**Rolipram, phosphodiesterase-4 inhibitor, reduced proteolysis in STZ-diabetic rats skeletal muscle**

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**Introduction and objectives:** Increase in the intracellular levels of cyclic AMP (cAMP) is essential for the inhibition of skeletal muscle proteolysis by catecholamines. Pharmacologic inhibition of cAMP phosphodiesterases (PDE) increases cAMP and decreases proteolysis in experimental models of muscle atrophy. Considering that PDE4 isoform accounts for the majority of PDE activity in skeletal muscles, the objective of this study was to evaluate the effects of rolipram (PDE4 inhibitor) on the activities of calpain, caspase and proteasome in skeletal muscles of diabetic rats.

**Materials and methods:** Male Wistar rats (80±10g) were injected with streptozotocin (60mg/kg, i.v.) to induce diabetes and were divided into groups (n=8): normal and diabetic rats treated with saline (i.p., NS and DS) or with 2 mg/kg rolipram (i.p., NROL and DROL). After 3 days of treatment, soleus and extensor digitorum longus (EDL) muscles were removed and the activities of proteasome, calpain and caspase-3 were made by the hydrolysis of specific substrates, with the release of 7-amido-4-methylcoumarin (AMC) that was measured fluorimetrically.

**Results and conclusions:** DS rats had a minor muscle mass when compared with NS. The activities of caspase and proteasome (μmol AMC/mg protein/min) were increased in EDL of DS rats (0.0163±0.0015 and 0.209±0.016, respectively) when compared with NS (0.0093±0.0009 and 0.152±0.008, respectively). The treatment of diabetic rats with rolipram decreased the activities of caspase (0.0127±0.0007) and proteasome (0.1495±0.0093) in EDL. DROL also showed a significant decrease in the activity of calpain (0.0533±0.0016) when compared with DS (0.0630±0.0043) and NS (0.0700±0.0064). Neither the insulin deficiency nor the rolipram treatment changed the proteases activities in soleus.

Muscle mass loss of diabetic rats may be due to the increased caspase activity, offering more substrates for the proteasome. Rolipram was effective in reduce proteolysis in EDL of diabetic rats, inhibiting both the proteasome and the proteases that release substrates for proteasomal degradation.

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**Key Words:** diabetes mellitus; skeletal muscle atrophy; rolipram