ANTITUMORAL POTENTIAL OF GREEN MICROALGAE EXTRACTS IN CHRONIC MYELOID LEUKEMIA (CML) IN VITRO MODEL

EL Silva [a,b], FL Oliveira [a], FP Mesquita [a], PFN Souza [a], MEA Moraes [a], FA Santos [a], GNA Senhorinho [b,c], C Laamanen [b], JA Scott [b], RC Montenegro [a]

[a] *Universidade Federal do Ceará (UFC), Fortaleza, Brazil*
[b] *Laurentian University, Sudbury, Canada*
[c] *Cambrian College, Sudbury, Canada*

Introduction: Bioprospected microalgae collected from Northern Ontario, Canada water bodies have been shown to produce bioactive molecules, including carotenoids, polysaccharides, vitamins, and lipids with high pharmacological potential. Several studies in Canada with these microalgae have confirmed extracts with antioxidant, antimicrobial, and anticancer activity. Chronic myeloid leukemia (CML) is a clonal hematopoietic stem cell disorder and accounts for approximately 30% of the incidence of adult leukemias. Despite the use of tyrosine kinase inhibitors (TKIs) has improved the treatment and the prognosis of patients with CML therapeutic failures and adverse effects make treatment difficult, highlighting the need for the study of new molecules with antileukemic potential. **Objective:** This study aims to evaluate the *in vitro* antileukemic potential of different microalgae extracts in the K-562 cell line. **Material and methods:** Bioprospected microalgae strains S5, P981 (*Coccomyxa sp.*), LL1 (*Scenedesmus sp.*), LL2A, and CC (*Chlamydomonas sp.*) were cultivated for 14 days in Bold's Basal Medium (BBM) with pH 7 under 16 hr:8 hr light-dark cycles, at 25°C, and were kept continuously agitated at 150 rpm. The microalgae were then harvested and methanol, ethanol, and aqueous extraction were performed on each strain. Tubes were placed under vacuum to evaporate the remaining solvent and the crude extract was weighted, DMSO was added to obtain a stock solution of microalgae extracts (ME) at 10 mg/mL. The CML *in vitro* model K-562 was plated in a 96-well plate and the microalgae extracts were added in a single dose (100 μg/mL) or in a concentration-response curve (200 μg/mL – 3.125 μg/mL) for 72 hours for evaluate the viability and the Half-maximal inhibitory concentration (IC_{50}) of the most cytotoxic ME, respectively by the MTT method. **Results:** Fifteen extracts were produced, the ethanolic extracts from CC, LL2A, and P981 presented the highest inhibition percentages in the CML cell line, being 53.67 %, 54.69 %, and 47.09 %, respectively, and were chosen for the definition of the IC_{50}. The extracts showed high antileukemic activity, being 80.22 μg/mL for CC, 91.93 μg/mL for LL2A, and 96.18 μg/mL for P918 ethanolic MEs. **Discussion:** Previous studies from bioprospected microalgae collected from Northern Ontario have shown their antimicrobial, antiviral, antioxidant as well as antitumoral activity against ovarian and breast cancer cell lines. Ethanolic extracts possess compounds such as alkaloids, flavonoids, glycosides, terpenoids, tannins, saponins, and reducing sugars being sources of compounds with pharmaceutical properties. Our results demonstrated the antileukemic activity with an IC_{50} of 80 – 96 μg/mL, corroborating with other studies *in vitro*. **Conclusion:** The initial results attested that the ethanolic extracts derived from green microalgae presented high antileukemic potential in the CML *in vitro* model, showing a promising source of new compounds with pharmacological activity. Further research is needed to visualize which compounds are present in the ethanolic ME that can confer its antileukemic activity and to better describe their mechanism of action *in vitro* and *in vivo*.

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PREVALÊNCIA DE PRESENÇA DE MUTAÇÃO DO GENE V617F JAK2 EM PACIENTES COM NEOPLASIAS MIELOPROLIFERATIVAS PHILADELPHIA NEGATIVO ATENDIDOS EM UM CENTRO DE REFERÊNCIA NO SUL DO BRASIL.

LPD Santos, MR Sagrilo, G Bellaver, BBC Paula, WF Silva, JC Salvador, V Weber, NM Mottecy, CCD Nascimento

Universidade Federal de Santa Maria (UFSM), Santa Maria, RS, Brasil

Originárias de uma proliferação clonal de um progenitor hematopoiético pruripotencial, as Neoplasia Mieloproliferativas (NMP) constituem um grupo heterogêneo de doenças que cursam com exacerbada hematopoiese com amplificação de uma ou mais linhagens celulares. Como consequência, as manifestações clínicas comuns às patologias que integram este grupo incluem: hipercelularidade da medula óssea, hematopoiese extramedular com esplenomegalia, desenvolvimento de fibrose medular, transformação para leucemia aguda e alto risco de hemorragia ou trombose. Um importantíssimo subgrupo das NMP, refere-se às doenças que não apresentam o gene de fusão BCR-ABL (Philadelphia) – Policitemia Vera (PV), Mielofibrose Primária (MP) e Trombocitemia Essencial (TE). A presença da mutação JAK2 V617F não só representa importante marco de clonalidade nestas patologias, como também é considerada critério maior para diagnóstico do subgrupo BCR-ABL negativo. Dessa forma, a produção de uma proteína alterada com atividade tirosino-quinase pela transcrição do gene mutado JAK2 V617F ativa constitutivamente a via JAK-STAT e outras vias downstream (RAS/MAPK e PI3K/Akt) levando a prejuízo na expressão de genes envolvidos no controle de apoptose e de proliferação celular das linhagens hematopoiéticas. Assim, a alteração genética está diretamente envolvida na elaboração das três doenças citadas que são fenotipicamente distintas em graus variados de prevalência de ocorrência. Em vista disso, o presente trabalho tem por objetivo observar se há concordância entre a literatura médica nacional e internacional entre as taxas de prevalência da mutação JAK2 V617F presentes entre as diferentes doenças que integram as Neoplasias Mieloproliferativas BCR-ABL negativo em um centro de referência de hematologia no sul do Brasil. Para tanto, após cálculo de tamanho amostral (n = 70) da população em análise (N = 209) e da consulta de prontuários do ambulatório de Neoplasias Mieloproliferativas BCR-ABL negativo de um Hospital (Centro de Referência) no