Sulfated polysaccharides isolated from *Caulerpa prolifera* promotes osteogenic differentiation of human mesenchymal stem cells

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Sulfated polysaccharides (SPs) from marine seaweeds have attracted attention due to their biological activities, including on stem cells differentiation through regulation of growth factor binding and signaling pathways. Here, we investigated the bioeffect of several SPs fractions isolated from *Caulerpa prolifera*, marine green seaweed, on osteogenic differentiation of human mesenchymal stem cells (hMSC). The SPs fractions were obtained from total extract precipitation, using different acetone volumes. hMSC isolated from Wharton jelly were treated with SPs samples, at different concentrations (0.1-10 ug/mL) and cell viability was evaluated for 24, 48 and 72 hours, by MTT assay. The osteogenic potential was examined based on alkaline phosphatase (ALP) activity and accumulation of calcium deposits accessed by Alizarin red S staining, after 5 and 21 days of treatment, respectively. We found that SPs effect depended on both sample and its concentration. Thus, CP0.5, CP0.7 and CP2.0 samples, at concentrations up to 1 µg/mL, induced an increase of 10-15% in cell proliferation ($p \leq 0.05$), whereas CP0.5 and CP0.7 samples, at 10 µg/mL, have an opposite effect, inhibiting 20-30% of cell proliferation. In addition, CP0.5 sample, at 5 µg/mL, increased 60% of ALP activity and 600% of calcium accumulation in comparison to negative control. Taking together our results suggest osteogenic activity of SPs from *C. prolifera* and their potential for development of alternative bone regeneration therapies. As far as we know, this is the first study demonstrating the osteogenic potential of SPs isolated from green seaweeds. Thereby, in the future, our aim will be to investigate the expression of other canonic molecular markers to elucidate the role of these SPs in hMSCs differentiation, contributing to the body of knowledge about marine-derived compounds and their possible pharmacological use.

Keywords: regenerative medicine, bone regeneration, osteoinductive effect.