

New cyclolignan and cytotoxic activity of some lignans from the fruits
of *Koelreuteria henryi*

Chu-Hung Lin (林居宏)¹, Hsun-Shuo Chang (張訓碩)^{1,2,3},
Kuo-Hsiung Lee (李國雄)⁴, Ih-Sheng Chen (陳益昇)^{1,2,3*}

¹School of Pharmacy, College of Pharmacy, Kaohsiung Medical University

²Graduate Institute of Natural Products, College of Pharmacy, Kaohsiung Medical University

³Research Center for Natural Products and Drug Development, Kaohsiung Medical University

⁴Natural Products Research Laboratories, UNC Eshelman School of Pharmacy, University of
North Carolina, Chapel Hill, North Carolina 27599

Koelreuteria henryi Dummer (Sapindaceae) is a large evergreen tree, endemic to Taiwan. The methanolic extract of the fruits of *K. henryi* showed strong cytotoxic activities against MCF-7 (Breast cancer cells), A549 (Lung cancer), KB (Epidermoid carcinoma of the nasopharynx), KB-VIN (Vincristine resistant) and MDA-MB-231 (Triple-negative breast cancer) cancer cell lines *in vitro*. The aim of this study is the isolation of chemical constituents and their cytotoxic activities from the fruits of this plant.

The methanolic extract of the fruits of *K. henryi* was partitioned with ethyl acetate and water, and the afforded ethyl acetate layer showed potent cytotoxic activities against MCF-7, A549, KB, KB-VIN, and MDA-MB-231 cancer cell lines. Previously, we reported 13 compounds, including three new lignans: keolreuterones A-C (**1**—**3**) and one isolated from nature for the first time, keolreuterone D (**4**), along with nine known compounds from the active ethyl acetate layer of this plant. Continuing investigation of the ethyl acetate layer of this species led to the isolation of one new lignan derivative, namely keolreuterone E (**5**). The structures of these new compounds were elucidated by ID, 2D NMR, UV, IR, ESIMS, and HRESIMS analysis.

Among the isolates, keolreuterone C (**3**) and austrobailignan-1 (**6**) displayed potent cytotoxicity against the KB, KB-VIN, and MCF-7 cancer cell lines, with IC₅₀ values of 5.800, 5.484 and 9.147; 0.045, 0.007 and 0.074 μ M, respectively.