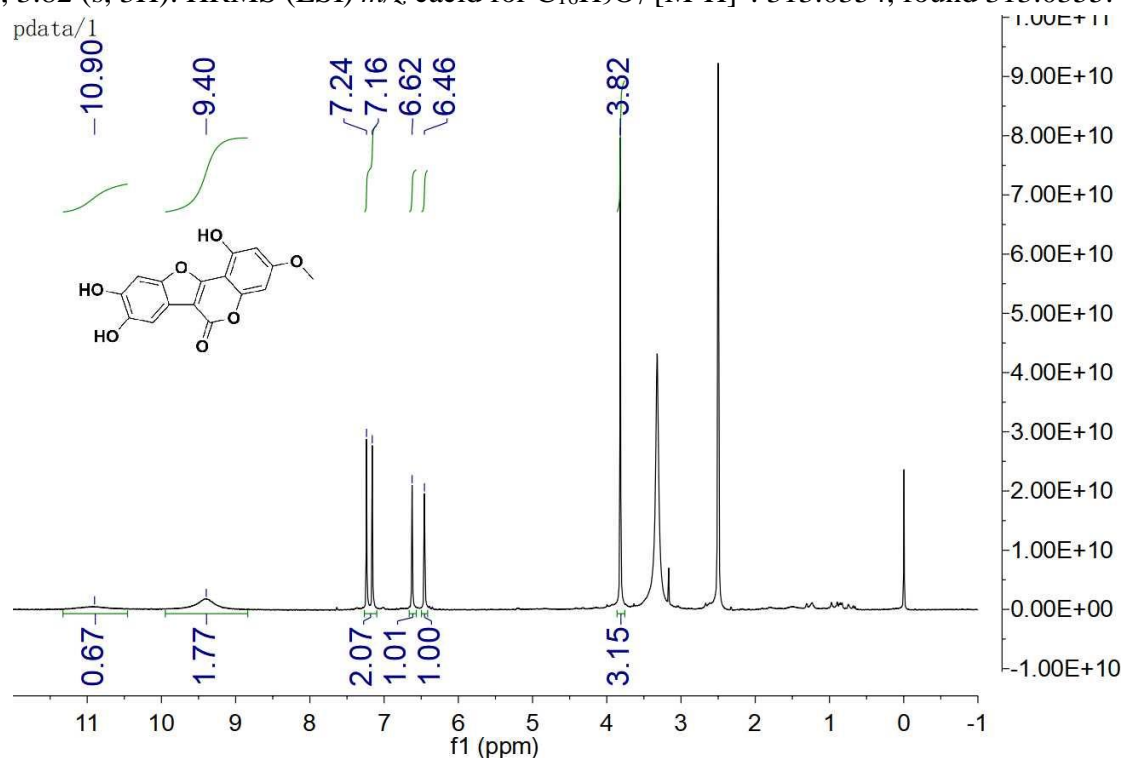


Figure S1 ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 1.

S2. ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 2

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 10.44 (s, 1H), 9.36 (s, 2H), 7.22 (s, 1H), 7.14 (s, 1H), 6.39 (d, $J = 2.0$ Hz, 1H), 6.35 (d, $J = 2.0$ Hz, 1H). HRMS (ESI) m/z calcd for $\text{C}_{15}\text{H}_7\text{O}_7$ $[\text{M-H}]^+$: 299.0197, found 299.0187.

