Effects of hidroalcoholic extract of *Parkinsonia aculeata* on mitochondrial integrity: *in vitro* and *in vivo* studies

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Mitochondrial permeability transition (MPT) is a non-selective inner membrane permeabilization that is involved in necrotic and apoptotic cell death under a variety of pathological situations. It has been shown by our group that *P. aculeata* hidroalcoholic extract (PAHE) has an antidiabetic property, and its benefic effect is related to the flavonoids content. On the other hand, the adverse side effects of PAHE have not been described yet. Here, we report PAHE effects (*in vitro* and *in vivo*) on rat liver mitochondria respiratory rates parameters (respiratory control, ADP/O, phosphorylating (State 3) and resting (State 4), and uncoupled state), on ROS production and on mitochondrial membrane integrity. PAHE *in vitro* significantly decrease about 45.11% respiratory control ratio when compared to control, this extract also decrease ROS production (15.52% to DCF measurement, and 21.52% to Amplex Red measurement) when compared to control. Furthermore, PAHE presence also disrupts the mitochondrial membrane potential followed by mitochondrial Ca\(^{2+}\) release when compared to control. PAHE-induced MPT *in vitro* was sensitive to cyclosporin A (inhibitor of cyclophilin), ADP (adenine nucleotide carrier ligand), EGTA (calcium quelator), *N*-ethylmaleimide (thiol reagent), catalase (antioxidant enzyme) and Mg\(^{2+}\), but insensitive to dithiothreitol (disulfide reducing agent). On the other hand, liver mitochondria isolated from *in vivo* PAHE-treated (125 mg/kg/day during 16 days) rats does not present any change in mitochondria respiratory rates parameters, ROS production or mitochondrial integrity when compared to mitochondria from non-treated rats. Collectively, these results suggests that PAHE elicit its adverse side effects via direct structural perturbation of mitochondria by direct decrease in mitochondrial respiratory control, and leads to MPT through mechanisms Ca\(^{2+}\)-dependent.

Keys Word: *P. aculeata*, mitochondrial permeability transition, reactive oxygen species.
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