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Apoptosis of Cancer Cells by Natural Substances

Adapted from :

"Cancer is DEAD : Cancer Killers from A to Z"

by Ignorance Isn't Bliss
http://www.ignoranceisfutile.org

Acai Berries

http://news.ufl.edu/2006/01/12/berries

Brazilian berry destroys cancer cells in lab, UF study shows

Extracts from acai berries triggered a self-destruct response in up to 86 percent of leukemia cells tested, said Stephen Talcott, an assistant professor with UF's Institute of Food and Agricultural Sciences. "Acai berries are already considered one of the richest fruit sources of antioxidants," Talcott said. "This study was an important step toward learning what people may gain from using beverages, dietary supplements or other products made with the berries."

Aloe-Emodin

http://www.ncbi.nlm.nih.gov/pubmed/16406939/

Aloe-Emodin Induces Apoptosis in T24 Human Bladder Cancer Cells

AE inhibited cell viability, and induced G2/M arrest and apoptosis in T24 cells. AE increased the levels of Wee1 and cdc25c, and may have led to inhibition of the levels of cyclin-dependent kinase 1 and cyclin B1, which cause G2/M arrest. AE induced p53 expression and was accompanied by the induction of p21 and caspase-3 activation, which was associated with apoptosis. In addition, AE was associated with a marked increase in Fas/APO1 receptor and Bax expression but it inhibited Bcl-2 expression.

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1573035/

Protein kinase C involvement in aloe-emodin- and emodin-induced apoptosis in lung carcinoma cell

This study demonstrated aloe-emodin- and emodin-induced apoptosis in lung carcinoma cell lines CH27 (human lung squamous carcinoma cell) and H460 (human lung non-small cell carcinoma cell). Aloe-emodin- and emodin-induced apoptosis was characterized by nuclear

morphological changes and DNA fragmentation.

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http://www.ncbi.nlm.nih.gov/pubmed/12175703

The antiproliferative activity of aloe-emodin is through p53-dependent and p21-dependent apoptotic pathway in human hepatoma cell lines

The aim of this study is to investigate the anticancer effect of aloe-emodin in two human liver cancer cell lines, Hep G2 and Hep 3B. We observed that aloe-emodin inhibited cell proliferation and induced apoptosis in both examined cell lines, but with different the antiproliferative mechanisms.

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http://cancerres.aacrjournals.org/content/60/11/2800.abstract

Aloe-emodin Is a New Type of Anticancer Agent with Selective Activity against Neuroectodermal Tumors

Here we report that aloe-emodin (AE), a hydroxyanthraquinone present in Aloe vera leaves, has a specific in vitro and in vivo antineuroectodermal tumor activity. The growth of human neuroectodermal tumors is inhibited in mice with severe combined immunodeficiency without any appreciable toxic effects on the animals. The compound does not inhibit the proliferation of normal fibroblasts nor that of hemopoietic progenitor cells. The cytotoxicity mechanism consists of the induction of apoptosis, whereas the selectivity against neuroectodermal tumor cells is founded on a specific energy-dependent pathway of drug incorporation. Taking into account its unique cytotoxicity profile and mode of action, AE might represent a conceptually new lead antitumor drug.

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http://www.ncbi.nlm.nih.gov/pubmed/15207375

Aloe-emodin induced in vitro G2/M arrest of cell cycle in human promyelocytic leukemia HL-60 cells

Aloe-emodin inhibited cell proliferation and induced G2/M arrest and apoptosis in HL-60 cells. Investigation of the levels of cyclins B1, E and A by immunoblot analysis showed that cyclin E level was unaffected, whereas cyclin B1 and A levels increased with aloe-emodin in HL-60 cells. Investigation of the levels of cyclin-dependent kinases, Cdk1 and 2, showed increased levels of Cdk1 but the levels of Cdk2 were not effected with aloe-emodin in HL-60 cells. The levels of p27 were increased after HL-60 cells were cotreated with various concentrations of aloe-emodin.

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http://www.ncbi.nlm.nih.gov/pubmed/17637488

Aloe-emodin-induced apoptosis in human gastric carcinoma cells

The purpose of this study was to investigate the anticancer effect of aloe-emodin, an

anthraquinone compound present in the leaves of Aloe vera, on two distinct human gastric carcinoma cell lines, AGS and NCI-N87. We demonstrate that aloe-emodin induced cell death in a dose- and time-dependent manner. Noteworthy is that the AGS cells were generally more sensitive than the NCI-N87 cells. Aloe-emodin caused the release of apoptosis-inducing factor and cytochrome c from mitochondria, followed by the activation of caspase-3, leading to nuclear shrinkage and apoptosis.

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http://www.ncbi.nlm.nih.gov/pubmed/17257888

Aloe-emodin induces in vitro G2/M arrest and alkaline phosphatase activation in human oral cancer KB cells

Aloe-emodin is a natural anthraquinone compound from the root and rhizome of Rheum palmatum. In this study, KB cells were treated with 2.5, 5, 10, 20, and 40 microM aloe-emodin for 1 to 5 days. The results showed that aloe-emodin inhibited cancer cells in a dose-dependent manner. Treatment with aloe-emodin at 10 to 40 microM resulted in cell cycle arrest at G2/M phase. The alkaline phosphatase (ALP) activity in KB cells increased upon treatment with aloe-emodin when compared to controls. This is one of the first studies to focus on the expression of ALP in human oral carcinomas cells treated with aloe-emodin. These results indicate that aloe-emodin has anti-cancer effect on oral cancer, which may lead to its use in chemotherapy and chemopreventment of oral cancer.

Anandamide

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC20983/

The endogenous cannabinoid anandamide inhibits human breast cancer cell proliferation

Anandamide was the first brain metabolite shown to act as a ligand of “central” CB1 cannabinoid receptors. Here we report that the endogenous cannabinoid potently and selectively inhibits the proliferation of human breast cancer cells in vitro. Anandamide dose-dependently inhibited the proliferation of MCF-7 and EFM-19 cells with IC50 values between 0.5 and 1.5 μM and 83–92% maximal inhibition at 5–10 μM. The proliferation of several other nonmammary tumoral cell lines was not affected by 10 μM anandamide. The anti-proliferative effect of anandamide was not due to toxicity or to apoptosis of cells but was accompanied by a reduction of cells in the S phase of the cell cycle. …These data suggest that anandamide blocks human breast cancer cell proliferation through CB1-like receptor-mediated inhibition of endogenous prolactin action at the level of prolactin receptor.

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http://onlinelibrary.wiley.com/doi/10.1002/pros.10190/abstract

Anti-proliferative and apoptotic effects of anandamide in human prostatic cancer cell lines

ANA induced a decrease of EGFR levels on LNCaP, DU145, and PC3 prostatic cancer cells by acting through cannabinoid CB1 receptor subtype and this leaded to an inhibition of the

EGF-stimulated growth of these cells. Moreover, the G1 arrest of metastatic DU145 and PC3 growth was accompanied by a massive cell death by apoptosis and/or necrosis while LNCaP cells were less sensitive to cytotoxic effects of ANA. The apoptotic/necrotic responses induced by ANA on these prostatic cancer cells were also potentiated by the acidic ceramidase inhibitor, N-oleoylethanolamine and partially inhibited by the specific ceramide synthetase inhibitor, fumonisin B1 indicating that these cytotoxic actions of ANA might be induced via the cellular ceramide production. The potent anti-proliferative and cytotoxic effects of ANA on metastatic prostatic cancer cells might provide basis for the design of new therapeutic agents for effective treatment of recurrent and invasive prostatic cancers.

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http://www.springerlink.com/content/h0m4052cq01vdba8/

Anandamide is an endogenous inhibitor for the migration of tumor cells and T lymphocytes

Cell migration is of paramount importance in physiological processes such as immune surveillance, but also in the pathological processes of tumor cell migration and metastasis development. The factors that regulate this tumor cell migration, most prominently neurotransmitters, have thus been the focus of intense investigation. While the majority of neurotransmitters have a stimulatory effect on cell migration, we herein report the inhibitory effect of the endogenous substance anandamide on both tumor cell and lymphocyte migration. …Using the specific agonist docosatetraenoylethanolamide (DEA), we have observed that the norepinephrine-induced migration of colon carcinoma cells is inhibited by the CB1-R. The SDF-1–induced migration of CD8+ T lymphocytes was, however, inhibited via the CB2-R, as shown by using the specific agonist JWH 133. Therefore, specific inhibition of tumor cell migration via CB1-R engagement might be a selective tool to prevent metastasis formation without depreciatory effects on the immune system of cancer patients.

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http://gut.bmj.com/content/54/12/1741.abstract

The endogenous cannabinoid, anandamide, induces cell death in colorectal carcinoma cells

These findings suggest anandamide may be a useful chemopreventive/therapeutic agent for colorectal cancer as it targets cells that are high expressors of COX-2, and may also be used in the eradication of tumour cells that have become resistant to apoptosis.

Apigenin
(Parsley, Celery, Coriander, Licorice, Majoram, Oregano, Rosemary, Tarragon, Citrus, Tea and Wheat)

http://www.ncbi.nlm.nih.gov/pubmed/11573952

Selective growth-inhibitory, cell-cycle deregulatory and apoptotic response of apigenin in normal versus human prostate carcinoma cells

The growth-inhibitory and apoptotic potential of apigenin was also observed in a variety of

prostate carcinoma cells representing different stage and androgen responsiveness. Apigenin may be developed as a promising chemopreventive and/or chemotherapeutic agent against prostate cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/14602723

Apigenin induces apoptosis in breast cancer cells

Apigenin is a low toxicity and non-mutagenic phytopolyphenol and protein kinase inhibitor. It exhibits anti-proliferating effects on human breast cancer cells. Here we examined several human breast cancer cell lines having different levels of HER2/neu expression and found that apigenin exhibited potent growth-inhibitory activity in HER2/neu-overexpressing breast cancer cells but was much less effective for those cells expressing basal levels of HER2/neu.

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http://www.ncbi.nlm.nih.gov/pubmed/10628390

Signal pathways involved in apigenin inhibition of growth and induction of apoptosis of human anaplastic thyroid cancer cells

Recently we demonstrated that several flavonoids can inhibit the proliferation of certain human thyroid cancer cell lines. Among the flavonoids tested, apigenin and luteolin are the most effective inhibitors of these tumor cell lines. In the present study, we investigated the signal transduction mechanism associated with the growth inhibitory effect of apigenin, using a human anaplastic thyroid carcinoma cell line, ARO.

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http://www.ncbi.nlm.nih.gov/pubmed/12032841

Induction of cell cycle arrest and apoptosis by apigenin in human prostate carcinoma cells

Apigenin, a common dietary flavonoid abundantly present in fruits and vegetables, may have the potential for prevention and therapy for prostate cancer. Here, we report for the first time that apigenin inhibits the growth of androgen-responsive human prostate carcinoma LNCaP cells and provide molecular understanding of this effect.

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http://www.ejcancer.info/article/S0959-8049

Induction of apoptosis by apigenin in leukaemia HL-60 cells

The potency of these flavonoids on these features of apoptosis were in the order of: apigenin>quercetin>myricetin>kaempferol in HL-60 cells treated with 60μM flavonoids. These results suggest that flavonoid-induced apoptosis is stimulated by the release of cytochrome c to the cytosol, by procaspase-9 processing, and through a caspase-3-dependent mechanism. The induction of apoptosis by flavonoids may be attributed to their cancer chemopreventive activity. Furthermore, the potency of flavonoids for inducing apoptosis may

be dependent on the numbers of hydroxyl groups in the 2-phenyl group and on the absence of the 3-hydroxyl group. This provides new information on the structure–activity relationship of flavonoids.

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http://ajpgi.physiology.org/cgi/content/abstract/285/5/G919

5,6-Dichloro-ribifuranosylbenzimidazole- and apigenin-induced sensitization of colon cancer cells to TNF–mediated apoptosis

Here we report that inhibition of CK2 in HCT-116 and HT-29 cells with the use of two specific CK2 inhibitors,
5,6-dichloro-ribifuranosylbenzimidazole (DRB) and apigenin, effected a synergistic reduction in cell survival when used in conjunction with TNF-. Furthermore, there was a demonstrable synergistic reduction in colony formation in soft agar with the use of the same combinations.

Arachidonyl Ethanolamide
(Cannabis)

http://www.ncbi.nlm.nih.gov/pubmed/15047233

Arachidonyl ethanolamide induces apoptosis of uterine cervix cancer cells via aberrantly expressed vanilloid receptor-1

The major finding was that AEA induced apoptosis of CxCa cell lines via aberrantly expressed vanilloid receptor-1, whereas AEA binding to the classical CB1 and CB2 cannabinoid receptors mediated a protective effect. Furthermore, unexpectedly, a strong expression of the three forms of AEA receptors was observed in ex vivo CxCa biopsies.

