Nobiletin, a Citrus Flavonoid, Prevents Systolic Functional Deterioration After Myocardial Infarction in Rats

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Objective

Abstract

Background: Nuclear acetylation of cardiomyocytes is being recognized as a critical event during maladaptive hypertrophy that leads to decompensated heart failure (HF). The acetylation is controlled by histone deacetylases and an intrinsic histone acetyltransferase (HAT), p300. We have reported that curcumin, a p300 HAT inhibitor, prevents systolic functional deterioration in two independent models of HF in adult rats, providing further evidence for the critical role of p300 HAT in HF. A natural compound, nobiletin, one of citrus flavonoids, has been reported to interfere with a coactivator, p300, and to suppress the transcriptional activation by GATA-4. In addition, nobiletin is able to activate PPARγ-dependent signals, which inhibit p300/GATA4-dependent transcriptional pathways. The goal of this study was to determine whether nobiletin is applicable to heart failure treatment in vivo.

Materials & Methods

Hypothesis

Purpose 1
To determine whether Nobiletin, a natural compound derived Citrus unshiu, prevents cardiac hypertrophy in primary cultured cardiomyocyte

Purpose 2
To examine the effect of Nobiletin on development of heart failure after myocardial infarction (MI) in rats

Results

Nobiletin improved the LV systolic function

Nobiletin suppressed PE-induced hypotrophy in cardiomyocytes

Nobiletin suppressed PE-induced ET-1/ANF promoter activity in cultured cardiomyocytes

Nobiletin significantly suppressed MI-induced increases in ET-1 and ANF levels in rat's hearts

Disclosures of Interest: Non

Background

Nobiletin is a candidate for heart failure treatment

We screened a natural product library

- Citrus acriflavus (Citrus x aurantium)
- Zizyphus jujuba (Zizyphus jujuba)
- ACA (Galangale) etc.

Cardiomyocyte

Hypertrophy

Nobiletin

- Polymethoxyflavonoids (PMFs)

- Function
  - Anti-tumor effects
  - Anti-inflammatory effects
  - Neuroprotective effects

1. Immunohistochemistry

2. Reporter assay

3. Myocardial infarction (MI) rats

Parameters at 1 week after operation in rats

Parameters at 7 weeks after operation in rats

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