Selective inducible nitric oxide synthase suppression by new bracteanolides from Murdannia bracteata.

Wang GJ, Chen SM, Chen WC, Chang YM, Lee TH.

Abstract

Murdannia bracteata has been used as a Taiwanese folk medicine for its anti-inflammatory properties. However, neither its active ingredients nor its anti-inflammatory actions are well defined. Nitric oxide (NO), overproduced by activated macrophages via inducible NO synthase (iNOS), is suggested to be a significant pathogenic factor in various inflammatory tissue injuries. In order to elucidate the anti-inflammatory actions of M. bracteata, the present study was designed to isolate its active constituents and examine its effects on iNOS in lipopolysaccharide (LPS)-activated macrophages. Two new hydroxybutenolides, bracteanolide A (1) and B (2), together with (+)-(R)-p-hydroxyphenyllactic acid (3) and isovitexin (4), were isolated and identified from M. bracteata by the NO production assay. All of the compounds inhibited NO production except 3. Their rank order of potency was 1>2>4. Among these, 1 significantly inhibited NO production, which is associated with its suppression on iNOS induction in a concentration-dependent manner, with an IC(50) of 33.27+/-0.86 microM. Nevertheless, isometric tension recordings in isolated endothelium-intact rat aorta revealed that 1-4 did not affect acetylcholine-induced endothelial NO-dependent relaxation, an index of endothelial NOS (eNOS) activity. The selective inhibition on iNOS provides a possible explanation for the anti-inflammatory use of M. bracteata.