Artemisinin
(Wormwood)

http://ar.iiarjournals.org/content/24/4/2277.abstract

Artemisinin Induces Apoptosis in Human Cancer Cells

Artemisinin is a chemical compound extracted from the wormwood plant, Artemisia annua L. It has been shown to selectively kill cancer cells in vitro and retard the growth of implanted fibrosarcoma tumors in rats. In the present research, we investigated its mechanism of cytotoxicity to cancer cells. …This rapid induction of apoptosis in cancer cells after treatment with DHA indicates that artemisinin and its analogs may be inexpensive and effective cancer agents.

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http://onlinelibrary.wiley.com/doi/10.1002/hed.20524/abstract

Effects of artemisinin and its derivatives on growth inhibition and apoptosis of oral

cancer cells

Artemisinin is of special biological interest because of its outstanding antimalarial activity. Recently, it was reported that artemisinin has antitumor activity. Its derivatives, artesunate, arteether, and artemeter, also have antitumor activity against melanoma, breast, ovarian, prostate, CNS, and renal cancer cell lines. Recently, monomer, dimer, and trimer derivatives were synthesized from deoxoartemisinin, and the dimers and the trimers were found to have much more potent antitumor activity than the monomers. …The deoxoartemisinin trimer was found to have greater antitumor effect on tumor cells than other commonly used chemotherapeutic drugs, such as 5-FU, cisplatin, and paclitaxel. Furthermore, the ability of artemisinin and its derivatives to induce apoptosis highlights their potential as chemotherapeutic agents, for many anticancer drugs achieve their antitumor effects by inducing apoptosis in tumor cells.

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http://www.ncbi.nlm.nih.gov/pubmed/19006645

Transferrin receptor-dependent cytotoxicity of artemisinin–transferrin conjugates on prostate cancer cells and induction of apoptosis

Artemisinin, a natural product isolated from Artemisia annua, contains an endoperoxide group that can be activated by intracellular iron to generate toxic radical species. Cancer cells over-express transferrin receptors (TfR) for iron uptake while most normal cells express nearly undetectable levels of TfR. We prepared a series of artemisinin-tagged transferrins (ART-Tf) where different numbers of artemisinin units are attached to the N-glycoside chains of transferrin (Tf). The Tf bearing approximately 16 artemisinins retains the functionality of both Tf and artemisinin. Reduction of TfRs by TfR siRNA transfection significantly impaired the ability of ART-Tf, but not dihydroartemisinin, to kill cells. We also demonstrate that the ART-Tf conjugate kills the prostate carcinoma cell line DU 145 by the mitochondrial pathway of apoptosis.

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http://www.cancerletters.info/article/S0304-3835

Transferrin overcomes drug resistance to artemisinin in human small-cell lung carcinoma cells

Multiple drug resistance is a significant problem in small-cell lung cancer (SCLC). Artemisinin (ART) is a natural product used to treat drug-resistant malaria. The drug is effective because the Fe2+ present in infected erythrocytes acts non-enzymatically to convert ART to toxic products. We tested the effects of ART on drug-sensitive (H69) and multi-drug-resistant (H69VP) SCLC cells, pretreated with transferrin (TF) to increase the intracellular Fe2+ level. …These data indicate the potential use of ART and TF in drug-resistant SCLC.

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http://www.ncbi.nlm.nih.gov/pubmed/18466355

Dihydroartemisinin induces apoptosis and sensitizes human ovarian cancer cells to carboplatin therapy

The present study was designed to determine the effects of artemisinin (ARS) and its derivatives on human ovarian cancer cells, to evaluate their potential as novel chemotherapeutic agents used alone or in combination with a conventional cancer chemotherapeutic agent, and to investigate their underlying mechanisms of action. Human ovarian cancer cells (A2780 and OVCAR-3), and immortalized non-tumourigenic human ovarian surface epithelial cells (IOSE144), were exposed to four ARS compounds for cytotoxicity testing. The in vitro and in vivo antitumour effects and possible underlying mechanisms of action of dihydroartemisinin (DHA), the most effective compound, were further determined in ovarian cancer cells. …These effects were also observed in in vivo ovarian A2780 and OVCAR-3 xenograft tumour models. In conclusion, ARS derivatives, particularly DHA, exhibit significant anticancer activity against ovarian cancer cells in vitro and in vivo, with minimal toxicity to non-tumourigenic human OSE cells, indicating that they may be promising therapeutic agents for ovarian cancer, either used alone or in combination with conventional chemotherapy.

Beta-Elemene
(Ginger Root)

http://www.springerlink.com/content/q576206712225035/

Antitumor effect of ß-elemene in non-small-cell lung cancer cells is mediated via induction of cell cycle arrest and apoptotic cell death

Beta-elemene is a novel anticancer drug, which was extracted from the ginger plant. However, the mechanism of action of beta-elemene in non-small-cell lung cancer (NSCLC) remains unknown. Here we show that beta-elemene had differential inhibitory effects on cell growth between NSCLC cell lines and lung fibroblast and bronchial epithelial cell lines. …These data indicate that the effect of beta-elemene on lung cancer cell death may be through a mitochondrial release of the cytochrome c-mediated apoptotic pathway.

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http://www.springerlink.com/content/pv97t35522411368/

Elemene displays anti-cancer ability on laryngeal cancer cells in vitro and in vivo

Elemene inhibited the growth of HEp-2 cells in vitro in a dose- and time-dependent manner with an IC50 of 346.5 μM (24 h incubation). Increased apoptosis was observed in elemene-administered cells. Elemene is suspected to enhance caspase-3 activity, and thus inhibit protein expression of eIFs (4E, 4G), bFGF, and VEGF. In vivo, the growth of HEp-2 cell-transplanted tumors in nude mice was inhibited by intraperitoneal injection of elemene. Compared with control groups, elemene significantly inhibited the protein expression of eIFs (4E and 4G), bFGF, and VEGF and decreased the MVD. Conclusions: Elemene inhibits the growth of HEp-2 cells in vitro and in vivo. These data provide useful information for further clinical study on the treatment of LSCC by elemene.

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http://www.springerlink.com/content/k579267014gnm588/

Antiproliferative effect of ß-elemene in chemoresistant ovarian carcinoma cells

In this study, we show that beta-elemene inhibited the proliferation of cisplatin-resistant human ovarian cancer cells and their parental cells, but had only a marginal effect in human ovary cells, indicating differential inhibitory effects on cell growth between ovarian cancer cells and normal ovary cells.

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http://en.cnki.com.cn/Article_en/CJFDTOTAL-REST200003019.htm

Effect of Local Arterial Infusion of ß_elemene on Breast Cancer Tissue Inhibition and Cell Apoptosis and Proliferation

The effect of local arterial infusion of ß_elemene on breast cancer tissue inhibition and cell apoptosis and proliferation was observed.

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http://www.ncbi.nlm.nih.gov/pubmed/18538921/

N-(beta-Elemene-13-yl)tryptophan methyl ester induces apoptosis in human leukemia cells

Beta-elemene is an active component of herb medicine Curcuma Wenyujin and N-(beta-elemene-13-yl)tryptophan methyl ester (ETME) was synthesized for increasing its antitumor activity. ETME induced apoptosis in human leukemia HL-60 and NB4 cells at concentrations less than 40 microM. The apoptosis induction ability of ETME was associated with the production of hydrogen peroxide (H(2)O(2)), the decrease of mitochondrial membrane potential, and the activation of caspase-3 that was blocked by catalase. ETME in combination with arsenic trioxide (As(2)O(3)), an agent used to treat acute promyelocytic leukemia, synergistically induced apoptosis in both cell lines by enhanced production of H(2)O(2). These data suggest that ETME induces apoptosis and synergizes with As(2)O(3) in leukemia cells through a H(2)O(2)-dependent pathway.

Beta-Glucan
(Mushrooms: Shiitake, Reishi, Maitake, Oyster Mushroom, Cauliflower Mushroom)

http://www.jimmunol.org/cgi/content/abstract/163/6/3045

ß-Glucan…Uses Antibodies to Target Tumors for Cytotoxic Recognition by Leukocyte Complement Receptor Type 3 (CD11b/CD18)

ß-Glucans were identified 36 years ago as a biologic response modifier that stimulated tumor rejection. In vitro studies have shown that ß-glucans bind to a lectin domain within complement receptor type 3 (CR3; known also as Mac-1, CD11b/CD18, or Mß2-integrin, that functions as an adhesion molecule and a receptor for factor I-cleaved C3b, i.e., iC3b) resulting in the priming of this iC3b receptor for cytotoxicity of iC3b-opsonized target cells. This investigation explored mechanisms of tumor therapy with soluble ß-glucan in mice. Normal mouse sera were shown to contain low levels of Abs reactive with syngeneic or allogeneic tumor lines that activated complement, depositing C3 onto tumors. Implanted tumors became

coated with IgM, IgG, and C3, and the absent C3 deposition on tumors in SCID mice was reconstituted with IgM or IgG isolated from normal sera. Therapy of mice with glucan- or mannan-rich soluble polysaccharides exhibiting high affinity for CR3 caused a 57–90% reduction in tumor weight. In young mice with lower levels of tumor-reactive Abs, the effectiveness of ß-glucan was enhanced by administration of a tumor-specific mAb, and in SCID mice, an absent response to ß-glucan was reconstituted with normal IgM or IgG. The requirement for C3 on tumors and CR3 on leukocytes was highlighted by therapy failures in C3- or CR3-deficient mice. Thus, the tumoricidal function of CR3-binding polysaccharides such as ß-glucan in vivo is defined by natural and elicited Abs that direct iC3b deposition onto neoplastic cells, making them targets for circulating leukocytes bearing polysaccharide-primed CR3. Therapy fails when tumors lack iC3b, but can be restored by tumor-specific Abs that deposit iC3b onto the tumors.

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http://www.ncbi.nlm.nih.gov/pubmed/17161824

Beta glucan induces proliferation and activation of monocytes in peripheral blood of patients with advanced breast cancer

Glucans are glucose polymers that constitute a structural part of fungal cell wall. They can stimulate the innate immunity by activation of monocytes/macrophages. In human studies it has been shown that beta glucan has an immunomodulatory effect and can increase the efficacy of the biological therapies in cancer patients. In this prospective clinical trial we assessed in vivo effects of short term oral beta glucan administration on peripheral blood monocytes and their expression of activation markers in patients with advanced breast cancer. …Oral beta glucan administration seems to stimulate proliferation and activation of peripheral blood monocytes in vivo in patients with advanced breast cancer.

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http://www.jimmunol.org/cgi/content/abstract/177/3/1661

Yeast ß-Glucan Amplifies Phagocyte Killing of iC3b-Opsonized Tumor Cells

Anti-tumor mAbs hold promise for cancer therapy, but are relatively inefficient. Therefore, there is a need for agents that might amplify the effectiveness of these mAbs. One such agent is -glucan, a polysaccharide produced by fungi, yeast, and grains, but not mammalian cells. -Glucans are bound by C receptor 3 (CR3) and, in concert with target-associated complement fragment iC3b, elicit phagocytosis and killing of yeast. -Glucans may also promote killing of iC3b-opsonized tumor cells engendered by administration of anti-tumor mAbs. In this study, we report that tumor-bearing mice treated with a combination of -glucan and an anti-tumor mAb show almost complete cessation of tumor growth.

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http://www.liebertonline.com/doi/abs/10.1089%2F107555302320825084

Chemosensitization of Carmustine with Maitake ß-Glucan on Androgen-Independent Prostatic Cancer Cells

This study demonstrates a sensitized cytotoxic effect of BCNU with ß-glucan in PC-3 cells, which was associated with a drastic (~80%) inactivation of Gly-I. Therefore, the BCNU/ß-

glucan combination may help to improve current treatment efficacy by targeting Gly-I, which appears to be critically involved in prostate cancer viability.

ß-Hydroxyisovalerylshikonin
(Lithospermum)

http://jb.oxfordjournals.org/cgi/content/abstract/125/1/17

ß-Hydroxyisovalerylshikonin Inhibits the Cell Growth of Various Cancer Cell Lines and Induces Apoptosis in Leukemia HL–60 Cells

ß-Hydroxyisovalerylshikonin (ß-HIVS), which was isolated from the plant, Lithosper-mium radix, inhibited the growth of various lines of cancer cells derived from human solid, tumors at low concentrations between 10-8 and 10-6 M. When HL-60 cells were treated with 10-6 M ß-HIVS for 3 h, characteristic features of apoptosis, such as DNA fragmentation, nuclear fragmentation, and activation of caspase-3–like activity, were observed.

