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## ABSTRACT BOOK

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**Results:** High glucose treated cells produce more ROS when compared with control groups. Moreover, hyperglycaemic conditions resulted in an increase in the activity of caspase 3 in differentiated cells. Significant changes in antioxidant enzymes were not observed. Results suggest alterations in mitochondrial function and cell injury.

**Conclusions:** The results indicate that hyperglycaemia causes mitochondrial degeneration in differentiated H9c2 myoblasts, mimicking what occurs in the human cardiomyocytes.

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## 2.39

## Relationship between the chemical structures of two derivatives of tacrine; relevance for mitochondrial dysfunction and hepatotoxicity

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**Background:** Tacrine therapy is associated with a serum aminotransferase elevation during therapy and has been linked to several instances of clinically apparent, acute liver injury, which can be connected to mitochondrial dysfunction. New tacrine derivatives proved to be less hepatotoxic than the original compound.

**Materials and methods:** Compounds pKa values were calculated using theoretical models. Liver biomarkers and mitochondrial bioenergetics were measured after treatment. We also assessed some parameters related to oxidative stress (e.g. lipid peroxidation and DNA oxidation).

**Results:** Liver biomarkers show that the novel compounds were less toxic than tacrine. Mitochondrial bioenergetics was significantly affected by tacrine, but the new derivative compounds did not induce any negative effect when used at the same concentration as tacrine. Mitochondrial calcium load capacity was significantly decreased by tacrine treatment but the new compounds did not interfere. Tacrine significantly increase lipid peroxidation and using the comet assay with cells digested in the presence of FPG enzyme shows that the DNA strand breaks were due oxidative processes.

**Conclusion:** The new tacrine derivative compounds do not interfere with mitochondrial bioenergetics, which is reflected in a lower hepatotoxicity. These differences could be justified based on the structural difference and in the pKa of the compounds that will be less accumulated in mitochondria when compared with tacrine.

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## 2.40

## *Mentha aquatica* L. extract affects mitochondrial bioenergetics

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**Background:** *Mentha aquatica* extracts are commonly used in food flavoring and pharmacology. In the present work, we evaluated the possible effects of *Mentha aquatica* L. (water mint) ethanolic extract on rat liver mitochondria bioenergetics.

**Materials and methods:** Rat liver mitochondria were isolated using conventional protocols. *M. aquatica* extracts were evaluated on mitochondrial membrane electric potential by using a tetraphenylphosphonium cation (TPP+)-selective electrode, while mitochondrial respiratory activity was evaluated using a Clark-type oxygen electrode, either in the presence of glutamate + malate and succinate as respiratory substrates. Mitochondrial osmotic volume changes were measured by the pseudo-absorbance changes at 520 nm with a suitable spectrophotometer-recorder set up.

**Results:** Incubation of *M. aquatica* extracts with isolated liver mitochondria resulted in a decrease in mitochondrial oxidative phsophorylation, reflected both by a decrease in respiratory parameters (state 3, respiratory control ratio -RCR, uncoupled respiration) and in membrane electric potential. This decrease can probably be related with the polyphenolic composition of the extract (mainly eriodictyol-7-*O*-rutinoside, luteolin-7-*O*-rutinoside, naringenin-7-*O*-rutinoside, hesperitin-7-*O*-rutinoside and rosmarinic acid), that can interact with membrane and change the inner mitochondrial membrane characteristics. Nevertheless, for the range of concentrations tested (up to 25 μg mg protein$^{-1}$) no significant increase in the inner mitochondrial membrane permeability was observed. Although decreasing the RCR, the *M. aquatica* extract did not affect the mitochondrial phosphorylative capacity, as estimated by the P/O ratio. Nevertheless, for highest concentrations (25 μg mg protein$^{-1}$ or higher) the inhibitory effect over mitochondrial respiratory chain (as reflected by uncoupled respiration) shows hindrance of mitochondrial respiratory maximal capacity.

**Conclusions:** Overall, the present study suggests that the consumption of *M. aquatica* leaves ethanolic extract should be regarded as hazardous, specially concerning high daily dosages.