QUINAZOLINE PD153035 INCREASES K^+ PERMEABILITY IN HEART MITOCHONDRIA: IMPLICATIONS FOR ITS CARDIOPROTECTIVE EFFECT

Renata A. Cavalheiro, Natalia M. Inada, Silvana Ap. Rocco, Rodrigo M. Marin, Kleber G. Franchini, Roger F. Castilho and Anibal E. Vercesi

Departamento de Patologia Clínica, Faculdade de Ciências Médicas,
Universidade Estadual de Campinas,
Campinas, SP, Brasil

Quinazoline PD153035 administration (≥1 nM) to isolated adult rat heart reduces tissue injury after transitory ischemia. PD153035, a potent inhibitor of tyrosine kinase, acts by competing with ATP. This study investigated whether the cardioprotective effects of PD153035 could be related to an increase in mitochondrial K^+ permeability, a mechanism related to cardioprotection. Isolated heart mitochondria from rats treated with PD153035 (32 mg/kg) presented an increased swelling in hyposmotic solutions containing K^+ salts as compared with the control. This effect was not observed in the presence of Li^+ or Na^+. Similar results were observed in isolated rat heart mitochondria incubated *in vitro* with 10 nM PD153035. PD153035-induced increase in mitochondrial volume, both *in vivo* and *in vitro,* was inhibited by ATP and 5-hydroxydecanoate, mitochondrial ATP-sensitive potassium channel (mitoK_{ATP}) antagonists. In addition, cardiac muscle fibers from PD153035-treated rats presented a slight increase in basal respiration supporting the higher mitochondrial K^+ permeability. PD153035-stimulated K^+ transport in heart mitochondria was associated with lower membrane potential supported by ATP hydrolysis under nonrespiring conditions. These results suggest that PD153035 increases K^+ permeability in heart mitochondria that can be related to the mitoK_{ATP} activation, implicating its cardioprotective role.
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