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Regeneration of mouse skeletal muscle after myotoxic injury is impacted by fucoidan supplementation

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Fucoidan is a complex polysaccharide, consisting of mainly l-fucose and sulfate groups but also containing mannose, glucose, xylose and glucuronic acid. Fucoidan is a natural extract derived from brown seaweeds which has been predominately researched for its antitumorigenic, antioxidant and anti-inflammatory actions (Fitton et al., 2015). Recently, evidence in animal models suggests fucoidan may also possess properties beneficial for skeletal muscle function (McBean et al., 2021). In this study we investigated whether treatment with a novel fucoidan blend improved skeletal muscle regeneration following myotoxin induced muscle injury in mice.

The animal studies were approved by the Animal Ethics Committee of La Trobe University, in accordance with NH&MRC guidelines. C57/BL6 male mice were allocated to fucoidan treatment or vehicle control groups and further allocated into one of either 7-, 14- or 21-days post injury or 21-days uninjured (N=5-6 each time point for each group). Barium Chloride ($BaCl_2$)-induced myotoxin injury of the Tibialis anterior (TA) was performed under anaesthesia with 2% isoflurane. Mice received fucoidan (400 mg/kg/day) or vehicle (equal volume saline) via oral gavage daily until experimental end point. For end point analyses, mice were anesthetised via IP injection of pentobarbitone (70 mg/kg), such that they were unresponsive to tactile stimuli. TA muscle function was assessed *in situ* following which, anaesthetized mice were humanely euthanized by cervical dislocation, and tissues were collected for molecular and histological analysis. Whole muscle experiments were complimented with primary mouse myoblast scratch and differentiation assays.

Both time ($P < 0.05$) and treatment ($P < 0.05$) were found to have a significant impact on force production with fucoidan treated mice producing significantly higher specific isometric tetanic force (kN/m^2) at 3-weeks post myotoxic injury ($P < 0.05$). Tetanic force in 3-week uninjured control and treated groups were not significantly different despite fibre cross-sectional area (CSA) of 3-week uninjured fucoidan treated mice displaying significantly smaller CSA ($P < 0.05$). Fucoidan treated mice at 1-week post injury were found to have a significant increase ($P < 0.05$) in the number of CD68 positive cells when compared with vehicle treated mice. Muscle wound healing, based on *in vitro* scratch wound of C2C12 mouse myoblasts, was assessed following incubation with either 100, 200 or 500 µg/mL fucoidan. Wound closure (%) in all fucoidan treated groups were significantly inhibited compared to control wound closure ($P < 0.05$).

Altogether our findings suggest that in addition to recent evidence suggesting a positive effect of fucoidan on muscle function, fucoidan supplementation can improve regeneration of mouse skeletal muscle function post myotoxic injury.

Fitton, J. H., Dell'Acqua, G., Gardiner, V.-A., Karpiniec, S. S., Stringer, D. N. & Davis, E. (2015). Topical benefits of two fucoidan-rich extracts from marine macroalgae. *Cosmetics*, **2**, 66-81

McBean SE, Church JE, Thompson BK, Taylor CJ, Fitton JH, Stringer DN, Karpiniec SS, Park AY, van der Poel C. (2021). Oral fucoidan improves muscle size and strength in mice. *Physiol Rep*. **9**(3):e14730