Chemical investigation of *Hyptis suaveolens* guided by xanthine oxidase inhibitory activity (I)

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Gout is a kind of metabolic diseases, caused by accumulation of uric acid crystals in the joints. Xanthine oxidase plays an important role in the production of uric acid. Thus, its inhibitor, allopurinol, is often used clinically for long-term gout therapy. This drug, however, might cause Stevens-Johnson syndrome. Therefore, the search for alternative drugs for treating gout is still in need. Our recent studies indicated that some constituents from *Hyptis rhomboides* are potent xanthine oxidase inhibitors.¹ Thus the aim of this research was to investigate whether the chemical constituents of the related native species, *H. suaveolens*, possess similar activity.

The ethanol extract of *H. suaveolens* stem was divided into fractions soluble in CH₂Cl₂, EtOAc, *n*-BuOH, and water via liquid-liquid partitioning. Further separation was conducted on the EtOAc-soluble fraction, which possesses the best anti-xanthine oxidase activity among these fractions. This effort led to the isolation of 14 compounds by combination of Sephadex LH-20, silica gel and reverse-phase columns, and semi-preparative RP-HPLC. Of these, two are new, i.e., 9'-methyl melitrate A and dimethyl melitrate A. The 12 known ones were identified as rosmarinic acid, caffeic acid, methyl melitrate A, melitric acid A, netpetoidin B, danshensu, methyl rosmarinate, oresbiusin A, ursolic acid, sagecoumarin, netpetoidin A, kaempferol-3-O-(4-O-acetyl- α -L-rhamnopyranoside). Their structures were elucidated by MS data and NMR (1D and 2D) spectroscopic analysis.

Through xanthine oxidase bioassay, netpetoidin A was found to possess the best inhibitory activity with the IC₅₀ values of 11.7 μ M (*cf.* allopurinol 5.3 μ M).¹

Reference

1. Tsai, S.-F., Lee, S.-S. Neolignans as xanthine oxidase inhibitors from Hyptis rhomboides, *Phytochemistry* **2014**, *101*, 121–127.