Parkinsonia aculeata aqueous extract fraction induces membrane permeability transition in rat liver mitochondria

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Mitochondrial permeability transition (MPT) is a non-selective inner membrane permeabilization that is involved in necrotic and apoptotic cell death in a variety of pathological situations. Strong evidences suggest that MPT is the consequence of oxidative damage to mitochondrial membrane proteins resulting in the formation of a proteinaceous pore, which causes mitochondrial calcium release, outer membrane rupture and leakage of pro-apoptogenic mitochondrial molecules. *P. aculeata* aqueous fraction (PAAF) has an antidiabetic effect already described, and its benefic effect is related to the flavonoids content. Adverse side effects of this extract have not been described yet. Here, we verified PAAF effects *in vitro* at rat liver mitochondria in a dose-dependent manner (0.01 – 0.1 mg/ml) at mitochondrial respiratory rates parameters (respiratory control, ADP/O, phosphorylating (State 3) and resting (State 4), and uncoupled state), ROS production and mitochondrial membrane integrity. PAAF significantly decrease respiratory control ratio and increase ROS production. Furthermore, PAAF presence also leads the mitochondria to membrane potential disruption followed by mitochondrial Ca²⁺ release. PAAF-induced MPT Ca²⁺-loaded was sensitive to cyclosporin A (inhibitor of cyclophilin), ADP (adenine nucleotide carrier ligant), EGTA (calcium quelator), N-ethylmaleimide (thiol reagent), catalase (antioxidant enzyme) and Mg²⁺, but insensitive to dithiothreitol (disulfide reducing agent). These results indicate that PAAF leads to a decrease in mitochondrial respiratory control and MPT at low concentrations through mechanisms dependent on Ca²⁺-induced altertations of ROS production.

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