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http://www.ncbi.nlm.nih.gov/pubmed/15031601

ß-Hydroxyisovalerylshikonin and Cisplatin Act Synergistically to Inhibit Growth and to Induce Apoptosis of Human Lung Cancer DMS114 Cells

beta-Hydroxyisovalerylshikonin (beta-HIVS) and cisplatin (CDDP) had a synergistic growth-inhibitory effect on cultured human small-cell lung carcinoma DMS114 cells, as well as on human leukemia U937 and epidermoid carcinoma A431 cells, while beta-HIVS and CDDP alone at the same respective concentrations had little effect.

Betulin
(Red Alder trees & White Birch trees, and the mushroom Chaga that grows on White Birch.)

https://www.thieme-connect.com/ejournals/abstract/plantamedica/doi/10.1055/s-0028-1088366

Anti-Cancer Effect of Betulin on a Human Lung Cancer Cell Line

Betulin is a representative compound of Betula platyphylla, a tree species belonging to the Betulaceae family. In this investigation, we revealed that betulin showed anticancer activity on human lung cancer A549 cells by inducing apoptosis and changes in protein expression profiles were observed.

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http://cancerres.aacrjournals.org/content/67/6/2816.abstract

Betulinic Acid Inhibits Prostate Cancer Growth

Betulinic acid is a pentacyclic triterpene natural product initially identified as a melanoma-specific cytotoxic agent that exhibits low toxicity in animal models. Subsequent studies show that betulinic acid induces apoptosis and antiangiogenic responses in tumors derived from multiple tissues;

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http://www.ncbi.nlm.nih.gov/pubmed/15363977

Apoptotic activity of betulinic acid derivatives on murine melanoma B16 cell line

Exposure of B16 cells to betulinic acid, 23-hydroxybetulinic acid and 3-oxo-23-hydroxybetulinic acid caused a rapid increase in reactive oxidative species production and a concomitant dissipation of mitochondrial membrane potential in a dose- and time-dependent manner, which resulted in cell apoptosis, as demonstrated by fluorescence microscopy, gel electrophoresis and flow-cytometric analysis. Cell cycle analysis further demonstrated that both 3-oxo-23-hydroxybetulinic acid and 23-hydroxybetulinic acid dramatically increased DNA fragmentation at the expense of G1 cells at doses as low as 12.5 and 25 microg/ml, respectively, thereby showing their potent apoptotic properties. Our results showed that hydroxylation at the C3 position of betulinic acid is likely to enhance the apoptotic activity of betulinic acid derivatives (23-hydroxybetulinic acid and 3-oxo-23-hydroxybetulinic acid) on murine melanoma B16 cells.

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http://www.ncbi.nlm.nih.gov/pubmed/9516843

Betulinic acid induces apoptosis in human neuroblastoma cell lines

Neuroblastoma has long been recognized to show spontaneous regression during fetal development and in the majority of stage 4s infants <1 year of age with disseminated disease. Stage 4s disease regresses with no chemotherapy in 50% of the patients. The mechanism by which this occurs is not understood but may be programmed cell death or apoptosis. Betulinic acid (BA) has been reported to induce apoptosis in human melanoma with in vitro and in vivo model systems.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1600-0625.2005.00352.x/abstract

Betulinic acid induces apoptosis in skin cancer cells

Betulinic acid (BA), a pentacyclic triterpene of plant origin, induces cell death in melanoma cells and other malignant cells of neuroectodermal origin. Little is known about additional biological effects in normal target cells. We show, in this study, that BA induces differentiation as well as cell death in normal human keratinocytes (NHK).

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http://onlinelibrary.wiley.com/doi/10.1002/hed.10231/abstract

Betulinic acid: A new cytotoxic compound against malignant head and neck cancer cells

In two HNSCC cell lines betulinic acid induced apoptosis, which was characterized by a dose-dependent reduction in cell numbers, emergence of apoptotic cells, and an increase in caspase activity. Western blot analysis of the expression of various Bcl-2 family members in betulinic acid–treated cells showed, surprisingly, a suppression of the expression of the proapoptotic protein Bax but no changes in Mcl-1 or Bcl-2 expression.

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http://www.ncbi.nlm.nih.gov/pubmed/15905055

In vivo and in vitro anti-inflammatory and anti-nociceptive effects of the methanol extract of Inonotus obliquus

The mushroom Inonotus obliquus (Fr.) Pilát (Hymenochaetaceae), has been traditionally used for the treatment of gastrointestinal cancer, cardiovascular disease and diabetes in Russia, Poland and most of Baltic countries. This study was designed to investigate the anti-inflammatory and anti-nociceptive effects of the methanol extract from Inonotus obliquus (MEIO) in vivo and in vitro. MEIO (100 or 200 mg/(kg day), p.o.) reduced acute paw edema induced by carrageenin in rats, and showed analgesic activity, as determined by an acetic acid-induced abdominal constriction test and a hot plate test in mice.

Blueberries

http://pubs.acs.org/doi/abs/10.1021/jf062915o

Effect of Anthocyanin Fractions from Selected Cultivars of Georgia-Grown Blueberries on Apoptosis and Phase II Enzymes

The response correlated positively with dose. The QR activity was lower in all cells treated with an anthocyanin fraction from Tifblue, Powderblue, Brightblue, and Brightwell cultivars than in control cells ($P < 0.05$). The activity decreased gradually when treated with increased concentrations of anthocyanin fractions (50-150 μg/mL) in the Tifblue and Powderblue cultivars. The GST activity was lower ($P < 0.05$) in cells treated with anthocyanin fractions from all of the cultivars and at all concentrations. These results indicated that apoptosis was confirmed in HT-29 cells when treated with anthocyanins from blueberry cultivars at 50-150 μg/mL concentrations, but these same concentrations decrease QR and GST activities rather than induce them.

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http://www.ncbi.nlm.nih.gov/pubmed/17487929

Availability of blueberry phenolics for microbial metabolism in the colon and the potential inflammatory implications

Blueberries are a rich source of phenylpropanoid-derived phytochemicals, widely studied for their potential health benefits. Of particular interest for colonic health are the lower molecular weight phenolic acids and their derivatives, as these are the predominant phenolic compounds detected in the colon. Blueberries contained a wide variety of phenolic acids, the majority of which (3371.14 ± 422.30 mg/kg compared to 205.06 ± 45.34 mg/kg for the free phenolic acids) were attached to other plant cell-wall components and therefore, likely to become

available in the colon. Cytokine-induced stimulation of the inflammatory pathways in colon cells was four-fold up-regulated in the presence of the free phenolic acid fraction. Incubation of the bound phenolic acids with human faecal slurries resulted in qualitative and quantitative differences in the phenolic compounds recovered. The metabolites obtained by incubation with faecal slurries from one volunteer significantly decreased (1.67 ± 0.69 ng/cm3) prostanoid production, whereas an increase (10.78 ± 5.54 ng/cm3) was obtained with faecal slurries from another volunteer. These results suggest that any potential protective effect of blueberry phenolics as anti-inflammatory agents in the colon is a likely result of microbial metabolism. Studies addressing a wide-range of well-characterised human volunteers will be required before such health claims can be fully established.

Broccoli

http://breastcancer.about.com/b/2010/05/11/broccoli-breast-cancer.htm

Natural Compound in Broccoli Slows Breast Cancer Stem Cells

In lab studies, when breast cancer cells were exposed to sulforaphane extract from broccoli, the growth of cancer stems cells slowed down and tumors shrank. The researchers speculate about the possible use of sulforaphane extract to prevent as well as treat breast cancer, someday.

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http://www.broccosprouts.com/health/sgsfactsheet.htm

Sprouts contain 3X the amount of Sulforaphane Glucosinolate

Johns Hopkins University researchers found that young broccoli sprouts, in particular, contained high concentrations of SGS. The scientists believe that SGS boosts the body's own antioxidant defense system, including Phase 2 detoxification enzymes, which promote long-lasting antioxidant activity in the body.

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http://www.activamune.com/

Diindolylmethane (DIM)

The Chairman of the Nutritional Sciences Department and the Director of the National Institutes of Health Cancer Research Program at the University of California at Berkeley were studying the biological properties of Diindolylmethane (DIM), a naturally occurring compound found in Brassica vegetables (broccoli, cauliflower, cabbage, kale, brussels sprouts), when they made a remarkable discovery: DIM is a potent activator of the immune response system. They patented their discovery and ActivaMune was launched as a first-in-class nutritional supplement to enhance the immune system and support multiple organs throughout the body: breast, prostate, cardiovascular, vision, skin and colon health. ActivaMune's unique and patented formula combines multiple nutrients for maximum effectiveness: Diindolylmethane (DIM), Sulforaphane, Selenium, Lycopene, Lutein, Zeaxanthin, Calcium and Vitamins C, D3 & E.

Caffeic Acid

(Sweetpotato Leaves, Propolis, Apples, White Grapes, White Wine, Olives, Olive Oil, Spinach, Cabbage, Turnips, Radish, Cauliflower, Bok Choy, Arugula, Kale, Asparagus, and Coffee)

http://pubs.acs.org/doi/abs/10.1021/jf0620259

Growth Suppression of Human Cancer Cells by Polyphenolics from Sweetpotato (Ipomoea batatas L.) Leaves

Sweetpotato leaves (Ipomoea batatas L.) contain a high content of polyphenolics that consist of caffeic acid, chlorogenic acid, 3,4-di-O-caffeoylquinic acid, 3,5-di-O-caffeoylquinic acid, 4,5-di-O-caffeoylquinic acid, and 3,4,5-tri-O-caffeoylquinic acid. We investigated the suppression of the proliferation of selected human cancer cells by phenolic compounds isolated from sweetpotato leaf. …Growth suppression of HL-60 cells by 3,4,5-tri-O-caffeoylquinic acid was determined to be the result of apoptotic death of the cells. These results indicate that 3,4,5-tri-O-caffeoylquinic acid may have potential for cancer prevention.

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http://www.springerlink.com/content/37t7896678842541/

Caffeic acid phenethyl ester induces mitochondria-mediated apoptosis in human myeloid leukemia U937 cells

Caffeic acid phenyl ester (CAPE), a biologically active ingredient of propolis, has several interesting biological properties including antioxidant, anti-inflammatory, antiviral, immunostimulatory, anti-angiogenic, anti-invasive, anti-metastatic and carcinostatic activities. Recently, several groups have reported that CAPE is cytotoxic to tumor cells but not to normal cells. In this study, we investigated the mechanism of CAPE-induced apoptosis in human myeloid leukemia U937 cells. Treatment of U937 cells with CAPE decreased cell viability in a dose-dependent and time-dependent manner.

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http://www.jbc.org/content/279/7/6017.short

Caffeic Acid Phenethyl Ester Induces Apoptosis by Inhibition of NF?B and Activation of Fas in Human Breast Cancer MCF-7 Cells

Our findings demonstrate that NF?B inhibition is sufficient to induce apoptosis and that Fas activation plays a role in NF?B inhibition-induced apoptosis in MCF-7 cells.

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http://www.ncbi.nlm.nih.gov/pubmed/11261888

The antioxidant caffeic acid phenethyl ester induces apoptosis associated with selective scavenging of hydrogen peroxide in human leukemic HL-60 cells

These results suggest that apoptosis induced by CAPE is associated with mitochondrial dysfunction, GSH depletion and selective scavenging of H2O2 in human leukemic HL-60

cells.

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http://www.ncbi.nlm.nih.gov/pubmed/15996024

Effect of caffeic acid phenethyl ester on proliferation and apoptosis of colorectal cancer cells in vitro

After HCT116 cells were exposed to CAPE (80, 40, 20, 10, 5, and 2.5 mg/L) for 24, 48, 72, 96 h, CAPE displayed a strong growth inhibitory effect in a dose- and time-dependent manner against HCT116 cells. FCM analysis showed that the ratio of G(0)/G(1) phase cells increased, S phase ratio decreased and apoptosis rate increased after HCT116 cells were exposed to CAPE (10, 5, and 2.5 mg/L) for 24 h. CAPE treatment was associated with decreased cytoplasmic beta-catenin, nuclear beta-catenin and a concurrent increase in beta-catenin protein expression at cell-cell junctions.

