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ANTICLASTOGENIC, ANTIGENOTOXIC AND APOPTOTIC ACTIVITY OF NATURAL POLYPHENOLS

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Modulation of events characteristic of carcinogenesis or of cancer cells is being emphasized as a rational strategy to combat cancer. This is achieved through chemoprevention by a variety of agents. Phenolic compounds, particularly polyphenols, have been shown to be highly active in this regard. Certain cellular and molecular events relevant to carcinogenesis are modified by polyphenols. The present investigation has been carried out to examine some of these aspects. Changes in ploidy of cells, non-random chromosome aberration and DNA damage are frequently associated with chemical toxicity and carcinogenesis. Manifestation of these events induced by H_2O_2 and *N*-methyl-*N*-nitro-*N*-nitrosoguanidine in cultured mammalian cells (CH V79) has been observed to be prevented by natural polyphenols. Polyphenols tested were curcumin, yakuchinone B, resveratrol, capsaicin, gallic acid and (-)-epigallocatechin gallate. Some of these compounds were very effective while others showed marginal activity. Apoptosis, a highly organized physiological mechanism to eliminate injured or abnormal cells, is also implicated in multistage carcinogenesis. Initiated cells or cells at promotional stage could be eliminated through apoptosis, thus preventing tumor progression. Induction of apoptosis in transformed cells is considered desirable as a mode of treatment for cancer. The above polyphenols have been tested for their ability to induce apoptosis in human leukemia derived cells (HL-60 and K 562), breast adenocarcinoma (MCF-7) and cervical epithelial carcinoma (HeLa) cell lines. Apoptosis was characterized by cytotoxicity, DNA synthesis, morphological features (chromatin condensation, apoptotic bodies) and DNA ladder formation. Leukemic cells were found to be more sensitive, and curcumin was the most active compound, others followed closely and capsaicin was least effective. The polyphenolic compounds used in these experiments have widespread occurrence in nature and are

consumed by humans through fruits, vegetables, beverages and medicine. Results show that these minor non-nutrient natural factors not only protect normal cells against genotoxic hazard but also eliminate cancer cells through induction of apoptosis.