Activation of Sirt1 by Silybinin Inhibits TNF-a Induced Inflammation in Fibroblasts

Abstract

Inflammation is one of main mechanisms of autoimmune disorders and a common feature of most diseases. Appropriate suppression of inflammation is a key resolution to treat the diseases. Silybinin has been shown to play a role in regulation of inflammation. Silybinin, has anti-inflammation property. However, the detailed mechanism is not fully understood. In this study, we investigated the anti-inflammation role of Silybinin in Bovine Fibroblast-like synoviocyte (BFLS). Upregulation of matrix metalloproteinases 9 (MMP-9), interleukin-1beta (IL-1b), IL-6 and inducible nitric oxide synthase (iNOS) were induced by tumor necrosis factor alpha (TNF-a) in BFLS and Silybinin suppressed overexpression of these pro-inflammatory molecules in a dose-dependent manner. Knockdown of Sirt1 by RNA interference caused 3T3 BFLS susceptible to TNF-a stimulation and diminished anti-inflammatory effect of resveratrol. We also explored potential anti-inflammatory mechanisms of resveratrol. Resveratrol reduced NF-kB subunit RelA/p65 acetylation, which is notably Sirt1 dependent. Silybinin also attenuated phosphorylation of mammalian target of rapamycin (mTOR) and S6 ribosomal protein (S6RP) while ameliorating inflammation. Our data demonstrate that Silybinin inhibits TNF-a-induced inflammation via Sirt1. It suggests that Sirt1 is an efficient target for regulation of inflammation. This study provides insight on treatment of inflammation-related diseases.

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activator, has anti-inflammation property. However, the detailedmechanism is not fully understood. In this study, we investigated the anti-inflammation role of Sirt1 in NIH/3T3 fibroblastcell line. Upregulation of matrix metalloproteinases 9 (MMP-9), interleukin-1beta (IL-1b), IL-6 and inducible nitric oxidesynthase (iNOS) were induced by tumor necrosis factor alpha (TNF-a) in 3T3 cells and resveratrol suppressed overexpressionof these pro-inflammatory molecules in a dose-dependent manner. Knockdown of Sirt1 by RNA interference caused 3T3cells susceptible to TNF-astimulation and diminished anti-inflammatory effect of resveratrol. We also explored potentialanti-inflammatory mechanisms of resveratrol. Resveratrol reduced NF-kB subunit RelA/p65 acetylation, which is notablySirt1 dependent. Resveratrol also attenuated phosphorylation of mammalian target of rapamycin (mTOR) and S6 ribosomalprotein (S6RP) while ameliorating inflammation. Our data demonstrate that resveratrol inhibits TNF-a-induced inflammationvia Sirt1. It suggests that Sirt1 is an efficient target for regulation of inflammation. This study provides insight on treatmentof inflammation-related diseases.