The acute effects of curcumin exposure on skeletal muscle contractile function

M. Grzelak, G.J. Pinniger and A.J. Bakker, School of Biomedical, Biomolecular and Chemical Sciences, The University of Western Australia, Crawley, WA 6009, Australia.

Curcumin, a component of turmeric, has been shown to exert anti-inflammatory, anti-oxidant and anti-cancer effects in animal models of human disease. Curcumin has been reported to alleviate the symptoms of muscular dystrophy in *mdx* mice (Pan *et al*, 2008). Although curcumin has been shown to have desirable effects on muscle damage and regeneration, little is known about its effects on muscle contractile function. Curcumin has inhibitory effects on sarcoplasmic reticulum (SR) function in SR vesicles *in vitro* (Logan-Smith *et al*, 2001; Sumbilla *et al*, 2002), suggesting possible adverse effects on muscle contraction. However, no such studies have examined the effect of curcumin on muscle function in intact skeletal muscle preparations. The aim of this study was to investigate the effects of curcumin exposure on skeletal muscle contractile function using isolated intact *extensor digitorum longus* (EDL) muscles of the mouse.

These experiments were conducted on EDL muscles from 7-9 week old ARC mice, with approval from the animal ethics committee of the University of Western Australia. Mice were anaesthetized using pentobarbitone (40mg/kg body weight, I.P.), and the EDL muscles were then surgically removed. Isolated EDL muscles were tied to a force transducer system using a surgical thread and maintained in a vertical organ bath filled with Krebs mammalian Ringer solution bubbled with Carbogen (95% O_2 and 5% CO_2) and maintained at 25°C. The contractile properties of EDL muscles were compared before and after exposure a 60 min exposure to either 100μM curcumin (dissolved in DMSO) or Krebs solution containing the equivalent DMSO concentration (control). The final DMSO concentration in all solutions was 0.05%. The effect of curcumin on the rate of muscle fatigue in response to 10 minute stimulation protocol was also assessed in curcumin and DMSO exposed EDL muscles.

In this study, no difference in maximum specific force was found between the two groups before exposure to curcumin or DMSO alone. However, 60 min exposure to curcumin (100μM) significantly decreased maximum specific force output by 14% compared to control EDL muscles exposed to DMSO alone (curcumin: 19.67 ± 0.73 N/cm^2, n=6 ; control: 23.02 ± 0.97 N/cm^2, n=6, P<0.05). Curcumin had no significant effect on peak force, the time to peak or the ½ relaxation times of twitch responses. The rate of muscle fatigue of the EDL muscles was significantly reduced after curcumin exposure compared to DMSO alone (significantly different all time points from 2-10 minutes, MANOVA, P<0.01, n=6).

The results of this study showed for the first time that curcumin (100 μM) has significant effects on contractile function of intact skeletal muscle preparations under physiological conditions. As the twitch contraction and relaxation times are sensitive to changes in SR function, these results are not consistent with previous findings that curcumin inhibits SR Ca^{2+} handling in SR vesicle preparations.

Pan Y, Chen C, Shen Y, Zhu C, Wang G, Wang X *et al.* (2008) Curcumin alleviates dystrophic muscle pathology in *mdx* mice. *Molecules and Cells* **25**(4), 531-537.

Logan-Smith MJ, Lockyer PJ, East JM & Lee AG. (2001). Curcumin, a molecule that inhibits the Ca^{2+}-ATPase of sarcoplasmic reticulum but increases the rate of accumulation of Ca^{2+}. *Journal of Biological Chemistry,* **276**(50), 46905-46911

Sumbilla C, Lewis D, Hammerschmidt T & Inesi G. (2002). The slippage of the Ca^{2+} pump and its control by anions and durcumin in skeletal and cardiac sarcoplasmic reticulum. *Journal of Biological Chemistry* **277**(16), 13900-13906.