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# Interference of sulphonylurea antidiabetica with mitochondrial bioenergetics under *in vivo* conditions[1]

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Sulphonylurea antidiabetica effectively inhibits the basal hepatic glucose production. Since it has been firmly established that lipophylic sulphonylurea drugs exerted an uncoupling effect on mitochondrial oxidative phosphorylation, a relationship between the reduction of hepatic gluconeogenesis and the insufficient energy supply due to sulphonylureas could be supposed. In this study we have investigated the effects of glibenclamide and gliquidone on mitochondrial bioenergetics in liver after peroral treatments of normal rats with different doses. The treatment of rats with 5 mg/kg glibenclamide or gliquidone daily for 14 days elicited only a marginal inhibition on mitochondrial oxidation capacity and remained without any effect on mitochondrial ATPase activity. Only the supermaximal dose 50 mg/kg for 14 day produced a significant damage in the mitochondrial functions. The basal respiration increased with 60–80 per cent, whereas the ADP- or DNP-stimulated oxygen consumption significantly decreased independently from the respiratory substrates investigated. Similar alterations were found in the mitochondrial ATPase activity after treatment with these drugs. No essential differences have been observed in the actions between glibenclamide and gliquidone.

However, the lowest dose applied in this study is many times higher than the usual therapeutic dose. Consequently, glibenclamide and gliquidone do not interact with mitochondrial bioenergetic processes under therapeutic conditions. On the other hand, in different liver and kidney damages we have no sufficient knowledge whether these drugs can be accumulated in these organs and therefore their elevated concentration may interfere with the mitochondrial energy metabolism.

**Keywords:** sulphonylurea antidiabetica, glibenclamide, gliquidon, mitochondrial bioenergetics, *in vivo* effects

[1] This paper is dedicated to the memory of Professor Tibor Kovács (1929–1994)

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