

Trans,trans-2,4-DECADIENAL INDUCES NON-SELECTIVE INNER
MITOCHONDRIAL MEMBRANE PERMEABILIZATION

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Lipid peroxidation mediated by a free radical chain mechanism produces a large number of reactive aldehydes as secondary products. Many of these aldehydes are cytotoxic and have been shown to form adducts with biomolecules, including glutathione, proteins and DNA. Reactive aldehydes are reportedly involved in important cellular processes such as the regulation of gene expression and activation of mitochondrial uncoupling pathways. The purpose of this study was to investigate the effects of *trans,trans*-2,4-decadienal (DDE), a lipid peroxidation product, in isolated rat liver mitochondria. DDE (180 μ M) treatment increases the rate of mitochondrial oxygen consumption, suggesting it promotes partial mitochondrial uncoupling. Moreover, extensive mitochondrial swelling upon treatment with DDE (900 nM-162 μ M) was observed by light scattering and transmission electron microscopy experiments. This effect was not prevented by the mitochondrial permeability transition inhibitor cyclosporin A. We also found a DDE concentration-dependent loss in the inner mitochondrial membrane potential, monitored by safranin O fluorescence. These results suggest that reactive aldehydes may play a role in mitochondrial dysfunction associated with oxidative stress.

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