



SENSITIVITY OF COLON CANCER CELLS TO DIETARY FLAVONOIDS

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Abstract — Drug resistance represents one of the major challenges to effective chemotherapeutic interventions against cancer. There is an urgent need for novel agents that could increase sensitivity to chemotherapy in cancer cells. Potential bioactive effects exerted by natural compounds led us to test the cytotoxic properties of anthocyanidins in human colorectal carcinoma metastatic cells and their role on the expression of genes involved in the development of drug resistance.

Index Terms — TRANS2CARE, colon cancer, anthocyanidins

1 BACKGROUND

Colon cancer is the third most common cancer in men and the second in women. It is the second leading cause of cancer death in the developed world. Lifetime risk of developing colon cancer has been estimated at 1:20 (5%).

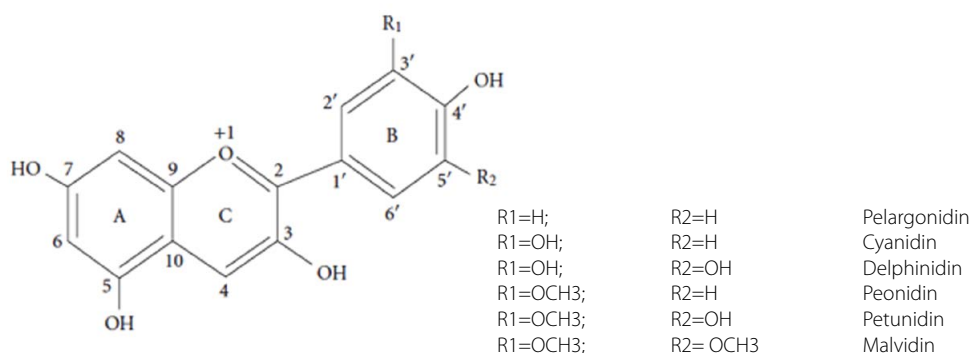
Together with surgery, chemotherapy is the cornerstone treatment for metastatic colorectal cancer. However, a high percentage of drug-resistant tumor forms represents a major challenge to modern medicine calling for new strategies and compounds able to reverse drug resistance.

Bioactive dietary components have raised a lot of interest recently in the field of cancer research. Many of them show anticancer properties and are seen as potential preventive and therapeutic agents.

2 OBJECTIVES

To assess the possible synergy of anthocyanidins* with cytotoxic drugs, especially their effect on the expression of certain genes involved in the development of drug resistance.

- plant pigments belonging to the group of dietary flavonoids, widely present in fruits, vegetables and flowers; anthocyanidins have been reported to exert anti-inflammatory and antioxidant activity in normal cells and numerous effects in cancer cells (eg. interaction with extrusion pumps, interaction with MAPKS and alteration of signal transduction pathways involved in cell proliferation, angiogenesis and apoptosis, reduction of GSTP expression, inhibition of topoisomerase I and II).



3 APPROACH & METHODS

General approach

Assessing the effect of long-term treatment with anthocyanidins on the expression of certain genes involved in the development of drug resistance using human cell culture models.

Methods

- Cells: metastatic colon cancer cells resistant to doxorubicin
- Treatment: anthocyanidins
- Cytotoxicity test (Alamar Blue)
- Uptake studies (doxorubicin uptake)
- Western blot
- qPCR
- Immunocytochemistry
- Cell cycle analysis – flow cytometry

4 RESULTS

- Drug resistance - we have identified conditions under which the tested anthocyanidins increase sensitivity of drug-resistant colon cancer cells. Mechanistic studies are ongoing.
- Cell cycle analysis - inhibition of drug-resistant cell proliferation after prolonged treatments with anthocyanidins was observed:

Long-term treatment with anthocyanidins decreases the number of cells in S phase while increasing the number of cells in G2/M phase suggesting inhibition of cell proliferation through induction of cell cycle arrest in G2 checkpoint phase

5 POTENTIAL NEW PRODUCTS & SERVICES

- Oral nutritional supplements for colon cancer patients
- “Local adjuvant therapy” for colon cancer patients

6 CURRENT COLLABORATIONS

With other researchers

Collaboration with:

- Maja Čemažar and Mitja Rak (Trans2Care, PP12, University of Primorska, Faculty of Health Sciences, Slovenia)
- Vanessa Nicolin (University of Trieste, Dep. of Medicine, Surgery and Health Sciences, Italy)

With associations

Collaboration with LILT (Italian ligue for the fight against cancer) and ASS1 (health agency in Trieste, Italy)

7 CONTACT OR COLLABORATIONS NEEDED

Collaborators for in vivo studies in mouse models of colon cancer.

8 COMMUNICATION TOOLS

- www.trans2care.eu

9 FUNDS NEEDED

9.1 For basic research (investigation of biological mechanisms): 100.000 €

9.2 For applied research (solutions for real-world problems): 350.000 €

9.2 For pilot & demonstrator activities (to develop a prototype): 500.000 €

10 CONCLUSION

The results of the ongoing study should help to understand if anthocyanidins can be used as sensitizing agents in metastatic colorectal cancer therapy.

ACKNOWLEDGEMENT

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