Capsaicin
(Hot Peppers)

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2857654/

Capsaicin Displays Anti-Proliferative Activity against Human Small Cell Lung Cancer in Cell Culture and Nude Mice Models via the E2F Pathway

BrdU assays and PCNA ELISAs showed that capsaicin displays robust anti-proliferative activity in four human SCLC cell lines. Furthermore, capsaicin potently suppressed the growth of H69 human SCLC tumors in vivo as ascertained by CAM assays and nude mice models. The second part of our study attempted to provide insight into molecular mechanisms underlying the anti-proliferative activity of capsaicin. We found that the anti-proliferative activity of capsaicin is correlated with a decrease in the expression of E2F-responsive proliferative genes like cyclin E, thymidylate synthase, cdc25A and cdc6, both at mRNA and protein levels.

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http://www.wjgnet.com/1007-9327/11/6254.pdf

Capsaicin-induced cell death in a human gastric adenocarcinoma cell line

Capsaicin, a pungent ingredient found in red pepper, has long been used in spices, food additives, and drugs. Cell death induced by the binding of capsaicin was examined in a human gastric adenocarcinoma cell line (AGS cells). Recently, a series of studies have demonstrated that capsaicin inhibits mutagenicity and DNA binding of some chemical carcinogens, possibly by suppressing their metabolic activation[16-18]. With cells in culture, capsaicin-inhibited proliferation of HeLa, ovarian carcinoma, and mammary adenocarcinoma by decreasing NADH oxidase activity[19]. Capsaicin can also alter the expression of tumor forming-related genes by mediating the overexpression of p53 and/or c-myc genes in a Korean stomach cancer cell line[20]. Capsaicin was found to induce apoptosis in T cells by increasing the reactive oxygen species and by a subsequent mitochondrial ransmembrane potential[21]. In this report, we examined the underlying mechanism by which capsaicin induces apoptotic cell death in a

human gastric adenocarcinoma cell line (AGS).

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http://www.springerlink.com/content/121j57kv01068g0q/

Capsaicin-induced apoptosis and reduced release of reactive oxygen species in MBT-2 Murine Bladder Tumor cells

Capsaicin, the major pungent ingredient in genusCapsicum, has recently been tried as an intravesical drug for overactive bladder and it has also been shown to induce apoptotic cell death in many cancer cells. In this study, we investigated the apoptosis-inducing effect and alterations in the cellular redox state of capsaicin in MBT-2 murine bladder tumor cells. Capsaicin induced apoptotic MBT-2 cell death in a time- and dose-dependent manner. The capsaicin-induced apoptosis was blocked by the pretreatment with Z-VAD-fmk, a broad-range caspase inhibitor, or AcDEVD-CHO, a caspase-3 inhibitor.

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http://www.spandidos-publications.com/or/21/3/665

Capsaicin-induced apoptosis in human breast cancer MCF-7 cells through caspase-independent pathway

Our results suggest that capsaicin induces cellular apoptosis through a caspase-independent pathway in MCF-7 cells, and that reactive oxygen species and intracellular calcium ion fluctuation has a minimal role in the process.

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http://www.ncbi.nlm.nih.gov/pubmed/17292493

TRPV6 mediates capsaicin-induced apoptosis in gastric cancer cells

In this study, both gastric cancer and normal epithelial cells were treated with capsaicin and examined for apoptosis by Annexin V binding. Our results showed that capsaicin induces apoptosis in both cells, although cancer cells are more susceptible. This susceptibility is dependent on the availability of TRPV6, a calcium-selective channel protein, as overexpression of TRPV6 in normal cells increased capsaicin-induced apoptosis and knockdown of TRPV6 in cancer cells suppressed this action. Our results further demonstrated that capsaicin increases mitochondrial permeability through activation of Bax and p53 in a JNK-dependent manner.

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http://www.medicalnewstoday.com/articles/41022.php

Capsaicin Shows Promise In Inhibiting Growth Of Pancreatic Cancer

“In our study, we discovered that capsaicin fed orally to mice with human pancreatic tumors was an extremely effective inhibitor of the cancer process, inducing apoptosis in cancer cells,” said Sanjay K. Srivastava, Ph.D., lead investigator and assistant professor, department of pharmacology, University of Pittsburgh School of Medicine. “Capsaicin triggered the

cancerous cells to die off and significantly reduced the size of the tumors."

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http://www.ncbi.nlm.nih.gov/pubmed/19592070

Capsaicin Mediates Cell Death in Bladder Cancer T24 Cells Through Reactive Oxygen Species Production and Mitochondrial Depolarization

RESULTS: CAP decreased the viability of T24 cells in a dose-dependent manner without marked apoptosis. CAP induced ROS production and mitochondrial membrane depolarization, thereby inducing cell death, not apoptosis, in T24 cells at a concentration of 100 microM or higher. Furthermore, these effects of CAP could be reversed by capsazepine, the antagonist of transient receptor potential vanilloid type 1 channel. In vivo experiment showed that CAP significantly slowed the growth of T24 bladder cancer xenografts as measured by size (661.80 +/- 62.03 vs 567.02 +/- 43.94 mm(3); P <.01).
CONCLUSIONS: CAP mediates cell death in T24 cells through calcium entry-dependent ROS production and mitochondrial depolarization, and it may have a role in the management of bladder cancer.

Carotenoids

(Carrots, Sweet Potato, Kale, Apricots, Mangos, Squash, Spinach, Kale, Collard Greens, Salmon, Shellfish, Egg Yolks, Hot Peppers, Brown Algae)

http://jn.nutrition.org/cgi/content/abstract/131/12/3303

Carotenoids Affect Proliferation of Human Prostate Cancer Cells

We investigated whether various carotenoids present in foodstuffs were potentially involved in cancer-preventing action on human prostate cancer. The effects of 15 kinds of carotenoids on the viability of three lines of human prostate cancer cells, PC-3, DU 145 and LNCaP, were evaluated. When the prostate cancer cells were cultured in a carotenoid-supplemented medium for 72 h at 20 μmol/L, 5,6-monoepoxy carotenoids, namely, neoxanthin from spinach and fucoxanthin from brown algae, significantly reduced cell viability to 10.9 and 14.9% for PC-3, 15.0 and 5.0% for DU 145, and nearly zero and 9.8% for LNCaP, respectively.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1349-7006.2003.tb01352.x/abstract

Serum carotenoids and mortality from lung cancer

Higher serum levels of carotenoids such as – and ß-carotenes may play a role in preventing death from lung cancer

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http://jn.nutrition.org/cgi/content/abstract/131/5/1574

Human Breast Cancer Cells Treated with Carotenoids or Retinoids

These results demonstrate that ER status is an important, although not essential factor for breast cancer cell response to carotenoid and retinoid treatments, and the mode of action of all-t-RA in MCF-7 and Hs578T cells is not through the induction of RAR. Other mechanistic pathways that are either followed by or concomitant with growth inhibition are possible.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.1435/abstract

Carotenoids, antioxidants and ovarian cancer risk in pre- and postmenopausal women

From a population-based study of 549 cases of ovarian cancer and 516 controls, we estimated the consumption of the antioxidant vitamins A, C, D and E and various carotenoids, including alpha- and beta-carotene and lycopene, using a validated dietary questionnaire. Multivariate logistic regression was used to calculate the exposure odds ratios adjusted for established ovarian cancer risk factors. Intakes of carotene, especially alpha-carotene, from food and supplements were significantly and inversely associated with risk for ovarian cancer, predominantly in postmenopausal women. Intake of lycopene was significantly and inversely associated with risk for ovarian cancer, predominantly in premenopausal women. Food items most strongly related to decreased risk for ovarian cancer were raw carrots and tomato sauce. Consumption of fruits, vegetables and food items high in carotene and lycopene may reduce the risk of ovarian cancer.

Ceramide

http://www.scbt.com/datasheet-201375.html

Ceramide mediates cancer therapy-induced apoptosis

Ceramide, which accumulates in response to different types of cellular stress such as chemo- and radiotherapy, strongly induced expression of CD95-L, cleavage of caspases and apoptosis. Antisense CD95-L as well as dominant-negative FADD inhibited ceramide- and cellular stress-induced apoptosis.

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http://cancerres.aacrjournals.org/content/61/3/1233.abstract

Induction of Apoptotic Cell Death and Prevention of Tumor Growth by Ceramide

We measured the levels of ceramide, a candidate lipid mediator of apoptosis, in human metastatic colorectal cancer and tested in vitro and in vivo effects of various ceramide analogues in inducing apoptosis in metastatic colon cancer. Human colon cancer showed a >50% decrease in the cellular content of ceramide when compared with normal colon mucosa.

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http://www.ncbi.nlm.nih.gov/pubmed/10421266

Multidrug resistance modulators and doxorubicin synergize to elevate ceramide levels and elicit apoptosis in drug-resistant cancer cells

These results demonstrate that MDR modulators can be used separately, in combination, or in conjunction with chemotherapy at clinically relevant concentrations to manipulate cellular ceramide levels and restore sensitivity in the drug resistant setting. As such, this represents a new direction in the treatment of cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/8046331

Ionizing radiation acts on cellular membranes to generate ceramide and initiate apoptosis

The present studies show that ionizing radiation, like TNF, induces rapid sphingomyelin hydrolysis to ceramide and apoptosis in bovine aortic endothelial cells. Elevation of ceramide with exogenous ceramide analogues was sufficient for induction of apoptosis. Protein kinase C activation blocked both radiation-induced sphingomyelin hydrolysis and apoptosis, and apoptosis was restored by ceramide analogues added exogenously. Ionizing radiation acted directly on membrane preparations devoid of nuclei, stimulating sphingomyelin hydrolysis enzymatically through a neutral sphingomyelinase. These studies provide the first conclusive evidence that apoptotic signaling can be generated by interaction of ionizing radiation with cellular membranes and suggest an alternative to the hypothesis that direct DNA damage mediates radiation-induced cell kill.

Cinnamaldehyde
(Cinnamon)

http://www.ncbi.nlm.nih.gov/pubmed/12860272

Cinnamaldehyde induces apoptosis by ROS-mediated mitochondrial permeability transition in human promyelocytic leukemia HL-60 cells

Cinnamaldehyde is an active compound isolated from the stem bark of Cinnamomum cassia, a traditional oriental medicinal herb, which has been shown to inhibit tumor cell proliferation. In this study, we investigated the effects of cinnamaldehyde on the cytotoxicity, induction of apoptosis and the putative pathways of its actions in human promyelocytic leukemia cells. … Taken together, our data indicate that cinnamaldehyde induces the ROS-mediated mitochondrial permeability transition and resultant cytochrome c release. This is the first report on the mechanism of the anticancer effect of cinnamaldehyde.

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http://www.ncbi.nlm.nih.gov/pubmed/16143316

Induction of apoptotic cell death by 2'-hydroxycinnamaldehyde is involved with ERK-dependent inactivation of NF-?B in TNF-a-treated SW620 colon cancer cells

These results demonstrate that HCA inhibits cell growth through induction of apoptotic cell death by ERK pathway-dependent NF-kappaB inactivation.

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http://www.biomedcentral.com/1471-2407/10/392

Cinnamon extract induces tumor cell death through inhibition of NF?B and AP1

Cinnamon extract strongly inhibited tumor cell proliferation in vitro and induced active cell death of tumor cells by up-regulating pro-apoptotic molecules while inhibiting NF?B and AP1 activity and their target genes such as Bcl-2, BcL-xL and survivin. Oral administration of cinnamon extract in melanoma transplantation model significantly inhibited tumor growth with the same mechanism of action observed in vitro.

Citral
(Lemon Grass)

http://www.ncbi.nlm.nih.gov/pubmed/18070620

An essential oil and its major constituent isointermedeol induce apoptosis in human leukaemia HL-60 cells

An essential oil from a lemon grass variety of Cymbopogon flexuosus (CFO) and its major chemical constituent sesquiterpene isointermedeol (ISO) were investigated for their ability to induce apoptosis in human leukaemia HL-60 cells because dysregulation of apoptosis is the hallmark of cancer cells. …The easy and abundant availability of the oil combined with its suggested mechanism of cytotoxicity make CFO highly useful in the development of anti-cancer therapeutics.

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https://www.thieme-connect.com/ejournals/abstract/plantamedica/doi/10.1055/s-2005-864146

Citral is a New Inducer of Caspase-3 in Tumor Cell Lines

Citral, 3,7-dimethyl-2,6-octadien-1-al, a key component of the lemon-scented essential oils extracted from several herbal plants such as lemon grass (Cymbopogon citratus), melissa (Melissa officinalis), verbena (Verbena officinalis) is used as a food additive and as a fragrance in cosmetics. In this study, we investigated the anti-cancer potential of citral and its mode of action. Concentrations of 44.5 µM, comparable to the concentration of citral in a cup of tea prepared from 1 g of lemon grass, induced apoptosis in several hematopoietic cancer cell lines. Apoptosis was accompanied by DNA fragmentation and caspase-3 catalytic activity induction. Citral activity (22.25 µM) was compared to a reference compound like staurosporine (0.7 µM), in respect to DNA fragmentation and caspase-3 enzymatic activity. The apoptotic effect of citral depended on the a,ß-unsaturated aldehyde group.

