Clerodane Diterpenoid with Anti-neuroinflammatory Activity in Vitro from Traditional Chinese Medicine Jin Guo Lan

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Abstract

The tuberous root of \textit{Tinospora sagittata} (Oliv.) Gagnep is the original plant of Traditional Chinese Medicine \textit{Tinosporae Radix} ("Jin Guo Lan"), which usually be used to treat pharyngeal arthralgia, carbuncle furuncle, bacillary dysentery, abdominal pain and inflammation. Twenty-six clerodane diterpenoids were isolated from \textit{T. sagittata}, including 8 new clerodane diterpenoids (tinotanoid A-H: 1-8), and 18 known ones (9-26). The absolute configurations of compounds 1, 2, 5, 8, 13, 17 and 20 were determined by single-crystal X-ray diffraction. Compound 1 is the first example of clerodane diterpenoid with a γ lactone ring which were constructed between C-11 and C-17. Compound 2 and 17 is a pair of epimer. Compounds 2, 12 and 17 showed excellent inhibitory activity on NO production with IC\textsubscript{50} values of 9.56±0.69, 9.11±0.53 and 11.12±0.70 μM, respectively, and the activities were significantly stronger than the positive control Minocycline (Mino) (IC\textsubscript{50} value was 23.57±0.92 μM). Moreover, compounds 2, 12 and 17 dramatically reduced the expressions of iNOS and COX-2 up-regulated by LPS treatment. Compounds 2 and 12 can significantly inhibit the levels of pro-inflammatory cytokines TNF-α, IL-1β and IL-6 that are increased by LPS stimulation.

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