Toxicity of statins on rat skeletal muscle mitochondria

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We investigated mitochondrial toxicity of four lipophilic stains (cerivastatin, fluvastatin, atorvastatin, simvastatin) and one hydrophilic statin (pravastatin). In L6 cells (rat skeletal muscle cell line), the four lipophilic statins (100 mu mol/l) induced death in 27-49% of the cells. Pravastatin was not toxic up to 1 mmol/l. Cerivastatin, fluvastatin and atorvastatin (100 mu mol/l) decreased the mitochondrial membrane potential by 49-65%, whereas simvastatin and pravastatin were less toxic. In isolated rat skeletal muscle mitochondria, all statins, except pravastatin, decreased glutamate-driven state 3 respiration and respiratory control ratio. Beta-oxidation was decreased by 88-96% in the presence of 100 mu mol/l of the lipophilic statins, but only at higher concentrations by pravastatin. Mitochondrial swelling, cytochrome c release and DNA fragmentation was induced in L6 cells by the four lipophilic statins, but not by pravastatin. Lipophilic statins impair the function of skeletal muscle mitochondria, whereas the hydrophilic pravastatin is significantly less toxic.
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