GN13 and HaCaT Cells Necrosis Promoted by Simvastatin is Prevented either by L-Carnitine or Piracetam

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Statins are competitive inhibitors of (HMG-CoA) reductase, which catalyzes the rate-limiting step in cholesterol synthesis. We have previously shown that simvastatin causes necrotic cell death mediated by mitochondrial permeability transition (MPT) in prostate cancer cells (PC3). This is prevented by L-carnitine and piracetam via a concentration dependent mechanism (1-12 µM). L-carnitine is a cofactor in the channeling of fatty acids inside the cell. Piracetam is a membrane stabilizer that improves the brain functions involved in processes of learning, memory, attention and consciousness. The present work was intended to evaluate the protection by L-carnitine or piracetam against cell necrosis promoted by simvastatin in non-tumorigenic immortalized cell line (HaCaT) and in primary fibroblasts cell line (GN13). In these cells simvastatin causes MPT associated with ROS generation followed by cell necrosis. Necrosis was associated with low levels of cellular ATP and confirmed by propidium iodide positive cells using flow cytometry. ROS generation was also measured by flow cytometry technique using the mitosox probe. Both L-carnitine or piracetam at 6 µM protected against simvastatin induced MPT, ROS generation and cell death. The association of L-carnitine and piracetam at 4 µM each showed addictive effects on the protection against cell necrosis promoted by simvastatin. We may conclude that these compounds protected against GN13 and HaCaT cells necrosis due to a primary inhibition of MPT. The data suggest that the effects of L-carnitine and piracetam on free fatty acids metabolism and mitochondrial membrane stabilization, respectively, acted in concert to protect these cells against MPT.

Keywords: L-carnitine, piracetam, simvastatin, Mitochondrial permeability transition.

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