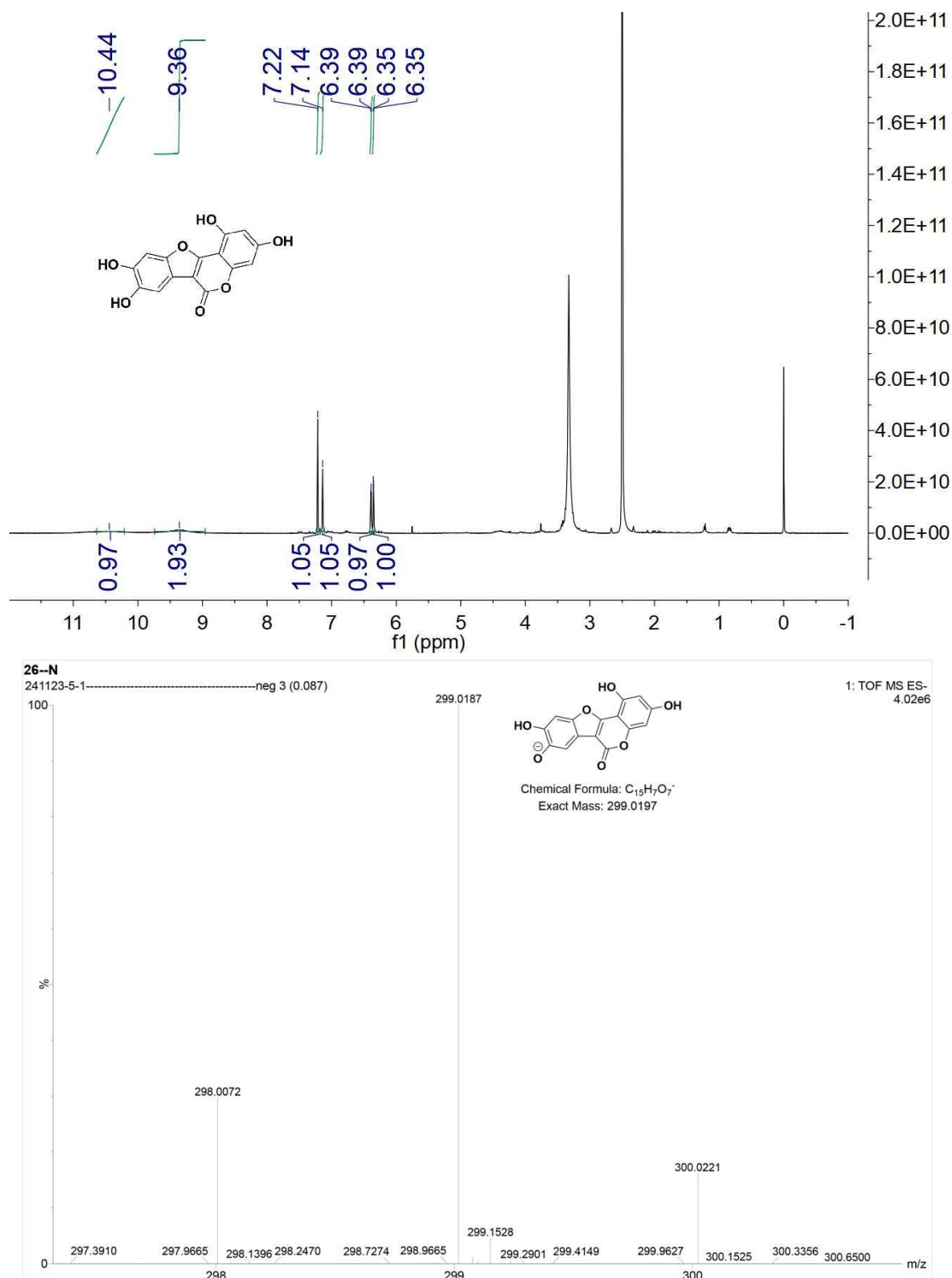


Figure S2 ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 2.

S3. ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 3

^1H NMR (400 MHz, $\text{DMSO-}d_6$) δ 7.58 (s, 1H), 7.36 (s, 1H), 6.82 (s, 1H), 6.69 (s, 1H), 4.03 (s, 3H), 3.91 (s, 3H), 3.88 (s, 6H). HRMS (ESI) m/z calcd for $\text{C}_{19}\text{H}_{15}\text{O}_7$ $[\text{M-H}]^+$: 355.0823, found 355.0827.

