

The Effect of Geranylgeraniol on Satellite Cells Myogenic State in Type 2 Diabetic Rats

NIGEL C. JIWAN¹, CASEY R. APPELL¹, RAOUL STERLING¹, CHWAN-LI SHEN², HUI-YING LUK¹

¹Applied Physiology Laboratory, Department of Kinesiology & Sport Management, Texas Tech University, Lubbock, TX

² Department of Pathology, Texas Tech University Health Sciences Center, Lubbock, TX

Category: Doctoral

Advisor / Mentor: Luk, Hui-Ying (HuiYing.Luk@ttu.edu)

ABSTRACT

Type 2 Diabetes (T2D) is associated with chronic inflammation, which can contribute to impaired satellite cells (SC) myogenic state that may result in muscle atrophy. Geranylgeraniol (GGOH) has shown to prevent muscle atrophy, reduce inflammatory markers, and increase SC content; however, the effect of GGOH on SC myogenic state in T2D rats is not known. **PURPOSE:** To examine the effects of GGOH on SC myogenic state and muscle cross-sectional area (CSA) in T2D rats. **METHODS:** 21 Sprague-Dawley rats were fed a control diet (CON; n=7), a high-fat diet with 35 mg/kg of streptozotocin (HFD; n=7), and HFD with 800mg/kg body weight of GGOH (GG; n=7). In the 8th week, the right soleus muscle was analyzed for protein expression for Pax7, MyoD, myostatin, and GAPDH, and protein content was normalized to GAPDH. The left soleus muscle was co-stained with Pax7, MyoD, and myostatin using immunohistochemistry and analyzed for muscle CSA. Counted SC were normalized to 100 fibers. **RESULTS:** A significant ($p < 0.05$) condition effect was observed for MyoD and myostatin protein expression. For MyoD, HFD (1.41 ± 0.09 A.U.) was lower than CON (2.24 ± 0.21 A.U.) and GG (2.62 ± 0.43 A.U.). For myostatin, HFD (0.42 ± 0.06 A.U.) was lower than CON (0.91 ± 0.09 A.U.). Additionally, a significant condition effect was observed for the number of cells that presented Pax7⁺/MyoD⁻ and Pax7⁺/myostatin⁺. For Pax7⁺/MyoD⁻, HFD (0.039 ± 0.004) and GG (0.035 ± 0.004) had lower cell counts than CON (0.064 ± 0.010). For Pax7⁺/myostatin⁺, HFD (0.034 ± 0.003) had lower cell counts than GG (0.065 ± 0.010) and CON (0.057 ± 0.004). A significant condition effect was observed for CSA where CON ($7099.89 \pm 187.33 \mu\text{m}^2$) was larger than HFD ($4351.02 \pm 127.46 \mu\text{m}^2$) and GG ($5584.61 \pm 208.01 \mu\text{m}^2$), while GG ($5584.61 \pm 208.01 \mu\text{m}^2$) was larger than HFD ($4351.02 \pm 127.46 \mu\text{m}^2$). **CONCLUSION:** GGOH supplementation to T2D rats mitigated muscle mass loss (increased MyoD expression with no change in MyoD⁺ SC). Despite no differences in SC myogenic state (proliferative and differentiation) among groups, GGOH appeared to mitigate the reduction in the quiescent SC pool (Pax7⁺/myostatin⁺) observed in HFD. Given the importance of quiescent SC pool on retaining myogenic potential, which is essential for muscle hypertrophy and regeneration, supplementing GGOH to T2D rats could improve muscle health.