A151 Neuroprotective phenylethanoid glycosides of *Callicarpa dichotoma*

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During our search for potential natural products against glutamate-induced neurotoxicity in primary cultures of rat cortical cells, we have discovered that the *n*-BuOH fraction of *Callicarpa dichotoma* Raeuschel (Verbenaceae) showed a significant protective activity. We isolated a new and nine known neuroprotective phenylethanoid glycosides against glutamate-induced neurotoxicity in the primary cultures of rat cortical cells from the *n*-BuOH fraction of *C. dichotoma* leaves and stems using bioactive-guided fractionation techniques. The chemical structures of nine known compounds were identified as forsythoside B, acteoside, 2'-acetylacteoside, poliumoside, brandioside, echinacoside, isoacteoside, cistanoside H, and *E*-tubuloside E, respectively by comparison of their spectral data with those reported in the literature (1). The spectroscopic data of the new compound was similar except for chemical shift of two olefinic protons of coumaric acid in *E*-tubuloside E. Thus, the chemical structure of new compound was identified as *Z*-tubuloside E. All phenylethanoid glycosides protected cortical cells from neurotoxicity induced by excessive glutamate to a significant degree at the concentrations ranging from 0.1 to 10 μM.

Reference: 1. Jimenez, et al. (1994) Nat. Prod. Rep., 11, 591-606.

A152 Monoamine oxidase (MAO) and inducible nitric oxide synthase (iNOS) inhibitory activity of *Salvia miltiorrhiza*.

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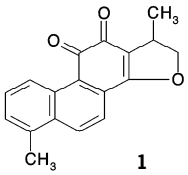
Danshen, the dried roots of *Salvia miltiorrhiza* Bunge (Lamiaceae), is a Chinese drug with clinical importance in the treatment of coronary heart diseases and other ailments. The drug has been subject to numerous phytochemical and pharmacological studies (1). In the course of our search for substances with activity on CNS-related targets, a lipophilic extract of Danshen showed a distinct activity in a kinetic MAO assay. LC-DAD-MS combined with HPLC-based bioactivity profiling revealed MAO inhibition in 5 out of 13 fractions of the extract. One of the active constituents was identified as dihydrotanshinone I (**1**). The compound inhibited MAO A (IC_{50} 36 μM) but had no effect on MAO B. The structurally related tanshinone II A (**2**) and cryptotanshinone (**3**), in contrast, were inactive. The abietane diterpene quinones represent a new class of MAO inhibitors with distinct isoenzyme selectivity.



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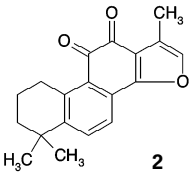

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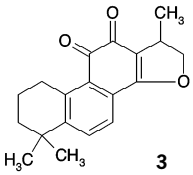

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The same extract was assayed for inhibition of inducible nitric oxide synthase in RAW-246.7 murine macrophages. HPLC-based activity profiling combined with LC-DAD-MS analysis revealed several peaks with marked inhibitory activity. Purification of active fractions by means of preparative LC, and structural analysis by LC-MS and NMR afforded known abietane diterpenoids.

References: 1. Tang, W. et al. (1992) Chinese Drugs of Plant Origin, Springer Berlin: 891-902.