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http://www.ncbi.nlm.nih.gov/pubmed/19656204

Citral inhibits cell proliferation and induces apoptosis and cell cycle arrest in MCF-7 cells

In this study, we investigated the effect of citral (3,7-dimethyl-2,6-octadienal), a key

component of essential oils extracted from several herbal plants, on the proliferation rate, cell cycle distribution, and apoptosis of the human breast cancer cell line MCF-7. The effects of this compound were also tested on cyclo-oxygenase activity. Citral treatment caused inhibition of MCF-7 cell growth (IC(50)-48 h: 18 x 10(-5)m), with a cycle arrest in G(2)/M phase and apoptosis induction. Moreover, we observed a decrease in prostaglandin E(2) synthesis 48 h after citral treatment. These findings suggest that citral has a potential chemopreventive effect.

Cocklebur

(Xanthium Strumarium)

http://www.anaturalhealingcenter.com/documents/Thorne/articles/lung_cancer9-4.pdf

Pharmacologically Active Natural Compounds for Lung Cancer

Regarding lung cancer, a methanolic extract of the leaves of Xanthium strumarium L. (Asteraceae) exhibited a strong inhibition of the proliferation of cultured human tumor cells, including A549 NSCLC cell line. The active constituents have been identified as 8-epi-xanthatin (Figure 1) and its epoxide, two xanthanolide sesquiterpene lactones. Their IC50 values have been calculated as 4.5 and 3.0 microM respectively, where the positive control cisplatin was 4.7 microM. (IC50 is the concentration of a compound needed to reduce growth of a population of cells by 50 percent in vitro. At higher concentrations (64 and 58 mM, respectively) the two xantholides showed a promising farnesyltransferase (FTase) inhibitory effect. 21 Farnesylation of certain oncoproteins (especially Ras proteins) is required for their oncogenic activity, and thus FTase inhibition could specifically stop Ras-mediated cellular proliferation. Synthetic FTase inhibitors have demonstrated activity against various human cancer cell lines, including NSCLC.22 An earlier study showed X. strumarium extracts are able to effectively inhibit tubuline polymerization in mammalian tissues,23 which could be a plausible explanation of these findings.

Coenzyme Q10

(Fish, chicken, peanuts, seasame seeds, pistachios, olive oil, soy beans, grapeseed, parsley, perilla, broccoli)

http://www.ishib.org/journal/19-2s3/ethn-19-02s3-17.pdf

Normalization of BCL-2 family members in breast cancer by Coenzyme Q10

Because of their integral role in intrinsic apoptosis any imbalance can lead to a variety of diseases; under expression can lead to degenerative diseases while over expression can lead to cancer and autoimmune disease. Due to their life or death role in the cell, Bcl-2 family members are currently the targets of many therapies in various disease states. Bcl-2 itself is over expressed in most tumors and all anti-apoptotic Bcl-2 family members are considered to have oncogenic potential. Conversely, the pro-apoptotic members are considered to be tumor suppressors and many mimetics are foci for cancer research. …Both pro- and anti-apoptotic protein levels were measured in the two breast cancer cell lines after Q10 exposure. Protein levels were measured at 4,8,12, and 24 hours respectively in order to capture evidence of Q10's normalizing influence on disrupted apoptotic function. In the MCF-7 cell line Bcl-2 levels were seen to significantly drop after only 4 hours of Q10 exposure.

Cuminum Cyminum
(Cumin Seeds)

http://findarticles.com/p/articles/mi_m0826/is_3_24/ai_n25378364/

Cumin: natures potent cancer combatant

This herb has been seen to effectively decrease the incidence of chemically induced tumors of the stomach, colon, and cervix. Its significant antioxidant activity and the ability to modulate the metabolism of carcinogens (toxins) explain its cancer-preventive prowess. Cumin seeds are known to induce the activity of glutathione-S-transferase, a protective enzyme that helps eliminate cancer-causing substances. Cumin offers a significant level of caffeic, chlorogenic, ferulic, and other phenolic acids that have anti-inflammatory potential.

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http://www.insipub.com/jasr/2009/1881-1888.pdf

Antitumor and Antibacterial Activities of …Cuminum Cyminum Seeds

1-(2-Ethyl, 6-Heptyl) Phenol (EHP), a biologically active compound formerly extracted bybenzene from Cuminum cyminum (cumin) Egyptian seeds and of activity against a number of fungalpathogens, exhibited antitumor activity against six types of tumor cell lines (HEPG2, HELA, HCT116,MCF7, HEP2, CACO2).

Curcumin
(Tumeric roots / powder, curry powder, yellow mustard)

http://news.bbc.co.uk/2/hi/health/8328377.stm

Turmeric Spice Kills Throat Cancer Cells

On Tuesday, the British Journal of Cancer published a propitious study from Cork Cancer Research Centre (“CCRC”) at the University College Cork in Ireland that found that curcumin —a compound in the curry spice turmeric—begins killing esophageal cancer cells within 24 hours. According to the CCRC study, curcumin ostensibly acts as a free radical scavenger that triggers a lethal cell death signal that causes cancerous cells in the throat to digest and kill themselves.

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http://www.cancerletters.info/article/S0304-3835

Induction of apoptosis in human lung cancer cells by curcumin

This study investigated the cellular and molecular changes induced by curcumin leading to the induction of apoptosis in human lung cancer cell lines—A549 and H1299. A549 is p53 proficient and H1299 is p53 null mutant. The lung cancer cells were treated with curcumin (0–160 μM) for 12–72 h. Curcumin inhibited the growth of both the cell lines in a

concentration dependent manner. Growth inhibition of H1299 cell lines was both time and concentration dependent. Curcumin induced apoptosis in both the lung cancer cell lines. A decrease in expression of p53, bcl-2, and bcl-XL was observed after 12 h exposure of 40 µM curcumin. Bak and Caspase genes remained unchanged up to 60 µM curcumin but showed decrease in expression levels at 80–160 µM. The data also suggest a p53 independent induction of apoptosis in lung cancer cells.

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http://www.ncbi.nlm.nih.gov/pubmed/8844727

Curcumin induces apoptosis in immortalized NIH 3T3 and malignant cancer cell lines

Curcumin, which is a widely used dietary pigment and spice, has been demonstrated to be an effective inhibitor of tumor promotion in mouse skin carcinogenesis. We report that curcumin induces cell shrinkage, chromatin condensation, and DNA fragmentation, characteristics of apoptosis, in immortalized mouse embryo fibroblast NIH 3T3 erb B2 oncogene-transformed NIH 3T3, mouse sarcoma S180, human colon cancer cell HT-29, human kidney cancer cell 293, and human hepatocellular carcinoma Hep G2 cells

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http://www.ncbi.nlm.nih.gov/pubmed/8844727

Curcumin induces apoptosis in human breast cancer cells

The aim of this study was to determine the mechanisms of curcumin-induced human breast cancer cell apoptosis. From quantitative image analysis data showing an increase in the percentage of cells with a sub-G0/G1 DNA content, we demonstrated curcumin-induced apoptosis in the breast cancer cell line MCF-7, in which expression of wild-type p53 could be induced. Apoptosis was accompanied by an increase in p53 level as well as its DNA-binding activity followed by Bax expression at the protein level. Further experiments using p53-null MDAH041 cell as well as low and high p53-expressing TR9-7 cell, in which p53 expression is under tight control of tetracycline, established that curcumin induced apoptosis in tumor cells via a p53-dependent pathway in which Bax is the downstream effector of p53. This property of curcumin suggests that this molecule could have a possible therapeutic potential in breast cancer patients.

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http://onlinelibrary.wiley.com/doi/10.1002/pros.1074/abstract

Curcumin inhibits proliferation, induces apoptosis, and inhibits angiogenesis of LNCaP prostate cancer cells in vivo

Curcumin causes a marked decrease in the extent of cell proliferation as measured by the BrdU incorporation assay and a significant increase in the extent of apoptosis as measured by an in situ cell death assay. Moreover, a significant decrease in the microvessel density as measured by the CD31 antigen staining was also seen.

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http://cancerres.aacrjournals.org/content/59/3/597.abstract

Chemopreventive Effect of Curcumin…during the Promotion/Progression Stages of Colon Cancer

The inhibition of adenocarcinomas of the colon was, in fact, dose dependent. Administration of curcumin to the rats during the initiation and postinitiation stages and throughout the promotion/progression stage increased apoptosis in the colon tumors as compared to colon tumors in the groups receiving AOM and the control diet. Thus, chemopreventive activity of curcumin is observed when it is administered prior to, during, and after carcinogen treatment as well as when it is given only during the promotion/progression phase (starting late in premalignant stage) of colon carcinogenesis.

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http://onlinelibrary.wiley.com/doi/10.1002/cncr.21904/abstract

Notch-1 down-regulation by curcumin is associated with the inhibition of cell growth and the induction of apoptosis in pancreatic cancer cells

Curcumin inhibited cell growth and induced apoptosis in pancreatic cancer cells. Notch-1, Hes-1, and Bcl-XL expression levels concomitantly were down-regulated by curcumin treatment. These results correlated with the inactivation of NF-?B activity and increased apoptosis induced by curcumin. The down-regulation of Notch-1 by small-interfering RNA prior to curcumin treatment resulted in enhanced cell growth inhibition and apoptosis.

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http://www.ncbi.nlm.nih.gov/pubmed/8950193

Curcumin, an antioxidant and anti-tumor promoter, induces apoptosis in human leukemia cells

Curcumin, widely used as a spice and coloring agent in food, possesses potent antioxidant, anti-inflammatory and anti-tumor promoting activities. In the present study, curcumin was found to induce apoptotic cell death in promyelocytic leukemia HL-60 cells at concentrations as low as 3.5 micrograms/ml.

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http://www.ncbi.nlm.nih.gov/pubmed/16376585

Antiproliferation and apoptosis induced by curcumin in human ovarian cancer cells

Curcumin, an active ingredient from the rhizome of the plant, Curcuma longa, has antioxidant, anti-inflammatory and anti-cancer activities. It has recently been demonstrated that the chemopreventive activities of curcumin might be due to its ability to inhibit cell growth and induce apoptosis. In the present study, we have investigated the effects of curcumin on growth and apoptosis in the human ovarian cancer cell line Ho-8910 by MTT assay, fluorescence microscopy, flow cytometry and Western blotting. Our data revealed that curcumin could significantly inhibit the growth and induce apoptosis in Ho-8910 cells. A decrease in expression of Bcl-2, Bcl-X(L) and pro-caspase-3 was observed after exposure to 40 microM curcumin, while the levels of p53 and Bax were increased in the curcumin-treated cells. These activities may contribute to the anticarcinogenic action of curcumin.

Daidzein
(Soybeans, Kwao Krua & Kudzu)

http://www.ncbi.nlm.nih.gov/pubmed/15304310

Biphasic effect of daidzein on cell growth of human colon cancer cells

LoVo cells were treated with 0.1, 1, 5, 10, 50 and 100 microM daidzein for 2, 3, 4 or 5 d. The results indicated that daidzein stimulated the growth of LoVo cells at 0.1 and 1 microM whereas at higher concentrations (10, 50 and 100 microM) cell growth was inhibited in a dose-dependent manner. Treatment of daidzein at 10, 50 and 100 microM resulted in cell cycle arrest at G0/G1 phase, DNA fragmentation and increases in caspase-3 activity. There were no changes in alkaline phosphatase activity (ALP), an indicator of cell differentiation, upon treatment with daidzein when compared to controls. These results indicate that daidzein has a biphasic effect on LoVo cell growth and its tumor suppressive effect is by means of cell cycle arrest and apoptosis but not through cell differentiation.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1048-891X.2004.14525.x/abstract

Effect of daidzein on cell growth, cell cycle, and telomerase activity of human cervical cancer in vitro

The inductive effects of apoptosis were more obviously observed in low-concentration groups. After HeLa cells were treated with daidzein, the expression of human telomerase catalytic subunit mRNA decreased. These meant that daidzein affected human nonhormone-dependent cervical cancer cells in several ways, including cell growth, cell cycle, and telomerase activity in vitro.

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http://www.ncbi.nlm.nih.gov/pubmed/15040033

Effects of daidzein on estrogen-receptor-positive and negative pancreatic cancer cells in vitro

Daidzein has antiproliferative effects on human estrogen-receptor-positive and negative pancreatic cancer cells, but their mechanisms may be different.

