

# Acrolein Inhibits NADH-Linked Mitochondrial Enzyme Activity: Implications for Alzheimer's Disease

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(Received 18 March 2003; Revised 08 May 2003; In final form 08 May 2003)

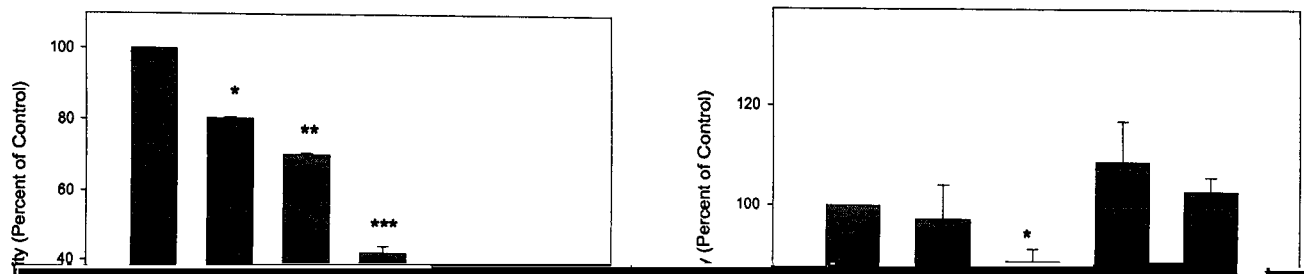
**In Alzheimer's disease (AD) brain increased lipid peroxidation and decreased energy utilization are found. Mitochondria membranes contain a significant amount of arachidonic and linoleic acids, precursors of lipid peroxidation products, 4-hydroxynonenal (HNE) and 2-propen-1-al (acrolein), that are extremely reactive. Both alkenals are known to**

**play a role in Alzheimer's disease (AD) brain (Butterfield *et al.*, 2001; 2002; Butterfield, 2002; Butterfield and Lauderback, 2002). An increase in protein oxidation (Hensley *et al.*, 1995), lipid peroxidation (Lovell *et al.*, 1995; Markesbery and Lovell, 1998), DNA oxidation (Lyras *et al.*, 1997; Lovell *et al.*, 2001), widespread**

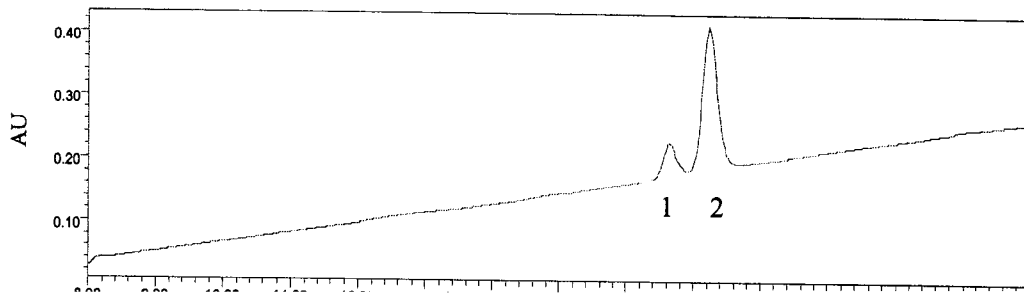
that convert oxidized nicotinamide adenine dinucleotide (NAD<sup>+</sup>) to the reduced form (NADH), which is vital to mitochondrial respiration and oxidative phosphorylation. In AD brain, KGDH is oxidatively modified by reactive alkenals (Gibson *et al.*, 1988). Lipoic acid is one part of the PDH and KGDH complexes and is susceptible to oxidative modification because of the two sulfhydryl groups contained in this cofactor. In the current study, the effect of acrolein on mitochondrial function was assessed by the activities of NADH-

## RESULTS AND DISCUSSION

In this study, we evaluated whether acrolein, at levels found in the AD brain (Lovell *et al.*, 2001), would affect the enzyme activity of pyruvate dehydrogenase or  $\alpha$ -ketoglutarate dehydrogenase. Figures 1 and 2 demonstrate that increasing nanomolar levels of acrolein significantly inhibit PHD and KGDH enzyme activity ( $p < 0.0006$  and  $p < 0.001$ , respectively). We

