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Fucoxanthin-rich ethanolic *Phaeodactylum tricornutum* extract ameliorates effects of diet-induced obesity in C57BL/6J mice

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The marine diatom microalga *Phaeodactylum tricornutum* is enriched in the ω-3 PUFA eicosapentanoic acid and the carotenoid fucoxanthin, two lipophilic constituents with proposed anti-obesity and anti-diabetic properties. We investigated the effect of an ethanolic *P. tricornutum* extract (PTE) on energy metabolism in obesity-prone mice fed a high fat diet (HFD). 6-8 week-old male C57BL/6J mice were switched to an HFD and, at the same time, received orally the vehicle or PTE (100 mg or 300 mg/kg body weight/day, providing ~2.4 mg fucoxanthin or ~7.1 mg fucoxanthin/kg body weight/day respectively). Body weight, body composition and food intake were monitored. After 26 days, blood and tissue samples were collected for biochemical, morphological and gene expression analyses. PTE-supplemented mice with the higher dose accumulated fucoxanthin metabolites in white adipose tissue (WAT) depots (1.48±0.76 µg fucoxanthinol/g *vs.* below detection in inguinal depot) and attained a significant 35% lower body weight gain, independent of decreased food intake. At the end of treatment they showed a significant 25% lower body fat content and reduced inguinal WAT adipocyte size compared to controls (adipocyte diameter 48.4±0.4 *vs.* 54.5±0.6 µm, $p<0.05$). PTE supplementation was associated with: lower expression of *Mest* (a marker of fat tissue expandability) in WAT depots; decreased expression of genes related to lipid uptake and turnover in visceral WAT; increased expression of genes key to fatty acid oxidation and thermogenesis (*Cpt1*, *Ucp1*) in subcutaneous WAT; and signs of thermogenic activation including higher UCP1 protein in interscapular brown adipose tissue. In conclusion, these data show the potential of PTE to ameliorate HFD-induced obesity *in vivo* through mechanisms that include changes in lipid and energy metabolism in adipose tissues. Knowledge on the anti-obesity action of *P. tricornutum* and its mechanisms may pave the way for novel uses of this microalga in the functional food and nutraceutical arena.