Pharmacologic Profile of the Selective Mitochondrial-\(K_{\text{ATP}}\) Opener BMS-191095 for Treatment of Acute Myocardial Ischemia

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**ABSTRACT**

ATP-sensitive potassium channel (\(K_{\text{ATP}}\)) openers as a class protect ischemic myocardium. The protective effects are independent of vasodilator activity and effects on action potential shortening, actions typically associated with sarcolemmal \(K_{\text{ATP}}\) activation. BMS-191095 is a novel mitochondrial \(K_{\text{ATP}}\) opener which protects ischemic myocardium while having no electrophysiologic or vasodilator effects (determined *in vitro* and *in vivo*). The cardioprotective effects were determined in isolated rat hearts subjected to ischemia and reperfusion. Protective effects were deduced from increased time to contracture formation during ischemia, improved reperfusion recovery of contractile function, and reduced reperfusion LDH release. The cardioprotective effects of BMS-191095 were observed at concentrations at which this compound selectively opened cardiac mitochondrial \(K_{\text{ATP}}\) channels. This effect was consistent with the pharmacologic profile of this agent. The protective effects were abolished by mitochondrial \(K_{\text{ATP}}\) inhibition. Unlike first-generation \(K_{\text{ATP}}\) openers, BMS-191095 is expected to protect ischemic myocardium with little hemodynamic sequelae and without any proarrhythmic potential. BMS-191095 is potentially useful clinically as a cardioprotective agent. It is also a useful tool for basic research.