COX-2 inhibition might be affected by contribution degree of COX-1 to intracellular PGs quantity. Therefore, the physiological roles of PGs derived from COX-1 as well as COX-2 even in many cancer cells with high expression of COX-2 require further investigation to establish COX-2 inhibition as a new modality for cancer treatment.

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Inhibition of DMBA-DNA adduct formation and modulation of TPA induced activation of AP-1 and NFkappaB transcription factors in mouse epidermis by naturally occurring plant phenols

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Mouse skin is one of the best animal models of chemical carcinogenesis which enables to study all stages of this process. Although most human skin cancers are not induced by chemicals, many events in this model could be extrapolated to humans. Moreover the biochemical changes observed in the mouse skin after application of tumor promoter 12-O-tetradecanoylphorbol acetate (TPA) are the same as those in humans after UVB radiation. Skin tumor initiator 7,12-dimethylbenz[a]anthracene (DMBA) is metabolically activated to syn- and anti-diol epoxides (DE), which form DNA adducts. The formation of dAdo adducts by DMBA diol-epoxides lead to mutation at the codon 61 of H-ras and consequently initiate tumorigenesis in mouse skin. Oncogenic H-ras can activate NFkappaB which similarly as AP-1 is considered to be a mediator of tumor promotion. In the present study we investigated the effects of topical application of plant phenols protocatechuic, chlorogenic and tannic acid on the DMBA-DNA adducts formation and the modulation of TPA induced activation of AP-1 and NFkappaB transcription factors in mouse epidermis. The application of these phenolic acids on mouse skin significantly reduced the DMBA binding to DNA. The most effective was tannic acid which almost completely inhibited the DMBADE-dAdo adduct formation. All phenols decreased the induced by TPA activation of the transcription factors AP-1 and NFkappaB by affecting their subunits expression, nuclear translocation and binding to specific sequence of DNA. Again the most efficient, particularly towards NFkappaB was tannic acid which increased the retention of IkappaBalfa in cytosol, reduced the nuclear translocation of p65 subunit and inhibited its binding to specific sequence of DNA.

In view of the important roles of the dAdo adducts activation in H-ras mutation and subsequent tumor initiation and AP-1 and NFkappaB in tumor promotion/progression the results of this study suggest that the ability of tannic acid and to lesser extent protocatechuic and chlorogenic acids to inhibit tumor development may be mediated by impairing signal transduction pathways leading to activation of AP-1 and NFkappaB.

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Experimental Therapy

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Immunotherapy with autologous dendritic cells in patients with hormone-refractory prostate carcinoma

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Currently there is no effective treatment available for metastatic prostate cancer. The enhancement of a normally weak immune response to tumor-antigens might therefore be a reasonable strategy in cancer treatment. Dendritic cells (DC) represent the most efficient antigen presenting cells, to initiate T cell responses in vitro and in vivo. For this reason autologous monocyte-derived DC, pulsed with peptides from multiple prostate antigens were used to vaccinate patients with hormone-refractory prostate cancer. Before application the DC were tested for maturation marker expression by flow cytometry and for migratory function. The DC vaccine is well tolerated and the induction of T cell responses and the course of the PSA-velocities are under investigation. The induction of an efficient immune response to over-expressed tumor antigens might be a strategy for the prevention of cancer.

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Selective cytotoxicity of an isolate from Cassia alata L. leaves

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In response for the continuing need for new therapeutics against cancer, leaf extracts of akapulko, Cassia alata L. were tested for their possible cytotoxic activity on five mammalian cell lines namely MCF-7, SkBr3, (both are breast cancer cells), T24 (urinary bladder cancer), Col 2 (Colon cancer) and A549 (non-small lung cancer) cell lines. The different mammalian cell lines were treated with methanol, hexane and ethyl acetate at different concentrations of 3.75, 7.5, 15, 25, 50, and 100 μg/ml. Doxorubicin, a known anticancer drug was also used to treat the cells and served as the positive control. The effects of the extracts were also tested on normal AA8 cells, from hamster ovary. The present study demonstrated that hexane (FB) caused remarkable cytotoxic effect on MCF-7, T24 and Col2 in a dose dependent manner as revealed by a low % cell survival using MTT assay and morphological investigation using light microscopy. Active FB fraction was then subjected to repeated and sequential chromatographic procedures following the bioactivity - directed fractionation and this yielded a TLC pure isolate, f6l. f6l was further evaluated using MTT, morphological and biochemical investigations and likewise showed a