Effect of curcumin exposure on skeletal muscle contractile function

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Curcumin, a component of the spice turmeric (*Curcuma longa*), reportedly alleviates the symptoms of muscular dystrophy in mdx mice (Pan *et al*., 2008) and decreases the expression of inflammatory mediators involved in muscle injury (Epstein *et al*., 2012). Based on these observations, curcumin may provide a new avenue for treatment of skeletal muscle damage and wasting. However, curcumin has also been reported to impair Ca^{2+} handling in sarcoplasmic reticulum (SR) vesicles (Bilmen *et al*., 2001; Logan-Smith *et al*., 2001) which could result in curcumin-induced muscle weakness. The aim of this study was to investigate the effects of curcumin exposure on skeletal muscle contractile function using skinned skeletal muscle preparations. Muscle fibres were isolated from the *extensor digitorum longus* (EDL) muscles of anaethetised ARC mice and Wistar rats (*Rattus norvegicus*). Mechanically skinned fibres were used to examine the effect of curcumin on excitation-contraction (E-C) coupling and SR function, based on Ca^{2+} loading and release characteristics. Curcumin (15 μM) reduced SR Ca^{2+} loading to 75.19 ± 5.29% (SEM) of control levels (P<0.001, n=9) but had no effect on the Ca^{2+} sensitivity of the contractile apparatus. Curcumin also decreased the peak of depolarisation-induced force (DIF) responses to 52.10 ± 7.97% of controls (P<0.0001, n=13). After curcumin washout, 7 fibres failed to respond to depolarisation with a force response, and in the remaining fibres, DIF responses were reduced to 14.94 ± 6.20% of controls (P<0.0001, n=6) Exposure to a low Mg^{2+}/caffeine Ca^{2+}-release solution shortly after resulted in large force responses similar in peak to control DIF responses (98.75 ± 4.20% of initial control measurements, P=0.78, n=6), indicating that the effects of curcumin on DIF were not due to SR Ca^{2+} depletion, or inhibition of SR Ca^{2+} release. The results of this study show that high doses of curcumin inhibit skeletal muscle force production, most likely through inhibitory effects on aspects of E-C coupling upstream from the SR.

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