Molecular Mechanism of the Inhibitory Effect of Trilinolein on Endothelin-1-Induced Hypertrophy of Cultured Neonatal Rat Cardiomyocytes

陳保羅;陳識中

Chen SC;Cheng JJ;Hsieh MH;Chu YL;Kao PF;Cheng TH;Chan P

摘要

Abstract

Trilinolein, isolated from the traditional Chinese herb Sanchi (Panax notoginseng [P. pseudoginseng var. notoginseng]), has been shown to have myocardial protective effects via its antioxidant ability. However, the cellular and molecular mechanisms of the protective effect of trilinolein in the heart remain to be elucidated. Oxidative mechanisms have been implicated in neonatal cardiomyocyte hypertrophy. We therefore have examined whether trilinolein attenuates reactive oxygen species (ROS) production and thus endothelin-1 (ET-1)-induced hypertrophy of cardiomyocytes. Cultured neonatal rat cardiomyocytes were stimulated with ET-1 (10 nM), and [3H]leucine incorporation and β-myosin heavy chain (β-MyHC) promoter activity were examined. Trilinolein (1 and 10 μM) inhibited the ET-1-induced increase of [3H]-leucine incorporation in a concentration-dependent manner. Trilinolein (1 and 10 μM) also inhibited ET-1-induced β-MyHC promoter activity in cardiomyocytes. We further examined the effects of trilinolein on ET-1-induced intracellular ROS generation by measuring a redox-sensitive fluorescent dye, 2´,7´-dichlorofluorescin diacetate, fluorescence intensity. Trilinolein (1 and 10 μM) inhibited ET-1-increased intracellular ROS levels in a concentration-dependent manner. This increase of ROS by ET-1 (10 nM) or H2O2 (25 μM) was significantly inhibited by trilinolein (10 μM) and N-acetylcysteine (10 mM). Moreover, ET-1- or H2O2-induced β-MyHC promoter activity and protein synthesis were also inhibited by trilinolein (10 μM). These data indicate that trilinolein inhibits ET-1-induced β-MyHC promoter activity, and subsequent hypertrophy via its antioxidant ability in cardiomyocytes.

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