EFFECTS OF DEHYDROMONOCROTALINE ON MITOCHONDRIAL PROCESSES

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The metabolite dehydromonocrotaline (DHM) is thought to be responsible for the toxicity of monocrotaline (MCT) *in vivo* but the exactly mechanism of action are not clear. In a previous study we found that DHM inhibits complex I of the respiratory chain interfering with mitochondrial respiration and oxidative phosphorylation. In the present work we evaluated the effects of DHM on NADH dehydrogenase activity in submitochondrial particles beside calcium transport and membrane permeability transition of mitochondria isolated from rat liver. DHM inhibited the NADH dehydrogenase activity presenting a tendency towards the competitive type of inhibition (K_i ~ 40 µM). DHM inhibited uptake and induced a poor efflux of calcium and membrane permeability transition of mitochondria in a concentration range between 50 and 250 µM. These effects were not inhibited by ruthenium red or cyclosporine A. We also evaluated the effects of DHM on oxidative status of mitochondria studying its effects on oxidation of mitochondrial NAD(P)H, generation of reactive oxygen species and lipid peroxidation but this parameters were not significantly affected by the compounds. The results discards the possibility of DHM induce the state of mitochondrial oxidative stress and indicate that its ability to inhibit the NADH dehydrogenase activity and affect calcium transport may be involved in the MCT mechanisms of citotoxicity.

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