

Efficacy of the combination of β -Hydroxy- β -methyl butyrate and R(+) Lipoic Acid in a cellular model of sarcopenia

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The decline of muscle mass and strength, known as sarcopenia, is a clinical problem associated with osteo-articular diseases, muscle disuse, cancer, renal failure, postmenopause, age and corticosteroid treatments. Aim of the present research was the evaluation of the pharmacological profile of the leucine metabolite β -Hydroxy- β -methyl butyrate (HMB) associated with the natural R(+) stereoisomer of lipoic acid (R(+))LA) in a cellular model of muscle wasting.

C2C12 cell line was used as myoblasts or differentiated in myotubes by 7 day culture with 2% horse serum. Cell damage was induced by dexamethasone. Dexamethasone toxicity was evaluated measuring cell viability (MTT assay) and apoptosis induction (caspase 3 activity) after 24h and 48h incubation of myoblasts with the glucocorticoid (0.01 – 300 μ M concentration range). One μ M dexamethasone (48h) decreased cell viability by about 50% and increased caspase 3 activity by 80%. R(+))LA (100 and 300 μ M) or HMB (1 and 3 mM) significantly prevented dexamethasone-induced cell mortality; efficacy was improved when 100 μ M R(+))LA was combined with 1mM HMB. The synergy fully prevented cell mortality and caspase 3 activation. R(+))LA (100 μ M) and HMB (1mM) significantly reduced dexamethasone evoked O_2^- production as well as protein carbonylation in myoblasts. In the early phase of myotube differentiation (72h) the combination synergistically preserved the number of myogenin-positive cells. In myotubes (7 day differentiation), R(+))LA (100 μ M) and HMB (1mM) reduced the dexamethasone-dependent damage evaluated as cell diameter and percentage of multinucleated cells. Finally, the mixture prevented the protein oxidative damage. These results highlight the protective effects of R(+))LA combined with HMB in myoblast- and myotube-cell cultures damaged by dexamethasone. These data offer a rationale to candidate the mixture as a therapeutic option for sarcopenia treatment.