flavonoids), some herbal dietary supplements and vitamins A, C, and E. However, in the majority of these studies natural antioxidants were administered i.v., thus in a way typical for pharmacological approach. In contrast, our studies were designed so as to represent truly nutritional approach in which animals undergoing chemotherapy were fed the diet enriched in a particular food item – red beetroot (*Beta vulgaris*) juice (RBJ).

In these experiments, we checked whether the dietary intervention with RBJ might have any impact on therapeutic efficacy of DOX. For this purpose, leukaemia L1210 bearing mice were treated with DOX and fed RBJ ad libitum (instead of water) for 7 or 14 days. DOX was very effective in prolonging survival time of leukaemia bearing mice (ILS about 400%). However, only in groups receiving DOX in combination with RBJ total cures were observed. These were not sporadic events but concerned about 50% of animals.

In accompanying experiments, healthy or leukaemia L1210 bearing mice were fed RBJ ad libitum instead of water for 7 days and then were treated with DOX applied in different schemes. Control mice received water to drink. From control and treated mice, bloods and hearts were collected and analysed for various markers of oxidative insult. In mice fed with RBJ prior to DOX treatment, the damage of DNA in cardiomyocytes was clearly decreased indicating marked protection offered by the employed dietary intervention. As RBJ on its own had no antitumor effect, one can speculate that the improved outcome of chemotherapy resulted from reduced cardiotoxicity.

Our research suggests then that appropriately designed dietary intervention may offer very considerable benefits to cancer patients.

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The role of the anti-hyperglycemic metformin, a potential chemopreventive agent, in regulating tumour angiogenesis

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Metformin is a biguanide drug used as a first-line therapy for the management of type 2 diabetes. It has been shown to decrease hyperglycemia primarily by suppressing hepatic gluconeogenesis and consequent glucose release from liver. Moreover, metformin increases insulin sensitivity, enhances peripheral glucose uptake, increases fatty acid oxidation, and decreases absorption of glucose from the gastrointestinal tract. Prospective studies unveil a possible role for metformin in preventing cardiovascular diabetic complication and cancer risk. Metformin is known to work in part through activation of AMP-activated protein kinase (AMPK). AMPK is involved in cancer cell growth and metabolism by modulation of gene expression and translation. It has been observed that metformin activates AMPK in human umbilical vein endothelial cells (HUVEC). Endothelial cells are part of the tumor microenvironment system, and play a key role in the inflammation-driven tumor angiogenesis and metastatisation. New blood vessel formation is fundamental to allow tumor feeding and modification in vessel permeability and physiology is required for tumor dissemination. Here we show an overview of the general metformin mechanisms of action. We carried out HUVEC morfogenesis assay in matrigel in presence of metformin. We found that the compound affects normal tube formation. Moreover we assessed the effect of metformin on cell viability by a crystal violet assay in presence of different doses of the drug. We also observed that this compound affected endothelial cell proliferation and migration. Our preliminary results highlight a potential role for metformin as angiogenic-modulating agent for new therapeutic approaches.

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Chemopreventive strategies for cardiotoxicity induced by anticancer drugs

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The use of chemotherapeutic agents, radiation therapy, and molecular targeted therapies are all approaches that can injure the cardiovascular system both at a central level by deteriorating the heart function, and in the periphery by enhancing hemodynamic flow alterations and thrombotic events often latently present in oncology patients. Cancer patients showing signs of cardiovascular disease induced by the antineoplastic therapy are currently treated for the specific disease. Moving towards a protective chemoprevention approach, several drugs may be useful to flank chemotherapy to reduce cardiotoxicity without losing, and possibly even enhancing, anti-tumor activity. Most of these are still at an experimental stage, however some could easily be considered for clinical trials. Antioxidants such as the glutathione (GSH) precursor and analogue N-acetyl-L-cysteine can be given to patients at relatively high levels with an excellent toxicity profile. Numerous antioxidants and free radical scavengers found in dietary components such polyphenols and flavonoids, vitamins, micronutrients, enzymes and hormones, such as selenium, zinc, coenzyme Q10 and melatonin also show promise. Several plant derivatives such as Gingko biloba, grape seed extracts as well as polyphenols previously investigated for their anti-angiogenic, anti-inflammatory and anti-cancer activities (Epigallocatechin-3-gallate (EGCG) from green tea, resveratrol from red wine, and curcumin from curry) have been found to have cardioprotective activity in experimental studies. Since damage to the endothelium appears to underlie the cardiotoxicity of a variety of chemotherapeutic drugs, agents that prevent endothelial cell apoptosis should provide protective effects. Interestingly, investigation of some anti-angiogenesis compounds, in particular those that target the NF-κB pathway, have also been found to render endothelial cells more resistant to apoptosis induced by external stimuli. These include NAC and deguelin, while xanthohumol and triterpenoids did not perturb endothelial cell viability in vitro. The concept is that these agents force the endothelial cell into a quiescent state that leads to increased resistance to apoptosis.