Abstract

Introduction: Colorectal cancer risks could be reduced by polyphenol-rich diets that inhibit tumour cell growth. Aims: To determine the polyphenolic profile of four fruit beverages (FbZn, FbZnFe, FbZnM and FbZnFeM) as affected by the presence of Zn with/without Fe and with/without skimmed milk, and the digestion conditions. To evaluate the antiproliferative activity of bioaccessible fractions against Caco-2 and HT-29 cells. To clarify whether cell cycle arrest and/or apoptosis is involved in their possible antiproliferative activity. Methods: The polyphenolic profiles were analyzed by RP-HPLC-DAD before and after in vitro gastrointestinal digestion. Cell proliferation and viability were measured using Trypan blue test, mitochondrial enzyme activity by means MTT test, cell cycle distribution using flow cytometry and apoptosis by means Hoechst dye. Results and discussion: The presence of zinc, iron and/or milk decreased the soluble extractable phenolic content before digestion probably by chelate formation, FbZn and FbZnFe being the samples with the highest soluble extractable phenolics. After digestion, a decrease in phenolics was observed in all zinc-fortified samples (up to 32% with respect to the original fruit beverages) - the FbZnFeM sample showing the lowest soluble extractable phenolic content, though with the lowest percentage decrease in phenolics (14%). FbZnM digest (~50 M total soluble extractable phenolics) was the sample that most inhibited Caco-2 and HT-29 cell proliferation after 24 h of incubation, without cytotoxicity. The specific combination of phytochemicals in FbZnM digest proved cytostatic and significantly suppressed proliferation through cell cycle arrest in the S-phase in both cell lines, without apoptosis.

Keywords
Fruit beverages, In vitro gastrointestinal digestion, Polyphenols, Colon cancer cells, Antiproliferative activity.