

The inhibitory effects of cyclodepsipeptides from the entomopathogenic fungus *Beauveria bassiana* on myofibroblast differentiation in A549 alveolar epithelial cells.

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Abstract

Pulmonary fibrosis (PF) is a chronic and fatal lung disease with few treatment options. Although the pathogenesis of PF is not clear, a chronic inflammatory response to continuous damage is considered the cause of pulmonary fibrosis. PF is characterized by excessive accumulation of extracellular matrix (ECM), therefore, inhibition of myofibroblast differentiation is a good therapeutic target for PF. As part of our continuing endeavor to explore biologically active metabolites from insect-associated microbes, we found that the MeOH extract of the culture broth from the entomopathogenic fungus *Beauveria bassiana* inhibited collagen induction and E-

cadherin down-regulation. In order to identify active compounds, we carried out chemical analysis of the MeOH extract with the assistance of LC/MS-guided isolation approach, which led to the successful identification of four cyclodepsipeptides 1–4. Among the isolates, compound 2 showed inhibitory effects on myofibroblast differentiation induced by TGF- β 1. Compound 2 inhibited induction of α -SMA and N-cadherin, which are myofibroblast markers, and blocked the accumulation of ECM proteins such as collagen and fibronectin. Overall these findings demonstrate that compound 2 can be used to attenuate pulmonary fibrosis by targeting myofibroblast differentiation.

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