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DEPRENYL INHIBITS POTENTIATED ARSENIC-INDUCED CYTOTOXICITY VIA THE INHIBITION OF C-JUN N-TERMINAL KINASE ACTIVATION

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A previous study showed that sulfur amino acid deprivation (SAAD) potentiated cytotoxicity induced by arsenic (As) and that activation of ERK1/2, p38 kinase and JNK1 was responsible for the potentiation of As toxicity. In the present study, we found for the first time that deprenyl a selective monoamine oxidase B inhibitor prevented potentiation of As toxicity by SAAD in a dose-dependent manner. Deprenyl inhibited the activation of JNK, but not p38 kinase or ERK1/2, which appeared to be responsible for decrease in the toxicity induced by SAAD or by SAAD plus As. Studies have shown that As induced cytotoxicity with activation of mitogen-activated protein kinases and that the activation of JNK was associated at least in part with the metal toxicity. Deprenyl inhibited the decrease in mitochondrial permeability induced by SAAD or by As. Mitochondrial permeability was restored by stable JNK1(-) transfection. As-induced JNK activation was also suppressed by deprenyl. Nonetheless, As-induced cytotoxicity was not improved by deprenyl treatment. These data provided evidence that deprenyl inhibited the JNK pathway and that the blockade of JNK activation by deprenyl contributed to prevention of SAAD-potentiated As toxicity, but not to the toxicity induced by As. Hence, the cytotoxicity of As appeared to result from other toxicological basis besides JNK activation.