Inducible nitric oxide synthase inhibitors of Chinese herbs II. naturally occurring furanocoumarins

王靜瓊
Wang CC;Lai JE;Chen LG;Yen KY;Yang LL

Abstract

Inducible nitric oxide synthase (iNOS)-dependent production of nitric oxide (NO) plays an important role in inflammation. The effects of various naturally occurring furanocoumarins on NO production in lipopolysaccharide (LPS)-activated RAW 264.7 macrophage cells were evaluated in vitro. The results showed that angelicin, pimpinellin, sphondin, byakangelicol, oxypeucedanin, oxypeucedanin hydrate, xanthotoxin, and cnidilin are potential NO production inhibitors, and their IC50 values for inhibition of nitrite production were 19.5, 15.6, 9.8, 16.9, 16.8, 15.8, 16.6, and 17.7 μg/mL, respectively. Distinct structure-activity relationships were also revealed for the NO production inhibitory activities of these furanocoumarins. Activities of the angelicin type such as pimpinellin and sphondin were more potent than those of the psoralen type. Presence of a methoxy at the C6 position in the angelicin type seemed to be essential to augment the activity. Western blot analysis demonstrated that only sphondin dose-dependently inhibited the expression of the iNOS protein at 2.5-20 μg/mL. However, iNOS enzyme activity was stimulated with LPS for 12 h and sphondin was administered (20 μg/mL) for 24 h, which did not reasonably inhibit iNOS enzyme activity. L-NAME (100 μM), a known specific inhibitor of iNOS, was employed as a positive control with the same protocol and showed more than 50% inhibition activity. The results demonstrate that the NO production inhibitory activity of sphondin is due to the effect of iNOS expression, but not by direct inhibition of iNOS enzyme activity. Thus, sphondin may act as a potent inhibitor of NO production under tissue-damaging inflammatory conditions.