Dihydroxybenzaldehyde
(Barley & Xanthium Strumarium seeds, Chaga Mushroom)

http://www.informaworld.com/index/905739960.pdf

Apoptotic cell death through inhibition of protein kinase CKII activity by 3,4-dihydroxybenzaldehyde purified from Xanthium strumarium

The CKII inhibitory compound was purified from the fruit of Xanthium strumarium by organic solvent extraction and silica gel chromatography. The inhibitory compound was

identified as 3,4-dihydroxybenzaldehyde by analysis with FT-IR, FAB-Mass, EI-Mass, (1)H-NMR and (13)C-NMR. 3,4-dihydroxybenzaldehyde inhibited the phosphotransferase activity of CKII with IC(50) of about 783 microM. Steady-state studies revealed that the inhibitor acts as a competitive inhibitor with respect to the substrate ATP. A value of 138.6 microM was obtained for the apparent K(i). Concentration of 300 microM 3,4-dihydroxybenzaldehyde caused 50% growth inhibition of human cancer cell U937. 3,4-dihydroxybenzaldehyde-induced cell death was characterised with the cleavage of poly(ADP-ribose) polymerase and procaspase-3. Furthermore, the inhibitor induced the fragmentation of DNA into multiples of 180 bp, indicating that it triggered apoptosis. This induction of apoptosis by 3,4-dihydroxybenzaldehyde was also confirmed by using flow cytometry analysis. Since CKII is involved in cell proliferation and oncogenesis, these results suggest that 3,4-dihydroxybenzaldehyde may function by inhibiting oncogenic disease, at least in part, through the inhibition of CKII activity.

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http://www.ncbi.nlm.nih.gov/pubmed/19022639

3,4-dihydroxybenzaldehyde purified from the barley seeds (Hordeum vulgare) inhibits oxidative DNA damage and apoptosis via its antioxidant activity

In antioxidant activity assay such as DPPH radical and hydroxyl radical scavenging assay, Fe(2+) chelating assay, and intracellular ROS scavenging assay by DCF-DA, 3,4-dihydroxybenzaldehyde was found to scavenge DPPH radical, hydroxyl radical and intracellular ROS. Also it chelated Fe(2+). In in vitro oxidative DNA damage assay and the expression level of phospho-H2A.X, it inhibited oxidative DNA damage and its treatment decreased the expression level of phospho-H2A.X. And in oxidative cell death and apoptosis assay via MTT assay and Hoechst 33342 staining, respectively, the treatment of 3,4-dihydroxybenzaldehyde attenuated H(2)O(2)-induced cell death and apoptosis. These results suggest that the barley may exert the inhibitory effect on H(2)O(2)-induced tumor development by blocking H(2)O(2)-induced oxidative DNA damage, cell death and apoptosis.

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http://www.liebertonline.com/doi/abs/10.1089/jmf.2008.1149

Cancer Cell Cytotoxicity of Extracts and Small Phenolic Compounds from Chaga

The phenolic components isolated from the 80% MeOH extracts had markedly greater cancer cell toxicity than the extracts themselves. In particular, two out of seven compounds showed strong cytotoxicity towards several tumor cell lines without giving rise to significant cell toxicity toward normal cells. For example, the 50% lethal dose for 3,4-dihydroxybenzalacetone was 12.2µmol/L in PA-1 cells but was 272.8µmol/L in IMR90 cells. Fluorescence-activated cell sorting analysis further revealed these phenolic ingredients have high potentiality for apoptosis induction in PA-1 cells.

Disulfiram
(Removes copper)

http://cancerres.aacrjournals.org/content/66/21/10425.abstract

Disulfiram, a Clinically Used Anti-Alcoholism Drug and Copper-Binding Agent, Induces Apoptotic Cell Death in Breast Cancer

Copper has been shown to be essential for tumor angiogenesis processes. Consistently, high serum and tissue levels of copper have been found in many types of human cancers, including breast, prostate, and brain, supporting the idea that copper could be used as a potential tumor-specific target. Here we report that the DSF-copper complex potently inhibits the proteasomal activity in cultured breast cancer MDA-MB-231 and MCF10DCIS.com cells, but not normal, immortalized MCF-10A cells, before induction of apoptotic cancer cell death. Furthermore, MDA-MB-231 cells that contain copper at concentrations similar to those found in patients, when treated with just DSF, undergo proteasome inhibition and apoptosis. In addition, when administered to mice bearing MDA-MB-231 tumor xenografts, DSF significantly inhibited the tumor growth (by 74%), associated with in vivo proteasome inhibition (as measured by decreased levels of tumor tissue proteasome activity and accumulation of ubiquitinated proteins and natural proteasome substrates p27 and Bax) and apoptosis induction (as shown by caspase activation and apoptotic nuclei formation).

Ellagic Acid

(Blackberries, Raspberries, Strawberries, Cranberries, Grapes, Walnuts, Pecans, Pomegranates, Wolfberry / Goji)

http://www.ncbi.nlm.nih.gov/pubmed/18595134

Ellagic acid induces apoptosis through inhibition of nuclear factor kappa B in pancreatic cancer cells

We show that ellagic acid, a polyphenolic compound in fruits and berries, at concentrations 10 to 50 mmol/L stimulates apoptosis in human pancreatic adenocarcinoma cells. Further, ellagic acid decreases proliferation by up to 20-fold at 50 mmol/L. Ellagic acid stimulates the mitochondrial pathway of apoptosis associated with mitochondrial depolarization, cytochrome C release, and the downstream caspase activation. Ellagic acid does not directly affect mitochondria. Ellagic acid dose-dependently decreased NF-kappa B binding activity. Furthermore, inhibition of NF-kappa B activity using IkB wild type plasmid prevented the effect of ellagic acid on apoptosis.

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http://www.cancerletters.info/article/S0304-3835

p53/p21(WAF1/CIP1) expression and its possible role in G1 arrest and apoptosis in ellagic acid treated cancer cells

Ellagic acid is a phenolic compound present in fruits and nuts including raspberries, strawberries and walnuts. It is known to inhibit certain carcinogen-induced cancers and may have other chemopreventive properties. The effects of ellagic acid on cell cycle events and apoptosis were studied in cervical carcinoma (CaSki) cells. We found that ellagic acid at a concentration of 10-5 M induced G1 arrest within 48 h, inhibited overall cell growth and induced apoptosis in CaSki cells after 72 h of treatment. Activation of the cdk inhibitory protein p21 by ellagic acid suggests a role for ellagic acid in cell cycle regulation of cancer cells.

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http://ar.iiarjournals.org/content/25/2A/971.short

Ellagic Acid Induced p53/p21 Expression, G1 Arrest and Apoptosis in Human Bladder Cancer T24 Cells

Ellagic acid significantly reduced the viable cells, induced G0/G1-phase arrest of the cell cycle and apoptosis. Ellagic acid also increased p53 and p21 and decreased CDK2 gene expression, that may lead to the G0/G1 arrest of T24 cells. Ellagic acid also promoted caspase-3 activity after exposure for 1, 3, 6, 12 and 24 h, which led to induction of apoptosis. Furthermore, the ellagic acid-induced apoptosis on T24 cells was blocked by the broad-spectrum caspase inhibitor (z-VAD-fmk).

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http://jn.nutrition.org/cgi/content/abstract/133/8/2669

Low Concentrations of Quercetin and Ellagic Acid Synergistically Influence Proliferation, Cytotoxicity and Apoptosis in MOLT-4 Human Leukemia Cells

Ellagic acid significantly potentiated the effects of quercetin (at 5 and 10 µmol/L each) in the reduction of proliferation and viability and the induction of apoptosis. Significant alterations in cell cycle kinetics were also observed. The synergy was confirmed by an isobolographic analysis of the cell proliferation data. The interaction of ellagic acid and quercetin demonstrated an enhanced anticarcinogenic potential of polyphenol combinations, which was not based solely on the additive effect of individual compounds, but rather on synergistic biochemical interactions.

Emodin

(Rheum Emodi / Himalayan rhubarb).

http://www.ncbi.nlm.nih.gov/pubmed/12892828

Emodin induces apoptosis of human cervical cancer cells

Emodin (1,3,8-trihydroxy-6-methylanthraquinone) is an active herbal component traditionally used in China for treating various ailments. Emodin exerts antiproliferative effects in many cancer cell lines and the actual molecular mechanism of which is still not clear. Since apoptosis could be a potential mechanism to explain these effects, we tested whether emodin induces cell death in human cervical cancer cells. Our results suggest that emodin exerts antiproliferative effects in human cervical cancer cells. Emodin inhibited DNA synthesis and induced apoptosis as demonstrated by increased nuclear condensation, annexin binding and DNA fragmentation in Bu 25TK cells in the presence of emodin. Moreover, we demonstrate for the first time in human cervical cancer cells that the apoptotic pathway involved in emodin-induced apoptosis is caspase-dependent and presumably through the mitochondrial pathway, as shown by the activation of caspases-3, -9 and cleavage of poly(ADP-ribose) polymerase.

Epigallocatechin

(Green Tea)

http://www.ncbi.nlm.nih.gov/pubmed/16945390

Role of epigallocatechin gallate (EGCG) in the treatment of breast and prostate cancer

Green tea and its major constituent epigallocatechin gallate (EGCG) have been extensively studied as a potential treatment for a variety of diseases, including cancer. Epidemiological data have suggested that EGCG may provide protective effects against hormone related cancers, namely breast or prostate cancer. Extensive in vitro investigations using both hormone responsive and non-responsive cell lines have shown that EGCG induces apoptosis and alters the expression of cell cycle regulatory proteins that are critical for cell survival and apoptosis. This review will highlight the important in vitro mechanistic actions elicited by EGCG in various breast and prostate cancer cell lines. Additionally, the actions of green tea/EGCG in in vivo models for these cancers as well as in clinical trials will be discussed.

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http://carcin.oxfordjournals.org/cgi/content/abstract/26/5/958

Epigallocatechin-3-gallate induces mitochondrial membrane depolarization and caspase-dependent apoptosis in pancreatic cancer cells

In pursuit of our investigations to dissect the molecular mechanism of EGCG action on pancreatic cancer, we observed that the antiproliferative action of EGCG on pancreatic carcinoma is mediated through programmed cell death or apoptosis as evident from nuclear condensation, caspase-3 activation and poly-ADP ribose polymerase (PARP) cleavage. EGCG-induced apoptosis of pancreatic cancer cells is accompanied by growth arrest at an earlier phase of the cell cycle.

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http://www.pnas.org/content/99/19/12455.abstract

Topical applications of caffeine or (-)-epigallocatechin gallate (EGCG) inhibit carcinogenesis and selectively increase apoptosis in UVB-induced skin tumors in mice

SKH-1 hairless mice were irradiated with ultraviolet B (UVB) twice weekly for 20 weeks. These tumor-free mice, which had a high risk of developing skin tumors during the next several months, were then treated topically with caffeine (6.2 μmol) or (-)-epigallocatechin gallate (EGCG; 6.5 μmol) once a day 5 days a week for 18 weeks in the absence of further treatment with UVB. Topical applications of caffeine to these mice decreased the number of nonmalignant and malignant skin tumors per mouse by 44% and 72%, respectively. Topical applications of EGCG decreased the number of nonmalignant and malignant tumors per mouse by 55% and 66%, respectively. Immunohistochemical analysis showed that topical applications of caffeine or EGCG increased apoptosis as measured by the number of caspase 3-positive cells in nonmalignant skin tumors by 87% or 72%, respectively, and in squamous cell carcinomas by 92% or 56%, respectively, but there was no effect on apoptosis in nontumor areas of the epidermis.

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http://www.ncbi.nlm.nih.gov/pubmed/17266926

A component of green tea, (-)-epigallocatechin-3-gallate, promotes apoptosis in T24 human bladder cancer cells

Bladder cancer is the fourth most common cancer in men and ninth most common in women. It has a protracted course of progression and is thus an ideal candidate for chemoprevention strategies and trials. This study was conducted to evaluate the chemopreventive/antiproliferative potential of (-)-epigallocatechin gallate (EGCG, the major phytochemical in green tea) against bladder cancer and its mechanism of action. Using the T24 human bladder cancer cell line, we found that EGCG treatment caused dose- and time-dependent inhibition of cellular proliferation and cell viability, and induced apoptosis. Mechanistically, EGCG inhibits phosphatidylinositol 3'-kinase/Akt activation that, in turn, results in modulation of Bcl-2 family proteins, leading to enhanced apoptosis of T24 cells. These findings suggest that EGCG may be an important chemoprevention agent for the management of bladder cancer.

