ABSTRACT

The central role of mitochondria in metabolism makes these organelles the object of varied and continuous research. In this study, it was required to establish the effects of selected cannabinoids and a hypoglycin metabolite - methylenecyclopropyl-pyruvate (MCPP) - on mitochondria. Experiments involving the cannabinoids were done *in vivo* and *in vitro*. The former was done to determine the possible effect of smoke obtained from marijuana (ganja) and hashish. Investigations of the effect of MCPP were done *in vitro* only and involved the use of mitochondria isolated from liver. Mitochondria from brain and liver of rats were used in investigations involving the cannabinoids.

The cannabinoids, especially Δ'-THC, satisfied all the requirements for classification as uncouplers. The one-half maximal activity, however, was low when compared to well-defined uncouplers. In addition, brain mitochondria appeared to be more resistant to uncoupling.

Smoke from marijuana and hashish appeared to have no significant effects on brain mitochondria. This, however, could probably be explained either by

a low Δ'-THC content of the substances used or the need to administer the drug over a longer period of time.

The uptake of tritium-labelled Δ'-THC by rat brain mitochondria within a five-minute period was, to some degree, a concentration-dependent process.

MCPP was capable of inhibiting oxidation of long- and medium-chain fatty acyl carnitines. The extent of the inhibition implicated butyryl-CoA dehydrogenase as the enzyme affected. Oxidation of citric acid cycle intermediate was not affected significantly.

The formation of malate from pyruvate and the disappearance of pyruvate were decreased in the presence of MCPP. A decline in the formation of ketone bodies and of the ratio β-hydroxybutyrate: acetoacetate was observed.

Only tentative hypotheses can be advanced to explain some of these findings.