

EFFECTS OF CAPSAICINOIDS IN DIFFERENT CONCENTRATIONS ON RAT LIVER MITOCHONDRIAL SWELLING

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ABSTRACT

Studying mitochondria and investigating in molecular levels are very significant for the estimation of medicinal properties of plants. Because mitochondria and MPTP are considered as specific “targets” not only for pathogens but also for pharmacological agents (Szewczyk et al., 2002). In folk medicine plants of *Capsicum annum* L family are well-known with their medicinal properties since ancient times. These plants are commonly named as leguminous red peppers.

Capsaicinoids are the main compounds giving bitter taste to pepper fruits. Yet 20 different capsaicinoids have been identified (Legin, 1996). Capsaicine and its analogs efficiently treat bronchial asthma, enuresis, inflammations of intestines, and different chronic deceases such as rheumatoid arthritis, osteoarthritis, neuralgia, and diabetic neuropathy (Kenji et al., 2010). However, the effects of capsaicinoids and proteins from red pepper *Capsicum annum* L. on membranes, mitochondria and in molecular levels have not been studied.

The aim of the work was to investigate the effects of capsaicinoids in different concentrations on rat liver mitochondrial swelling.

MATERIAL AND METHODS

Isolation of mitochondria

Mitochondria were isolated from the livers of white rats, weighed 120-140 g, by conventional differential centrifugation (Schneider, Hogeboom, 1951). Composition of isolation medium: 250 mM sucrose, 10 mM Tris-HCl, 1 mM EDTA, and pH 7.4.

Measurement of the mitochondrial inner membrane permeability

The kinetics of swelling of mitochondria was studied by the changes of optical density at 540 nm. Composition of the incubation medium (IM) for energized mitochondria: 200 mM sucrose, 20 μ M EGTA, 5 mM succinate, 20 mM Tris-HCl, 1 mM KH_2PO_4 , 20 mM HEPES, 2 μ M rotenone (He et al., 2003).

Drugs and chemicals

These given chemical reagents were used: EGTA, EDTA, cyclosporine A ("Sandoz", Switzerland), rotenone, tris-HCl (Serva, Germany), Sucrose (Russia), CaCl_2 ("Sigma", USA).

RESULTS AND DISCUSSION

It is known that activation of the mitochondrial permeability transition in matrix cause volume increase, outer membrane rupture and release of proapoptotic intermembrane space signalling molecules such as cytochrome c (Smaili et al., 2000). The mitochondrial permeability transition is Ca^{2+} dependent, CsA- sensitive and cause mitochondrial dysfunction. MPTP activation is associated with both apoptosis by the mitochondrial pathway and necrosis due to a damage of mitochondria. In this regard that fruit proteins are inductors of MPTP, we can assume that these components will act on the cancer cell death.

In these conditions red pepper seed proteins in 10, 15, 30, 65 μ g/ml concentrations did not significantly influence to MPTP and higher concentrations; 100, 130, 200 μ g/ml inhibited mitochondria swelling only to 3- 6% (results are not shown). Protein fractions were isolated from the fruits and seeds of red pepper had opposite effects on MPTP.

Lower concentration range of capsaicinoids 5-25 μ g/ml did not meaningly affect the speed of mitochondria swelling and MPTP condition. Addition of 30 μ g/ml of capsaicinoids sum into IM showed that they own membrane activity.

In this concentration mitochondria swelling lowered till $24.4 \pm 2.0\%$ compared to control. Capsaicinoids concentrations increase in IM inhibited mitochondria swelling more. Capsaicinoids in $130 \mu\text{g/ml}$ inhibited mitochondrial swelling till $84.4 \pm 3.0\%$, comparing to control.

These obtained results demonstrate that capsaicinoids inhibit MPTP and own membrane activity. It is known that MPTP change into the open state when exposed to low concentrations of Ca^{2+} . Thus the mitochondria swell rapidly, and compounds with a molecular weight 1.5 kD pass through the pore. Antioxidants and chelators of divalent cations inhibit swelling of mitochondria, i.e. MPTP turn into the closed condition. Capsaicinoid molecules probably affect one of components of MPTP and cause it to close. For example, in various pathologies MPTP is in an open state, resulting in increased ROS formation and lipid peroxidation. The inhibitory effect on the MPTP capsaicinoids might be possibility to use the studied alkaloids up as corrective agents.

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