Effect of the Acyl-Coa Synthetase Inhibitor Triacsin C on Mitochondrial Energetics


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Introduction: Obesity and excessive weight gain represent the fifth leading risk for global deaths and are often implicated in cardiovascular disease, diabetes and cancer. Immediate therapeutic actions are highly sought after to slow the escalating progress of these conditions, as enhancing body energy dissipation. Acyl-CoA synthetase (ACS) up-regulation is frequently associated with obesity and hyperlipidemic profiles in rat and human livers. ACS catalyzes the first step of fatty acid metabolism using free fat acids (FFA), CoA and ATP to form acyl-CoA. To investigate the effects of ACS activity on mitochondrial energetics in hepatocytes we firstly tested the effects of the ACS selective inhibitor triacsin C (1 - 20 µM) on isolated rat liver mitochondria.

Material and Methods: Rat liver mitochondria were isolated by differential centrifugation; mitochondrial respiration was measured using a Clark-type electrode; reactive oxygen species (ROS) release was monitored by spectrophotometric assay using Amplex Red; mitochondrial swelling was monitored spectrophotometrically at 540 nm. Results and Discussion: Triacsin C, from 2 µM concentration, increased ROS release and Ca\(^{2+}\)-induced mitochondrial permeability transition when compared to controls in a dose dependent manner. Only 20 µM triacsin C significantly reduced respiratory control ratio due to an increase in resting respiration. Conclusions: Triacsin C at concentrations up to 1 µM can be used to reduce ACS activity in hepatocytes avoiding direct changes in mitochondrial energetics.

Key words: obesity, mitochondria, acyl-CoA synthetase, triacsin C