Pharmacognosy-2013
International Conference and Exhibition on
Pharmacognosy, Phytochemistry & Natural Products
October 21-23, 2013 Radisson Blu Plaza Hotel, Hyderabad, India

Role of curcumin in amelioration of hypobaric hypoxia induced skeletal muscle atrophy: *in vitro* and *in vivo* studies

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Abstract

Hypobaric hypoxia, which prevails at high altitude causes loss of body mass, decreased growth and increased oxidative stress inducing various deleterious cellular effects. Despite a number of studies reporting skeletal muscle atrophy as an important consequence of exposure to hypobaric hypoxia, the underlying mechanism is still to be uncovered. Recent studies have suggested the manifestation of high altitude induced oxidative stress in skeletal muscle atrophy that leads to early attainment of muscle fatigue. Upregulation of calpain and ubiquitin proteasome pathway were found to have important role in chronic hypoxia induced skeletal muscle loss. Recently, the role of curcumin in ameliorating skeletal muscle atrophy during a number of catabolic conditions has gained much attention. The present study explores the role of curcumin in ameliorating hypoxia induced muscle atrophy using both *in vitro* and *in vivo* models. The experiments were conducted on L6 skeletal muscle cell line and rat as animal model. For chronic hypoxia exposure male Sprague Dawley rats (n=12 each group) weighing about 180-200 g were exposed to 7,620 m for 3, 7, 14 days. After hypoxic exposure effect of curcumin on physical performance, total protein and myofibrillar protein were estimated. Calpain activity, proteasome activity were measured in muscle homogenates. Our results reveal that exposure of muscle myotubes to hypoxia results in increased oxidative stress which causes activation of NF-κB in the muscle cells. Addition of curcumin to the cells before exposure to hypoxia led to decreased NF-κB leads which further declined the activity ubiquitin–proteasome pathway and calpains subsequently ameliorating protein loss under hypoxic conditions. In the animals Curcumin administration prevented the decrease in physical performance of rats during treadmill running exercise. Curcumin restored the total protein content of skeletal muscle by decreasing the degradation of myofibrillar proteins. Administration of curcumin also led to decreased expression of MURF-1, ubiquitinated protein and μ-calpain.