

Cucurbitane triterpenoid from *Momordica charantia* induces apoptosis and autophagy in breast cancer cells, in part, through peroxisome proliferator-activated receptor γ activation

翁靖如 Jing-Ru Weng^{1,*}, 白禮源 Li-Yuan Bai^{2,3}, 邱昌芳 Chang-Fang Chiu^{2,4}, 胡景嵐 Jing-Lan Hu¹, 邱士娟 Shih-Jiuan Chiu⁵, and 吳佳昀 Chia-Yung Wu¹

¹Department of Biological Science and Technology, China Medical University, Taichung, 40402 Taiwan, ²Division of Hematology and Oncology, Department of Internal Medicine; ³Cancer Center, China Medical University Hospital, Taichung, 40402 Taiwan, ⁴College of Medicine, China Medical University, Taichung, 40402 Taiwan, ⁵School of Pharmacy, Taipei Medical University, Taipei, 11031, Taiwan

Although the anti-tumor activity of the crude extract of wild bitter melon (*Momordica charantia* L.) has been reported, its bioactive constituents and the underlying mechanism remain undefined. Here, we report that 3 β ,7 β -dihydroxy-25-Methoxycucurbita-5,23-diene-19-al (DMC), a cucurbitane-type triterpene isolated from wild bitter melon, induced apoptotic death in breast cancer cells through peroxisome proliferator-activated receptor (PPAR) γ activation. Luciferase reporter assays indicate the ability of DMC to activate PPAR γ , and pharmacological inhibition of PPAR γ protected cells from DMC's antiproliferative effect. Western blot analysis indicates that DMC suppressed the expression of many PPAR γ -targeted signaling effectors, including cyclin D1, CDK6, Bcl-2, XIAP, cyclooxygenase-2, and NF- κ B. Moreover, DMC inhibited mTOR-p70S6K signaling through Akt downregulation and AMPK activation. Together, the ability of DMC to modulate multiple PPAR γ -targeted signaling pathways provides a mechanistic basis to account for the antitumor activity of wild bitter melon.

Keywords: *Momordica charantia*, PPAR γ , triterpene, autophagy, apoptosis