EFFECT OF 4-PHENYL BUTYRATE TREATMENT DURING MYOTUBES DIFFERENTIATION

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Introduction and objectives The maintenance of glycemia is obtained through a complex mechanism of homeostasis that involved many organs and hormones. Skeletal muscle is the main tissue that has glucose uptake stimulated by insulin. 4-phenyl butyrate (4-PBA) is a chemical chaperone used to revert endoplasmic reticulum (ER) stress increased in diabetic and obesity models. Has been described that 4-PBA can alters mitochondrial bioenergetics and the existence of a correlation between ER stress and mitochondria dysfunction in obesity, so is important to identify molecules able to regulate the homeostasis of these two organelles. Materials and Methods L6 myoblasts were grown in medium high (25 mM) or low glucose (5 mM) supplemented with 10% of fetal bovine serum. Differentiation into myotubes was induced in a medium with 2% of horse serum, changed every 2-3 days for 7 days. Treatment with 1 mM 4-PBA was made during the differentiation and control cells were treated with vehicle (DMSO). On the last day of differentiation, mitochondrial respiration was performed though specifics inhibitors in OROBOROS instrument, cellular viability was analyzed by MTT assay and protein expression was determined by Western Blot. Results and Conclusions Treatment with 1 mM of 4-PBA did not change cellular viability, despite glucose concentrations. Myosin expression was significantly decreased in the group treated with 1 mM of 4-PBA in high glucose concentration when compared to high glucose group, however low glucose concentration did not differ from low glucose group. The expression of BiP, a ER stress marker, did not differ between all groups. Treatment with 1 mM of 4-PBA increased mitochondrial proton leak in both glucose concentrations. Therefore, we conclude that 4-PBA inhibits myotubes differentiation growing in high glucose concentration media by a mechanism not related to ER stress but that involves mitochondrial function.

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Key Words
4-PBA; mitochondria; skeletal muscle