Evening Primrose

http://news.bbc.co.uk/2/hi/health/4395826.stm

Plant oil acts like cancer drug

Scientists have pinpointed how evening primrose oil fights breast tumours. It is down to a substance in the oil called gamma-linolenic acid that acts on the same receptor in tumours as the powerful breast cancer drug Herceptin. Unlike Herceptin, which blocks the Her-2/neu receptor, GLA interferes with the gene carrying the DNA code needed to make the receptor work. The US work in the Journal of the National Cancer Institute applies to about 30% breast cancers.

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http://www.ncbi.nlm.nih.gov/pubmed/14580681

Caspase-independent apoptosis induced by evening primrose extract in Ehrlich ascites tumor cells

The EPE-induced translocation of AIF was suppressed with the addition of catalase, suggesting that the rapid intracellular peroxide levels after addition of EPE triggers off induction of apoptosis, which is AIF-mediated and caspase-independent.

Figs
(Ficus carica)

http://pubs.acs.org/doi/abs/10.1021/np000592z

Suppressors of Cancer Cell Proliferation from Fig (Ficus carica) Resin

A mixture of 6-O-acyl-ß-d-glucosyl-ß-sitosterols, the acyl moeity being primarily palmitoyl and linoleyl with minor amounts of stearyl and oleyl, has been isolated as a potent cytotoxic agent from fig (Ficus carica) latex and soybeans. Identity was established by spectroscopic

methods (NMR, MS) and confirmed by chemical synthesis. Both the natural and the synthetic compounds showed in vitro inhibitory effects on proliferation of various cancer cell lines.

Fisetin

(Acacia greggii, Acacia berlandieri, yellow dye young fustic from Rhus cotinus / Eurasian smoketree, Butea frondosa / parrot tree, Gleditschia triacanthos, Quebracho colorado, genus Rhus, Callitropsis nootkatensis / yellow cypresses, & mangoes)

http://carcin.oxfordjournals.org/cgi/content/abstract/29/5/1049

Fisetin, a novel dietary flavonoid, causes apoptosis and cell cycle arrest in human prostate cancer LNCaP cells

There was also induction of mitochondrial release of cytochrome c into cytosol, downregulation of X-linked inhibitor of apoptosis protein and upregulation of second mitochondria-derived activator of caspase/direct inhibitor of apoptosis-binding protein with low pI on treatment of cells with fisetin. Treatment of cells with fisetin also resulted in significant activation of caspases-3, -8 and -9. Pretreatment of cells with caspase inhibitor (Z-VAD-FMK) blocked fisetin-induced activation of caspases. These data provide the first evidence that fisetin could be developed as an agent against PCa.

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http://carcin.oxfordjournals.org/cgi/content/abstract/30/2/300

A plant flavonoid fisetin induces apoptosis in colon cancer cells by inhibition of COX2 and Wnt/EGFR/NF-B-signaling pathways

Fisetin treatment of cells also inhibited the activation of EGFR and nuclear factor-kappa B (NF-B). Finally, the formation of colonies in soft agar was suppressed by fisetin treatment. Taken together, we provide evidence that the plant flavonoid fisetin can induce apoptosis and suppress the growth of colon cancer cells by inhibition of COX2- and Wnt/EGFR/NF-B-signaling pathways. We suggest that fisetin could be a useful agent for prevention and treatment of colon cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/15572302

Flavonoids Induce Apoptosis in Human Leukemia U937 Cells Through Caspase- and Caspase-Calpain-Dependent Pathways

At lower concentrations, these compounds were also able to sensitize these cells to apoptosis induced by tumor necrosis factor-. Regarding the mechanisms, galangin, luteolin, chrysin, and quercetin induced apoptosis in a way that required the activation of caspases 3 and 8, but not caspase 9. In contrast, an active role of calpains in addition to caspases was demonstrated in apoptosis induced by fisetin, apigenin, and 3,7-dihydroxyflavone. Our data show evidence of the proapoptotic properties of some flavonoids that could support their rational use as chemopreventive and therapeutic agents against carcinogenic disease.

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http://cancerres.aacrjournals.org/content/68/20/8555.abstract

Fisetin Inhibits Androgen Receptor Signaling and Tumor Growth in Athymic Nude Mice

Treatment with fisetin in athymic nude mice implanted with AR-positive CWR22R?1 human PCa cells resulted in inhibition of tumor growth and reduction in serum PSA levels. These data identify fisetin as an inhibitor of AR signaling axis and suggest that it could be a useful chemopreventive and chemotherapeutic agent to delay progression of PCa.

Fucoidan

(brown seaweed such as Kombu, Limu Moui, Bladderwrack, Wakame, Mozuku, and Hijiki)

http://www.ncbi.nlm.nih.gov/pubmed/19801840

Apoptosis inducing activity of fucoidan in HCT-15 colon carcinoma cells

The antitumor activity of fucoidan from Fucus vesiculosus was investigated in human colon carcinoma cells. The crude fucoidan, a polysaccharide composed predominantly of sulfated fucose, markedly inhibited the growth of HCT-15 cells (human colon carcinoma cells). After HCT-15 cells were treated with fucoidan, several apoptotic events such as DNA fragmentation, chromatin condensation and increase of the population of sub-G1 hypodiploid cells were observed. …Furthermore, the induction of apoptosis was also accompanied by a strong activation of extracellular signal-regulated kinase (ERK) and p38 kinase and an inactivation of phosphatidylinositol 3-kinase (PI3K)/Akt in a time-dependent manner. These findings provide evidence demonstrating that the pro-apoptotic effect of fucoidan is mediated through the activation of ERK, p38 and the blocking of the PI3K/Akt signal pathway in HCT-15 cells. These data support the hypothesis that fucoidan may have potential in colon cancer treatment.

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http://www.ncbi.nlm.nih.gov/pubmed/19754176

Fucoidan induces apoptosis through activation of caspase-8 on human breast cancer MCF-7 cells

Fucoidan is an active component of seaweed that has been shown to inhibit proliferation and induce apoptotic cell death in several tumor cells. However, the detailed mechanisms underlying this process have not yet been elucidated. In the present report, we investigated the effect of fucoidan on the induction of apoptosis in human breast cancer MCF-7 cells. Our data demonstrated that fucoidan reduced the viable cell number of MCF-7 cells in a dose- and time-dependent manner. In contrast, fucoidan did not affect the viable cell number of normal human mammary epithelial cells. Results from the apoptosis assay demonstrated that fucoidan induced internucleosomal DNA fragmentation, chromatin condensation, activation of caspase-7, -8, and -9, and cleavage of poly(ADP ribose) polymerase.

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http://pubs.acs.org/doi/abs/10.1021/jf9010406

Fucoidan Induces Apoptosis of Human HS-Sultan Cells (Leukemia)

Fucoidan-induced apoptosis was accompanied by the activation of caspase-3 and was partially prevented by pretreatment with a pan-caspase inhibitor, Z-VAD-FMK. The mitochondrial potential in HS-Sultan cells was decreased 24 hr after treatment with fucoidan, indicating that fucoidan induced apoptosis through a mitochondrial pathway. When HS-Sultan was treated with 100 mg/mL fucoidan for 24 hr, phosphorylation of ERK and GSK markedly decreased. In contrast, phosphorylation of p38 and Akt was not altered by treatment with fucoidan. L-Selectin and P-selectin are known to be receptors of fucoidan; however, as HS-Sultan does not express either of these selectins, it is unlikely that fucoidan induced apoptosis through them in HS-Sultan. The neutralizing antibody, Dreg56, against human L-selectin did not prevent the inhibitory effect of fucoidan on the proliferation of IM9 and MOLT4 cells, both of which express L-selectin; thus it is possible fucoidan induced apoptosis though different receptors. These results demonstrate that fucoidan has direct anti-cancer effects on human HS-Sultan cells through caspase and ERK pathways.

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http://www.spandidos-publications.com/mmr/1/4/537

Fucoidan, a major component of brown seaweed, prohibits the growth of human cancer cell lines in vitro

The results revealed that cell proliferation was suppressed in 13 cell lines in a time- and/or dose-dependent manner; this suppression was marked in the hepatocellular carcinoma, cholangiocarcinoma and gallbladder carcinoma cell lines. In contrast, proliferation of the neuroblastoma and 1 of the 2 ovarian carcinoma cell lines was not affected.

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http://www.britannica.com/bps/additionalcontent/18/37697185/Inhibitory-Effect-of-Fucoidan-on-Huh7-Hepatoma-Cells-Through-Downregulation-of-CXCL12

Inhibitory Effect of Fucoidan on Huh7 Hepatoma Cells (Liver Cancer) Through Downregulation of CXCL12

Western blotting revealed that the amount of Œ±-fetoprotein was decreased by 1.0 mg/ml of fucoidan in Huh7 cells, whereas it was unchanged in HepG2 cells. In Huh7 cells, CXCL12 mRNA expression was significantly downregulated by 1.0 mg/ml of fucoidan, whereas CXCR4 mRNA expression was unchanged by fucoidan. CXCL12 and CXCR4 mRNA were barely expressed in HepG2 cells. In addition, 1.0 mg/ml of fucoidan mildly arrested the cell cycle and induced apoptosis in Huh7 cells. The findings suggest that fucoidan exhibits antitumor activity toward Huh7 cells through the downregulation of CXCL12 expression.

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http://www.liebertonline.com/doi/abs/10.1089/jmf.2008.1114

Ethyl Alcohol Extracts of Hizikia fusiforme Sensitize AGS Human Gastric Adenocarcinoma Cells (Bone Marrow Cancer)

Resistance to tumor necrosis factor-related apoptosis-inducing ligand (TRAIL)-induced apoptosis has been reported in some cancer cells, including AGS human gastric

adenocarcinoma cells. Hizikia fusiforme is a commonly used brown seaweed species in Korea that possesses potent antibacterial, antifungal, and anti-inflammatory activities. In this study, we demonstrated that treatment with TRAIL in combination with subtoxic concentrations of ethyl alcohol extract of H. fusiforme (EAHF) sensitized TRAIL-resistant AGS cells to TRAIL-mediated apoptosis. Combined treatment with EAHF and TRAIL increased chromatin condensation, DNA fragmentation, and sub-G1-phase DNA content.

Genistein

(Lupin, Fava Beans, Soybeans, Kudzu, Psoralea, Coffee, & Flemingia Vestita)

http://www.ncbi.nlm.nih.gov/pubmed/9795970

Genistein-induced G2-M arrest, p21WAF1 upregulation, and apoptosis in a non-small-cell lung cancer cell line

Our results showed that genistein can upregulate p21WAF1 expression in genistein-treated cells. From these results, we conclude that genistein may act as an anticancer agent, and further studies may prove its efficacy in non-small lung cancer cells. Thus the biological effects of genistein may, indeed, be due to the modulation of cell growth, cell death, and cell cycle regulatory molecules.

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http://www.ncbi.nlm.nih.gov/pubmed/7833143

Growth-inhibitory effects of the natural phyto-oestrogen genistein in MCF-7 human breast cancer cells

The low incidence of breast cancer in countries with a flavonoid-rich soy-based diet and the protection afforded by soy-derived products against experimental mammary tumours in rats suggest that genistein and other isoflavonoid compounds may exert an anti-tumour activity. We analysed the effects of genistein on cell number and cell cycle progression (flow cytometric analysis of propidium iodide-stained nuclei) of human breast cancer cells (MCF-7) in vitro. Genistein produced a significant, dose-dependent inhibition of MCF-7 cell growth with an ID50 of approximately 40 microM after 72 h of incubation.

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http://www.ncbi.nlm.nih.gov/pubmed/10050261

Genistein-induced upregulation of p21WAF1, downregulation of cyclin B, and induction of apoptosis in prostate cancer cells

Here we report that genistein inhibits PCa cell growth in culture in a dose-dependent manner, which is accompanied by a G2/M cell cycle arrest. Cell growth inhibition was observed with concomitant downregulation of cyclin B, upregulation of the p21WAF1 growth-inhibitory protein, and induction of apoptosis. Collectively, these results provide experimental evidence for a novel effect of genistein on cell cycle gene regulation, resulting in the inhibition of cell growth and ultimate demise of tumor cells.

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http://www.ncbi.nlm.nih.gov/pubmed/10762754

Genistein induces apoptosis and topoisomerase II-mediated DNA breakage in colon cancer cells

The present study was undertaken to determine if (a) genistein induces topo II-mediated DNA damage in HT-29 colon cancer cells; and (b) if this damage is required to induce apoptosis. DNA damage was evaluated using the comet assay. Apoptosis was determined by the ethidium bromide/acridine orange staining technique. DNA breakage was noted within 1 h of treatment. Apoptosis was only induced with high concentrations (>/=60 microM) of genistein. Marked inhibition of HT-29 cell growth was evident at concentrations ranging from 60 to 150 microM. This was associated with a cell cycle arrest at G(2)/M. Similar findings were obtained in SW-620 and SW-1116 colon cancer cell lines. Aclarubicin, a topo II antagonist, reduced genistein-induced DNA breaks but did not reduce apoptosis. These data suggest that, in colon cancer cells, topo II serves as the enzymatic target of genistein. Furthermore, topo II-mediated DNA cleavage is not required for the induction of apoptosis.