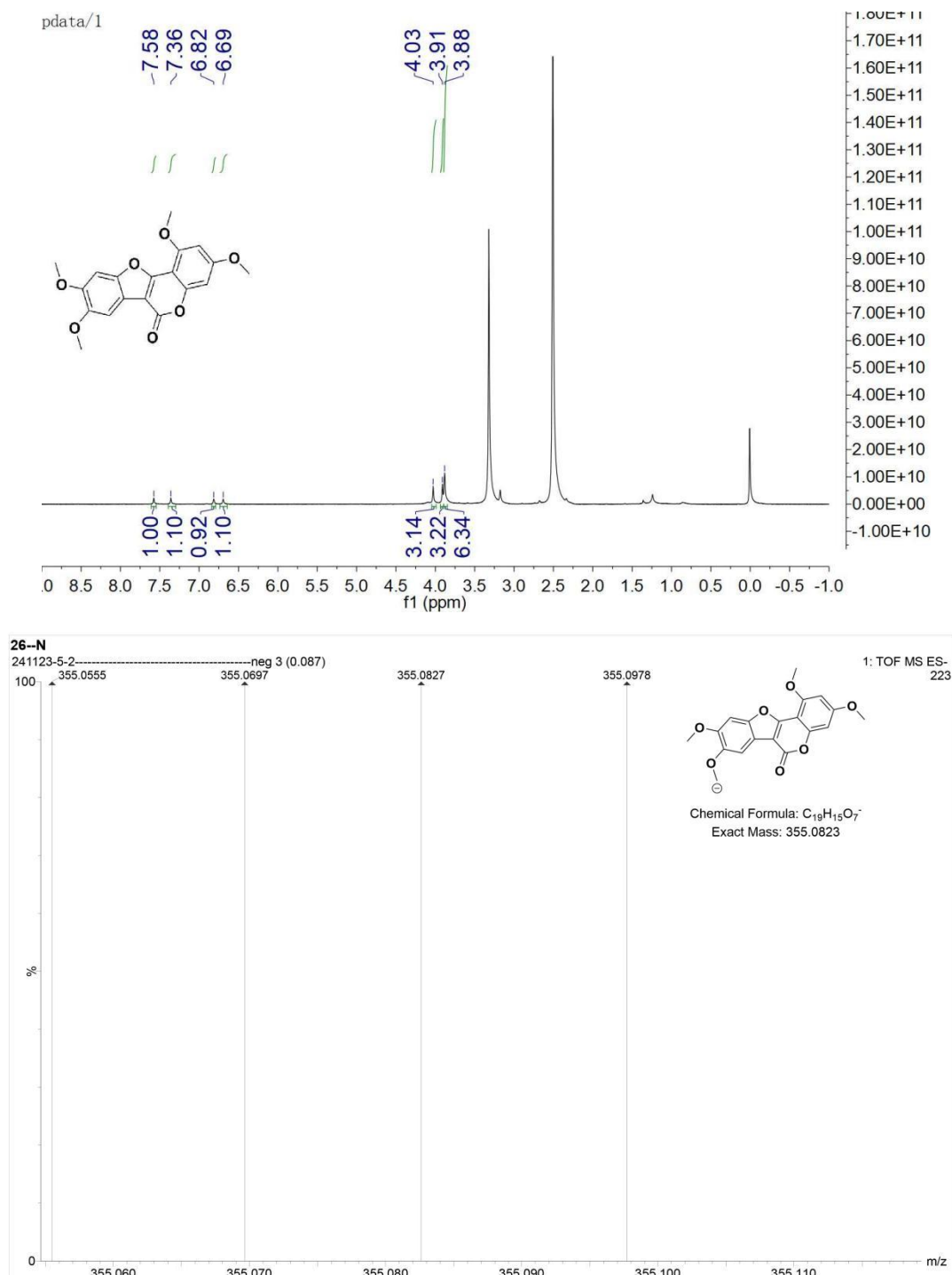


Figure S3 ^1H NMR (400 MHz) Spectrum and HRMS Chromatogram of Compound 3.

S4. Levels of AST and UREA in Mice from the Subacute Toxicity Assay.

To evaluate the systemic toxicity of WDL, the levels of aspartate aminotransferase (AST) and UREA in the serum of treated mice were measured. No significant differences were observed between the control and WDL-treated groups, indicating that topical application of 15% WDL did not induce hepatic or renal toxicity (Figure S4).

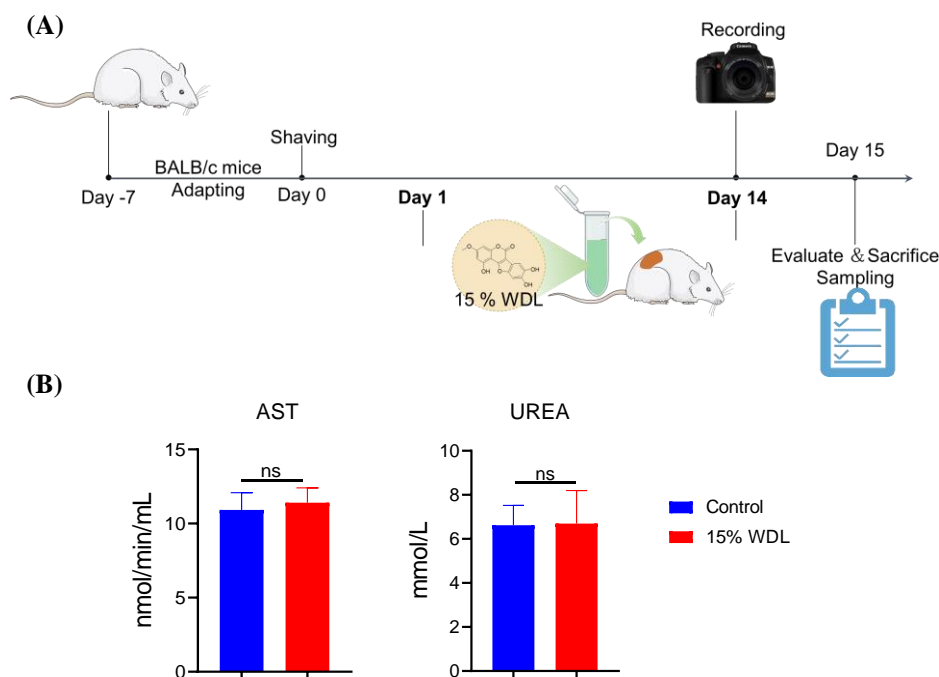


Figure S4 (A) Schematic representation of the subacute toxicity study. (B) Serum levels of AST and UREA. Data are presented as mean \pm SEM ($n = 10$ independent experiments), with no statistically significant differences between groups.