P46 A Sesquiterpene, Dehydrocostus Lactone, Inhibits the Expression of inducible Nitric Oxide Synthase and TNFα in LPS-Activated Macrophages

H.J. Lee, N.Y. Kim, D.H. Sohn,[1] S.H. Lee,[2] J.-H. Ryu

College of Pharmacy, Sookmyung Women's University, Seoul 140-742, [1]College of Pharmacy and Medicinal Resources Research Center, Wonkwang University, [2]Department of Physiology, Ajou University, Suwon 110-460, Korea

An enhanced formation of nitric oxide (NO) is an important mediator of hypotention, peripheral vasodilation and vascular hyporeactivity to vasoconstrictor agents in endotoxaemia. And tumor necrosis factor (TNFα), as a primary mediator of circulatory shock has been known to induce inducible nitric oxide synthase (i-NOS), leading to excessive production of NO. We isolated two sesquiterpene lactone compounds from *Saussurea lappa* and their structures were elucidated as dehydrocostus lactone and costunolide. These compounds inhibit the production of both NO and TNFα by LPS (1 μg/ml)-activated Raw 264.7 cells. NO was measured spectrophotometrically as nitrite by the Griess reagent and TNFα by ELISA. Dehydrocostus lactone (IC_{50} : 3.0 μM) and costunolide (IC_{50} : 4.5 μM) inhibited the production of NO in LPS-activated Raw 264.7 cells by suppressing inducible nitric oxide synthase enzyme expression. These compounds also decreased the TNFα levels in LPS-activated system *in vitro* and *in vivo*.