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A reduction of the final tumor volume (p = 0.03) and an overexpression of VASH (p = 0.01), assuming that the Q3G group had a reduction of the final tumor volume (p < 0.04) as well. Increased VASH expression (p = 0.03) and decreased vascular proliferation (p < 0.05). It was found an inversely proportional relationship between the tumor growth of human colon adenocarcinoma/HT-29 and VASH expression (p < 0.05).

Conclusion: Flavonoids HR and Q3G demonstrated antangiogenic potential in colon adenocarcinoma/HT-29 when administered prophylactically and therapeutically, respectively. Q3G showed direct inhibition of the neovascular proliferation.

No conflict of interest.

**[54]** Anti-cancer properties of secondary metabolites derived from marine bacteria

L. Lee-Jones, O. Wang, S. Bohan, O. Martin, P.E. Linton, \(^1\)Manchester Metropolitan University, Healthcare Science, Manchester, United Kingdom

Background: Natural combinatorial chemistry has been occurring in plants and microorganisms throughout evolutionary history and consequently is far more sophisticated than that achievable in the laboratory by current combinatorial chemical procedures. This makes natural products an invaluable source of novel bioactive molecules which could lead to the development of novel pharmaceutical compounds to treat cancer.

Methods and Materials: Samples were collected from Heysham, West Lancashire. Marine bacteria were isolated to pure culture from marine tidal surfaces including marine invertebrates, molluscs and marine plants using actinomycete-seawater culture media. Resultant pure cultures were grown in organic circuits, including oncogenes and tumor suppressor genes such as P53 and ING2.

Method: For the experiment, 25 athymic mice were used and randomly divided into 5 groups: control, therapeutic Q3G and HR, prophylactic Q3G and HR. All animals were implanted with colon adenocarcinoma (HT-29) tumor cell line under subcutaneous tissue. Control animals had their tumor growth measured and assessed as a standard curve for comparative analysis. Prophylactic groups were gavaged with their respective drugs for 5 days prior to tumor implantation, while animals from therapeutic groups were gavaged only when their tumors reached volumes equal to or greater than 100mm\(^3\). After an evaluation of tumor growth the animals were euthanized, their tumors resected and stored for histological analysis and immunohistochemistry.

Results and Discussion: From an initial pilot study of 12 extracts derived from several strains of actinomycetes, 5/12 demonstrated anti-proliferative properties that were more potent than the hydroxyurea (positive) control. Evaluation of the bioactive properties of the remaining panel of extracts (n = 82) is now underway. Marine bacteria represent a largely untapped resource with enormous potential as a source of novel bioactive compounds.

No conflict of interest.

**[55]** Flavonoids Q3G and hydrolyzed rutin demonstrated antitumor activity in colon adenocarcinoma – in vivo study

D. Priolli, D.D.C. Silva, A.C. Duarte, G.D.C. Orfali, N.P. Martinez, \(^1\)São Francisco University, Medicine Course. \(^2\)São Francisco University, Medicine Course. \(^3\)São Francisco University, Medicine Course.

Background: Flavonoids are polyphenolic compounds widely distributed in the plant kingdom, whose importance lies in its beneficial physiological effects, including antioxidant and anti-proliferative effects. Carcinogenesis is a complex process that involves metabolic and cell proliferative changes by alteration in organic circuits, including oncogenes and tumor suppressor genes such as P53 and ING2.

Method: For the experiment, 25 athymic mice were used and randomly divided into 5 groups: control, therapeutic Q3G and HR, prophylactic Q3G and HR. All animals were implanted with colon adenocarcinoma (HT-29) tumor cell line under subcutaneous tissue. Control animals had their tumor growth measured and assessed as a standard curve for comparative analysis. Prophylactic groups were gavaged with their respective drugs for 7 days prior to tumor implantation, while animals from therapeutic groups were gavaged only when their tumors reached volumes equal to or greater than 100mm\(^3\). After an evaluation of tumor growth the animals were euthanized, their tumors resected and stored for histological analysis and immunohistochemistry.

**Results and Discussion:** Histological analysis showed poorly differentiated adenocarcinoma with the presence of signet ring cell. There was a reduction of tumor growth in all groups tested in the control group (p = 0.00). Immunohistochemical analysis revealed a reduction in the expression of p53 (p = 0.00) in all groups compared to control group. There was no difference in the expression of ING2 (p = 0.97). The drugs tested exhibited tumor growth inhibition and involvement in antiproliferative pathways mediated by the p53 protein, corroborating literature data showing activation of apoptotic mitochondrial pathway of flavonoid.

Conclusions: Flavonoids Q3G and HR demonstrated antitumor activity. Reduction of tumor growth was observed in all groups, moreover it was directly proportional to the reduction in mutated p53 expression in the therapeutic Q3G group (p = 0.03), indicating a potential pro-apoptotic action and cell cycle arrest (G1 / S phase) through p53 signaling pathways.

No conflict of interest.