Antitumor Activity of the Polysaccharides Obtained from *Gayralia oxysperma*: Chemical Structure Correlation and Mechanism of Action

Mariana M. de Carvalho, Luciana G. Ferreira, Cristiane R. Zuconelli, Juliana Ropelatto, Miguel D. Noseda, Franciely G. Colodi, Sheila M.B. Winnischofer, M. Eugênia Duarte Noseda*

Laboratório de Glicobiologia Estrutural de Carboidratos - Algas Marinhas (GLICAM). Departamento de Bioquímica e Biologia Molecular, Setor de Ciências Biológicas, Universidade Federal do Paraná, Paraná, Brasil.

* Autor para correspondência (e-mail): nosedaeu@ufpr.br

Green seaweeds biosynthesize polysaccharides with potential for antitumor therapy. This work describes the antitumor activity of the native and partially depolymerized polysaccharides obtained from *G. oxysperma*. Correlations of chemical structure and biological activity were proposed. The sulfated heterorhamnans from *G. oxysperma* were obtained by aqueous extraction (80 °C) resulting OX fraction (25.7% of NaSO₃). In order to obtain partially depolymerized fragments, OX was submitted to controlled Smith degradation, originating OXS (34.3% of NaSO₃), which was fractionated (DEAE-Sephacel) to give OXSb (33.7% of Na₂SO₃, Mw = 109.3 kDa) and OXSc (41.1% of Na₂SO₃, Mw = 251.1 kDa). OXSb and OXSc contain 3- and 2-linked rhamnosyl units (2:1 and 1.7:1, respectively). These units are partially branched at C-2 or C-3. Noteworthy OXSc presents higher content of 3,4-sulfated 2-linked rhamnose residues when compared to OXSb (3.25:1). The antitumor activity of OX, OXS, OXSb and OXSc using human glioblastoma cell lines (U87MG) showed that all of them were able to reduce the cell viability at 100 µg/ml for 48 hours. In these conditions, the cell cycle assay revealed that OX, OXS and OXSc increased the percentage of cells in G1 phase. These results are in agreement with the genic expression assay, which showed an increase in p53/p21 levels. For OXSb, the increase of cells in G1 phase could only be observed after 72 hours of treatment. Although all the fractions evaluated present similar mechanism of action, OXSc was more cytotoxic than OXSb. This feature could be attributed at least in part to the major content of dissulfated units and higher molecular weight of OXSc. Therefore, chemical structure and antitumor activity studies indicate that the cytotoxicity displayed by the sulfated heterorhamnans from *G. oxysperma* against U87MG cell lines is correlated with an appropriate molar weight and specific pattern of sulfation.

Keywords: green seaweed, sulfated heterorhamnans, glioblastoma

Acknowledgements: CNPq, CAPES and Fundação Araucária