# Paraquat causes hepatocytes death via oxidative stress-induced JNK/ERK activation regulated mitochondria-dependent apoptosis pathway

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**Abstract:**

Paraquat (1,1'-dimethyl-4,4'-bipyridium dichloride, PQ), a common herbicide used all over the world, is toxic to human beings and causes severe injuries to multiple organs, including lung and liver. However, the toxicological effects and molecular mechanisms of PQ-induced on hepatocytes are mostly unclear. In this study, we found that PQ significantly reduced the cell viability in rat hepatocytic cell line H4-II-E cells. Treatment of H4-II-E cells with PQ also induced several features of mitochondria-dependent apoptotic signals, including loss of mitochondrial membrane potential (MMP), increase in cytosolic cytochrome c release, activation of PARP and caspase-3/-7, and increased oxidative stress injuries such as reactive oxygen species

(ROS) generation and glutathione depletion. These PQ-induced apoptotic-related signals could be effectively reversed by antioxidant NAC. Moreover, PQ increased the phosphorylation of JNK and ERK1/2, but not p38. Pharmacological inhibitors SP600125, PD98059, and NAC significantly attenuated PQ-induced cytotoxicity, caspase-3/-7 activation, MMP loss, and inhibited the phosphorylation of JNK and ERK1/2. Taken together, these results suggest that PQ exerts its cytotoxicity on hepatocytes by inducing apoptosis via an oxidative stress-induced JNK and ERK1/2 activation regulated mitochondria-dependent signaling pathway.