

## **Evaluation of antiproliferative effect and cell cycle arrest on HT29 cells of different plant-derived natural extracts- Correlation of response with composition**

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**Background:** Colorectal cancer is the second most frequent malignant disease in Europe. Treatments for recurrent and metastatic diseases remain a centre of clinical attention. While continuing efforts have been made for discovering new molecular target-based molecules, there is an emerging interest in chemotherapeutic application of natural substances. In fact, between 1981 and 2002, almost 74% of all drugs approved for cancer therapy were: (i) natural products, (ii) based on natural products or (iii) mimicked natural products in one form or another. Phytochemicals, namely polyphenols and terpenes, presented in plants, fruits and vegetables have shown to have potential anticancer effect. The mechanisms by which these compounds inhibit tumorigenesis include inhibition of tumour cell mediated protease activity, attenuation of tumour angiogenesis, induction of cell cycle arrest and promotion of apoptosis.

**Objective:** This work is part of a project aiming at correlating the structure of natural anticancer biomolecules present in different natural matrices with their anticancer activity. For that we evaluated the antiproliferative effect and cell cycle arrest on human colon cancer cells (HT29) of several highly fractionated plant extracts containing different classes of phytochemicals.

**Methods:** Highly fractionated extracts from cherries, cactus pear, olive and cork were obtained using clean extraction and separation technologies, namely high pressures extraction, membrane process and adsorption technology. The extracts were analyzed for their content in phytochemicals, including polyphenols and terpenes using chromatographic and spectrophotometric assays. The antiproliferative effect of these extracts was evaluated in a

human intestinal cancer cell line, namely HT29. In these assays HT29 cells were incubated with different concentrations of natural extracts derived from fruits and plants and cell viability was measured by MTT and MTS assays. Cells were also analyzed by Flow Citometry aiming at evaluating the effect of natural extracts on the induction of cell cycle arrest. The antiproliferative effect of standard compounds alone was also performed. The results obtained were correlated with phytochemical composition of plant-based natural extracts.

**Results:** Cherry, cactus pear, olive and cork-based natural extracts inhibited HT29 cell growth in a time and dose dependent manner. Moreover all extracts induced cell cycle arrest and this effect varied according with extracts composition. In particular, cherry and olive extracts, that contained perillyl alcohol and hydroxytyrosol, respectively, induced cell cycle arrest on G1 phase suggesting that these compounds were the major responsible for this effect.

**Conclusion:** Our study demonstrated that cherry, cactus pear, olive and cork-based natural extracts inhibit the growth of HT29 through cell cycle modulation. These natural extracts have the potential to be further exploited for the discovery and development of new chemotherapeutic agents for colon cancer.

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