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NUTTASIRI SAEYIB : INHIBITION OF ENERGY-LINKED FUNCTIONS OF ISOLATED RAT LIVER MITOCHONDRIA BY AMIODARONE. THESIS ADVISOR : ASSO.PROF. PRAKORN CHUDAPONGSE, Ph.D. 100 pp. ISBN 974-581-111-4.

Amiodarone had a biphasic effect on respiratory activity of rat liver mitochondria supported by NAD^+-linked substrates or succinate. Initially, amiodarone uncoupled the mitochondria which was followed by marked inhibition of state 4 respiration. This compound exhibited some DNP-like effects on oxidative phosphorylation, e.g., the uncoupling effect was not inhibited by oligomycin, lowered ADP/O ratio as well as RCI value and activated the oligomycin-sensitive ATPase activity. However, in contrast to DNP, the amiodarone-induced uncoupling activity is almost unaffected by varying pH of incubation medium. Amiodarone inhibited mitochondrial respiration (state 4, state 3 and state 3u) supported by NAD^+-linked susbstrates or succinate but did not affect respiration when ascorbate + TMPD were electron donors. These results supported previous finding that amiodarone inhibited the respiratory chain at the levels of complex I and complex II. DTT did not alter the uncoupling and inhibitory effects of this compound on mitochondrial respiration. The inhibition of mitochondrial respiration incuced by amiodarone was diminished by Mg^{2+} but enhanced by bovine serum albumin. Amiodarone did not inhibit the mitochondrial MAO activity. The molecular mechanism of the biphasic effect of amiodarone is unclear. Nevertheless, the mitochondrial actions of amiodarone are likely to be involved in the pharmacological and/or toxicological effects of this compound.