

Effects of Methylglyoxal on Skeletal Muscle Myosin and Isolated Myofibrils

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Methylglyoxal (MG) is a highly reactive dicarbonyl, from multiple metabolic origins, that reacts with cellular proteins to form cross-links of amino groups, generating “advanced glycation end products” (AGE). This modification has been implicated in the development of diabetic complications. Despite their physiological importance, little is known about effects of MG in skeletal muscle. Rabbit psoas skinned-fiber bundles and purified myosin were incubated in relaxing solution without (control group) or with 10mM MG for 24h. Myosin Ca²⁺ATPase activity, tryptophan and AGE fluorescence were measured. In fibers, maximum isometric tension (P₀), Ca sensitivity and cooperativity were measured. Ca²⁺ affinity was reduced in the MG-fiber preparation compared to control (pCa₅₀ 6.0 vs 5.8, respectively). The Hill coefficient increased in the MG-group (nH=3.4 vs 2.5). When control fibers were incubated for 5, 15, 30 and 90min with 10mM MG, P₀ was inhibited by 18.6, 22.3, 27.2 and 68% respectively. After 90 min with MG (32% residual tension), fibers exposed to 5mM glutathione for 15min recovered to 60% of P₀. In purified MG-myosin, Ca²⁺ATPase activity was reduced 35% compared to control. The non-tryptophan (AGE) fluorescence spectrum (ex.368nm) of MG persisted after 24h dialysis, suggesting a stable interaction between myosin and MG. Increased tryptophan fluorescence (ex.280nm) indicated that MG induced a myosin conformational change. These *in-vitro* experiments show that single-fiber contractile activation properties as well as myosin enzymatic and structural functions are affected by incubation with MG. Our next step is to establish MG dose-response curves.

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