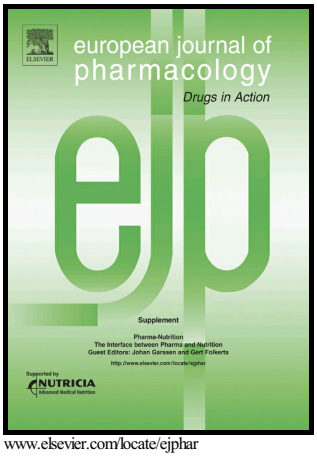

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MAPKs-mediated modulation of the myocyte voltage-gated K^+ channels is involved in ethanol-induced rat coronary arterial contraction

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Abstract

Acute coronary arterial spasm is contributory to ethanol-induced heart ischemic events. The present experiments were designed to study contractive effect of ethanol in isolated rat coronary arteries (RCAs) stimulated mildly with vasoconstrictors and involvement of voltage-gated potassium (K_V) channels and mitogen-activated protein kinases (MAPKs) of rat coronary arterial smooth muscle cell (RCASMC) in the spasm. The vascular tension was recorded with a wire myograph. K_V currents of single freshly isolated RCASMC were assessed with patch clamp. Phosphorylation of RCASMC MAPKs (p38 MAPK and p44/42 MAPK) was assayed by Western blots. Mild stimulation, which was defined as 5%-20% of 60 mM KCl-induced contraction, with thromboxane A_2 mimetic U46619, endothelin-1 or KCl tremendously increased contractive response of RCAs to ethanol (0.8-8.0 mg/ml). Ethanol (8 and 25 mg/ml) reduced the maximal K_V currents by 53.6 % and 56.6 % respectively without concentration-dependence. Both ethanol (8.0 mg/ml) and U46619 (0.3 μM) enhanced phosphorylation of p38 MAPK and p44/42 MAPK and there was a pronounced synergism between them. MAPK pathway inhibition with p38 MAPK inhibitor SB239063 and p44/42 MAPK inhibitor PD98059