Discovery of New Filicinic Acid-based Meroterpenoids from *Hypericum japonicum*

Linzhen Hu¹, Yonghui Zhang², Yong Chen¹, Zhenzhen Wang², Rongrong Wu¹, Shuying Tian¹, Yongbo Xue²

¹*School of Life Science, Hubei University, China,* ²*School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, China*

Natural products have been utilized sophisticatedly as traditional medicines for millennia¹. In recent decades, an increasing discovery of natural products provided prolific sources of new chemical entities served as therapeutic drugs or lead compounds². The genus *Hypericum* (Guttiferae) has triggered wide investigations of the scientific community³, owing to phloroglucinol derivatives possessing diversiform structures, and appealing bioactivities such as antidepressant⁴, antibacterial⁵, anticancer⁶, and antiviral⁷ properties. In our continuous course of systematic study on the genus *Hypericum*^{8,9}, one pair of enantiomers ($\pm$)-hyperjaponols H (**1a/1b**), two pairs of epimers hyperjaponols J-M (**3-6**), as well as hyperjaponol I (**2**), six new hetero-Diels-Alder adducts of polymethylated phloroglucinol and sesquiterpene motifs giving shape to filicinic acid⁻ based meroterpenoids, along with 6/6/10 ring skeletons (Figure 1), were isolated from the entire herbs of *Hypericum japonicum*. Their structures with absolute configurations were characterized on the extensive analyses of NMR spectra, ECD calculations, and the experimental ECD data. The aforementioned metabolites exhibited moderate inhibitory effects on lytic replication of Epstein-Barr virus (EBV).

References

1. Clardy, J.; Walsh, C., *Nature* **2004**, *432*, 829-837.
2. Li, J. W. H.; Vederas, J. C., *Science* **2009**, *325*, 161-166.
3. Ciochina, R.; Grossman, R. B., *Chem. Rev.* **2006**, *106*, 3963-3986.
4. Richard, J. A. *Eur. J. Org. Chem.* **2014**, *2014*, 273-299.
5. Oya, A.; Tanaka, N.; Kusama, T.; Kim, S. Y.; Hayashi, S.; Kojima, M.; Hishida, A.; Kawahara, N.; Sakai, K.; Gono, T.; Kobayashi, J., *J. Nat. Prod.* **2015**, *78*, 258-264.
6. Zhang, S.; Yin, J.; Li, X.; Zhang, J.; Yue, R.; Diao, Y.; Li, H.; Wang, H.; Shan, L.; Zhang, W., *BMC Cancer* **2014**, *14*, 689-699.
7. Singh, I. P.; Bharate, S. B., *Nat. Prod. Rep.* **2006**, *23*, 558-591.
8. Hu, L.; Zhang, Y.; Zhu, H.; Liu, J.; Li, H.; Li, X. N.; Sun, W.; Zeng, J.; Xue, Y.; Zhang, Y., *Org. Lett.* **2016**, *18*, 2272-2275.
9. Zhu, H.; Chen, C.; Yang, J.; Li, X. N.; Liu, J.; Sun, B.; Huang, S. X.; Li, D.; Yao, G.; Luo, Z.; Li, Y.; Zhang, J.; Xue, Y.; Zhang, Y., *Org. Lett.* **2014**, *16*, 6322-6325.