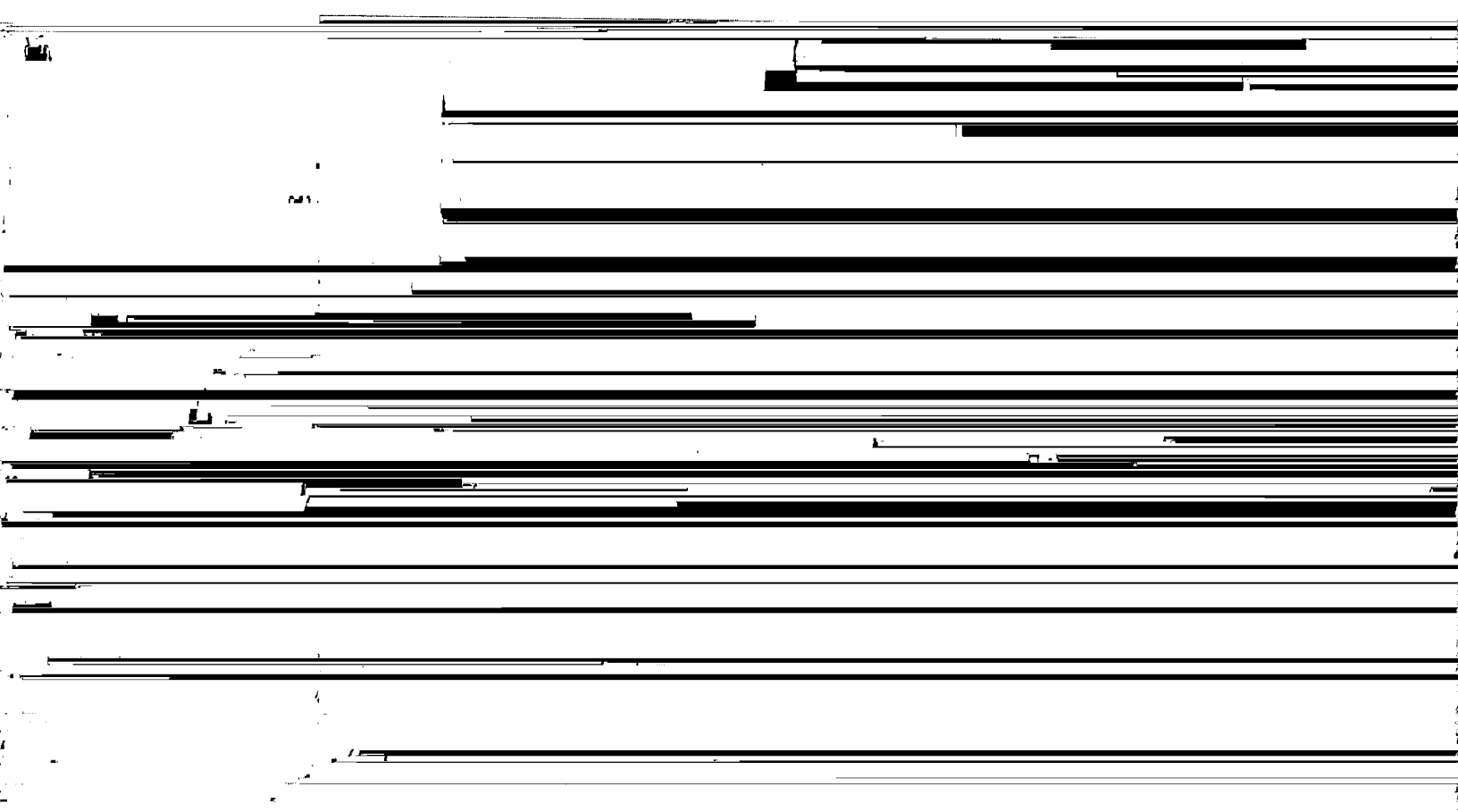


A



Minutes

B



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