Isosteviol as potassium channel opener to lower intracellulr calcium concentrations in cultured aortic smooth muscle cells

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摘要

Abstract

Isosteviol is a derivative of stevioside, a constituent of Stevia rebaudiana, and is commonly used as a non-caloric sugar substitute in Japan and Brazil. The present study attempted to elucidate the role of potassium (K (+)) channels in the action of isosteviol on intracellular calcium concentrations ([Ca (2+)]i) in cultured vascular smooth muscle (A7r5) cells using the Ca (2+)-sensitive dye Fura-2 as an indicator. The increase of [Ca (2+)]i in A7r5 cells produced by vasopressin (1 micromol/L) or phenylephrine (1 micromol/L) was attenuated by isosteviol from 0.01 micromol/L to 10 micromol/L. The attenuation by isosteviol of the vasopressin- and phenylephrine-induced increase in [Ca (2+)]i was inhibited by glibenclamide, apamin and 4-aminopyridine but not by charybdotoxin. Furthermore, the inhibitory action of isosteviol on [Ca (2+)]i was blocked when A7r5 cells co-treated with glibenclamide and apamin in conjunction with 4-aminopyridine were present. Therefore, not only did the ATP-sensitive potassium (K (ATP)) channel affect the action of isosteviol on [Ca (2+)]i modulation in A7r5 cells, but also those on the small conductance calcium-activated potassium (SK (Ca)) channels and voltage-gated (Kv) channels. However, the blockers of large-conductance Ca (2+)-activated potassium channels failed to modify the inhibitory action of isosteviol on [Ca (2+)]i. The obtained results indicated that a decrease of [Ca (2+)]i in A7r5 cells by isosteviol is mainly mediated by the selective opening of K (ATP) channel or/and SK (Ca) channel. Alteration in the Kv channel also plays a critical role in the inhibitory action of isosteviol