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Short communication

Cytoprotective action of the potassium channel opener NS1619 under conditions of disrupted calcium homeostasis

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Abstract:
Cytoprotective properties of potassium channel openers (KCOs) have been demonstrated in several models of cell injury, mainly in ischemia-reperfusion-induced damage of cardiac muscle. The mechanism responsible for the observed cytoprotection and the relative contribution of plasma membrane or inner mitochondrial membrane potassium channels regarding the beneficial effects exerted by KCOs remain unclear.
Our work demonstrates the cytoprotective properties of NS1619, an opener of large-conductance calcium-activated potassium channels (BK_{Ca} channels), using C2C12 myoblasts injured by calcium ionophore A23187 treatment. Application of two BK_{Ca} channel inhibitors, paxilline and iberiotoxin, abolished this cytoprotective effect. At concentrations of 10–100 μM, NS1619 increased the respiration rate and decreased mitochondrial membrane potential ($\Delta\psi$) in C2C12 cells in a dose-dependent manner. At a concentration of 0.2 μM, paxilline, which effectively abolished the protective effect of NS1619, failed to counteract the opener-induced mitochondrial depolarization and increase in cellular respiration. This result indicates that the NS1619-mediated increase in the survival rate of A23187-treated C2C12 cells occurs in a manner distinct from its effect on mitochondrial functioning and suggests that activation of BK_{Ca} channels in the plasma membrane is the mechanism responsible for cytoprotection by NS1619.

Key words: BK_{Ca} channel, mitochondria, cytoprotection, NS1619, calcium