CONTAMINATION BY ROUGH MICROSONES OF RAT LIVER MITOCHONDRIA DURING POISONING BY CARBON TETRACHLORIDE

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Rat liver mitochondria suffer a loss of function during poisoning by carbon tetrachloride (CCl₄). The nadir of function occurs 40 hrs. after CCl₄ administration (male CFN strain rats, 180-230g., 1.1 ml CCl₄/kg., i.p.), marked by a loss of ATP synthesis coupled to respiration (respiratory control ratio of 2.0 cf. 5.4 for controls) and an abnormal morphology. Swollen structures, as well as highly condensed, pleomorphic forms are seen in micrographs of isolated mitochondria instead of the uniform, spherical condensed profile of control mitochondria. Outstanding in micrographs of the mitochondrial fraction is a marked increase in rough microsomes in the preparations from the poisoned animals, Fig. 1 and Fig. 2. Since restoration of mitochondrial structure and function is evident after 40 hrs. (Brabec, et al., 1974), preceded by an increased incorporation in vivo of amino acids into mitochondrial protein (Brabec, et al., 1976), it was considered that the rough microsomal fractions represent part of the cellular mitochondrial repair system. Others have demonstrated that compartmentalization of the rough endoplasmic reticulum occurs, resulting in the translation of specific mRNAs (Shore and Tata, 1977). To determine if the rough microsomal elements contribute to the disruption of mitochondrial function, mitochondrial pellets from chloramphenicol-protected, CCl₄-poisoned rats were also examined. Simultaneous administration of CCl₄ and chloramphenicol (100mg/kg) increase the rat's tolerance of CCl₄ and largely prevent mitochondrial damage (Brabec, et al., 1976). Fig. 3 displays mitochondria from protected rats poisoned with CCl₄. Rough microsomal contamination is evident although these mitochondria were of high integrity (respiratory control ratio: 4.6) and normal appearance. In vivo amino acid incorporation into mitochondrial protein was highest in protected rats, supporting the proposition that the contamination by rough microsomes represents a fragment of endoplasmic reticulum specific for the synthesis of mitochondrial proteins during restoration following damage induced by CCl₄. This study was supported by PHS grant ES 01024.

Fig. 1-3. Electron micrographs of rat liver mitochondria prepared by conventional differential centrifugation methods. The arrows indicate masses of rough microsomes. Fig. 1, control mitochondria. Fig. 2, mitochondria isolated from a CCl₄-poisoned rat. Fig. 3, mitochondria from a chloramphenicol-protected rat. 12000×