

# Antiproliferative effect of isosteviol on angiotensin-II-treated rat aortic smooth muscle cells

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摘要

## Abstract

Isosteviol is a derivative of stevioside, a constituent of *Stevia rebaudiana*, which is commonly used as a noncaloric sugar substitute in Japan and Brazil. The aims of this study were to examine whether isosteviol alters angiotensin-II-induced cell proliferation in rat aortic smooth muscle cells. Cultured rat aortic smooth muscle cells were preincubated with isosteviol, then stimulated with angiotensin II, after which [<sup>3</sup>H]thymidine incorporation and endothelin-1 secretion were examined. Isosteviol (1-100 μmol/l) inhibits angiotensin-II-induced DNA synthesis and endothelin-1 secretion. Measurements of 2'7'-dichlorofluorescein diacetate, a redox-sensitive fluorescent dye, showed an isosteviol-mediated inhibition of intracellular reactive oxygen species generated by the effects of angiotensin II. The inductive properties of angiotensin II on extracellular signal-regulated kinase (ERK) phosphorylation were found reversed with isosteviol and antioxidants such as N-acetylcysteine. In summary, we speculate that isosteviol inhibits angiotensin-II-induced cell proliferation and endothelin-1 secretion via attenuation of reactive oxygen species generation. Thus, this study provides important insights that may contribute to the effects of isosteviol on the cardiovascular system