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http://clincancerres.aacrjournals.org/content/6/1/230.abstract

The Potential of Soybean Foods as a Chemoprevention Approach for Human Urinary Tract Cancer

Furthermore, both genistein and combined isoflavones exhibited a significant tumor suppressor effect in vivo ($P < 0.05$). The results justify the potential use of soybean foods as a practical chemoprevention approach for patients with urinary tract cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/12657953

Prevention of metastatic pancreatic cancer growth in vivo by induction of apoptosis with genistein, a naturally occurring isoflavonoid

In vivo, genistein significantly improved survival, almost completely inhibited metastasis, and increased apoptosis in an orthotopic model of pancreatic cancer. In vitro genistein treatment resulted in apoptosis in all pancreatic cancer cell lines tested, and this appeared to be mediated by activation of caspase-3.

Ginger

http://www.ncbi.nlm.nih.gov/pubmed/12969783

Dietary ginger constituents, galanals A and B, are potent apoptosis inducers in Human T lymphoma Jurkat cells

The effects of the constituents isolated from ginger species including curcumin, 6-gingerol and labdane-type diterpene compounds on cell proliferation and the induction of apoptosis in the cultured human T lymphoma Jurkat cells were studied. Among the tested compounds, galanals A and B, isolated from the flower buds of a Japanese ginger, myoga (Zingiber mioga

Roscoe), showed the most potent cytotoxic effect. …In conclusion, the results from this study provide biological evidence that ginger-specific constituents other than curcuminoids are potential anticancer agents.

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http://www.ncbi.nlm.nih.gov/pubmed/17706603

Ginger ingredients reduce viability of gastric cancer cells via distinct mechanisms

We found that 6-gingerol, a phenolic alkanone isolated from ginger, enhanced the TRAIL-induced viability reduction of gastric cancer cells while 6-gingerol alone affected viability only slightly. 6-Gingerol facilitated TRAIL-induced apoptosis by increasing TRAIL-induced caspase-3/7 activation. 6-Gingerol was shown to down-regulate the expression of cIAP1, which suppresses caspase-3/7 activity, by inhibiting TRAIL-induced NF-kappaB activation. As 6-shogaol has a chemical structure similar to 6-gingerol, we also assessed the effect of 6-shogaol on the viability of gastric cancer cells. Unlike 6-gingerol, 6-shogaol alone reduced the viability of gastric cancer cells. 6-Shogaol was shown to damage microtubules and induce mitotic arrest. These findings indicate for the first time that in gastric cancer cells, 6-gingerol enhances TRAIL-induced viability reduction by inhibiting TRAIL-induced NF-kappaB activation while 6-shogaol alone reduces viability by damaging microtubules.

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http://pubs.acs.org/doi/abs/10.1021/jf0624594

6-Shogaol (Alkanone from Ginger) Induces Apoptotic Cell Death of Human Hepatoma p53

In conclusion, we provide here a novel modality that can help to eradicate a p53 mutant of human hepatoma cells by using a natural consistent isolated form of ginger. These data also provide evidence to reaffirm the notion that consumption of certain foodstuffs can be beneficial to health because some of the constituents contained in them may be anticarcinogenic.

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http://www.ncbi.nlm.nih.gov/pubmed/10025876

Induction of apoptosis in HL-60 cells by pungent vanilloids, [6]-gingerol and [6]-paradol[/size]

[6]-Paradol, another pungent phenolic substance found in ginger and other Zingiberaceae plants, also has a vanilloid structure found in other chemopreventive phytochemicals including curcumin. In the present study, [6]-gingerol and [6]-paradol were found to exert inhibitory effects on the viability and DNA synthesis of human promyelocytic leukemia (HL-60) cells. The cytotoxic and antiproliferative effects of both compounds were associated with apoptotic cell death. The above results suggest that [6]-gingerol and [6]-paradol possess potential cytotoxic/cytostatic activities.

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http://onlinelibrary.wiley.com/doi/10.1002/mc.20374/abstract

Multiple mechanisms are involved in 6-gingerol-induced cell growth arrest and apoptosis in human colorectal cancer cells

The results suggest that 6-gingerol stimulates apoptosis through upregulation of NAG-1 and G1 cell cycle arrest through downregulation of cyclin D1. Multiple mechanisms appear to be involved in 6-gingerol action, including protein degradation as well as ß-catenin, PKCe, and GSK-3ß pathways.

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http://www.ncbi.nlm.nih.gov/pubmed/17683926

Gingerol inhibits metastasis of MDA-MB-231 human breast cancer cells

In conclusion, we have shown that [6]-gingerol inhibits cell adhesion, invasion, motility and activities of MMP-2 and MMP-9 in MDA-MB-231 human breast cancer cell lines.

Ginsenoside
(Ginseng Root)

http://www.ncbi.nlm.nih.gov/pubmed/10972198

Anti-proliferative effect of ginseng saponins on human prostate cancer cell line

Ginseng is a medicinal herb widely used in Asian countries, and many of its pharmacological actions are attributed to the ginsenosides. In a study of the anti-proliferative activity of ginsenosides using human prostate carcinoma LNCaP cell line, ginsenoside Rg3 displayed growth inhibitory activity. The cells lost its adherent property after incubation in the presence of 250 microM of ginsenoside for 48h.

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http://www.ncbi.nlm.nih.gov/pubmed/9618279

An Intestinal Bacterial Metabolite of Ginseng Protopanaxadiol Saponins Has the Ability to Induce Apoptosis in Tumor Cells

Our previous study demonstrated that the in vivo anti-metastatic effect induced by oral administration of ginseng protopanaxadiol saponins was mediated by their metabolic component M1, and that the growth, invasion and migration of tumor cells were inhibited by M1 but not by ginsenosides. Here we investigated the inhibitory mechanism of M1 on the growth of tumor cells. M1 inhibited the proliferation of B16-BL6 mouse melanoma cells in a time- and dose-dependent manner, with accompanying morphological changes at the concentration of 20 microM. In addition, at 40 microM M1 induced apoptotic cell death within 24 h. Fluorescence microscopy revealed that dansyl M1 entered the cytosol and quickly reached the nuclei (approximately 15 min). Western blot analysis revealed that M1 rapidly up-regulated the expression of p27Kip1, but down-regulated the expression of c-Myc and cyclin D1 in a time-dependent manner. Thus, the regulation of apoptosis-related proteins by M1 is responsible for the induction of apoptotic cell death, and this probably leads to the anti-metastatic activity in vivo.

http://www.ncbi.nlm.nih.gov/pubmed/10503876

Antitumor activity of a novel ginseng saponin metabolite in human pulmonary adenocarcinoma cells resistant to cisplatin

The in vitro antitumor activity of a novel ginseng saponin metabolite, 20-O-beta-D-glucopyranosyl-20(S)-protopanaxadiol (IH-901), was examined against four human cancer cell lines and one subline resistant to cisplatin (CDDP). The growth inhibitory activity of the compound was estimated by MTT tetrazolium assay. The mean concentrations of IH-901 needed to inhibit the proliferation of the cells by 50% (IC50) were 24.3, 25.9, 56.6 and 24.9 microM against human myeloid leukemia (HL-60), pulmonary adenocarcinoma (PC-14), gastric adenocarcinoma (MKN-45) and hepatoma (HepG2) cell lines, respectively. These values are higher than that of CDDP. In the CDDP-resistant PC/DDP cell line, the IC50 values of IH-901 and CDDP were 20.3 and 60.8 microM, respectively. These results suggest that IH-901 is not cross-resistant to CDDP in this cell line and could be a candidate for the treatment of CDDP resistant pulmonary cancer.

Grape Seed Extract

http://clincancerres.aacrjournals.org/content/15/1/140.abstract

Induction of Apoptosis in Human Leukemia Cells by Grape Seed Extract Occurs via Activation of c-Jun NH2-Terminal Kinase

Conclusions: The result of the present study showed that GSE induces apoptosis in Jurkat cells through a process that involves sustained JNK activation and Cip1/p21 up-regulation, culminating in caspase activation.

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http://carcin.oxfordjournals.org/cgi/content/short/23/11/1869

Grape seed extract induces apoptotic death of human prostate carcinoma DU145 cells

Together, these results suggest that GSE possibly causes mitochondrial damage leading to cytochrome c release in cytosol and activation of caspases resulting in PARP cleavage and execution of apoptotic death of human PCA DU145 cells. Furthermore, GSE-caused caspase 3-mediated apoptosis also involves other pathway(s) including caspase 9 activation.

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http://www.springerlink.com/content/k87838352613h062/

Synergistic Anti-Cancer Effects of Grape Seed Extract and Conventional Cytotoxic Agent Doxorubicin Against Human Breast Carcinoma Cells

In quantitative apoptosis studies, GSE and Dox alone and in combination showed comparable apoptotic death of MCF-7 cells, however, a combination of the two was inhibitory to Dox induced apoptosis in MDA-MB468 cells. This was further confirmed in another estrogen receptor-negative MDA-MB231 cell line, in which GSE and Dox combination strongly

inhibited cell growth but did not show any increase in apoptotic cell death caused by Dox. Together, these results suggest a strong possibility of synergistic efficacy of GSE and Dox combination for breast cancer treatment, independent of estrogen receptor status of the cancer cell.

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http://www.informaworld.com/smpp/content%7Edb

Grape Seed Extract Induces Cell Cycle Arrest and Apoptosis in Human Colon Carcinoma Cells

We reported recently that GSE inhibits CRC cell HT29 growth in culture and nude mice xenograft. Because GSE is available commercially through different vendors, here we assessed whether GSE from 2 different manufacturers produces comparable biological effects in a panel of human CRC cell lines. Our results show that irrespective of source, GSE strongly inhibits LoVo, HT29, and SW480 cell growth, with a G1 arrest in LoVo and HT29 cells but an S and/or G2/M arrest in SW480 cell cycle progression. GSE also induced Cip/p21 levels in all 3 cell lines. Furthermore, an induction of apoptosis was observed in all 3 cell lines by GSE. Taken together, our findings suggest that GSE could be an effective CAM agent against CRC possibly due to its strong growth inhibitory and apoptosis-inducing effects.

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http://www.cancerci.com/content/9/1/29

Induction of apoptosis in HeLa cells by chloroform fraction of seed extracts of Nigella sativa

Methanolic, n-Hexane and chloroform extracts of Nigella sativa seedz effectively killed HeLa cells. The IC50 values of methanolic, n-hexane, and chloroform extracts of Nigella sativa were 2.28 µg/ml, 2.20 µg/ml and 0.41 ng/ml, respectively. All three extracts induced apoptosis in HeLa cells. Apoptosis was confirmed by DNA fragmentation, western blot and terminal transferase-mediated dUTP-digoxigenin-end labeling (TUNEL) assay. Western Blot and TUNEL results suggested that Nigella sativa seed extracts regulated the expression of pro- and anti- apoptotic genes, indicating its possible development as a potential therapeutic agent for cervical cancer upon further investigation.

Hispolon
(Phellinus Linteus / Mushroom)

http://www.ncbi.nlm.nih.gov/pubmed/18423410

Hispolon induces apoptosis in human gastric cancer cells

Severe side effects and complications such as gastrointestinal and hematological toxicities because of current anticancer drugs are major problems in the clinical management of gastric cancer, which highlights the urgent need for novel effective and less toxic therapeutic approaches. Hispolon, an active polyphenol compound, is known to possess potent antineoplastic and antiviral properties. …Furthermore, hispolon potentiated the cytotoxicity of chemotherapeutic agents used in the clinical management of gastric cancer. These results

suggest that hispolon could be useful for the treatment of gastric cancer either as a single agent or in combination with other anticancer agents.

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http://www.ncbi.nlm.nih.gov/pubmed/19477214

Hispolon from Phellinus linteus has antiproliferative effects via MDM2-recruited ERK1/2 activity in breast and bladder cancer cells

The MDM2 proto-oncogene is overexpressed in many human tumors. Although MDM2 inhibits tumor-suppressor function of p53, there exists a p53-independent role for MDM2 in tumorigenesis. Therefore, downregulation of MDM2 has been considered an attractive therapeutic strategy. Hispolon extracted from Phellinus species was found to induce epidermoid and gastric cancer cell apoptosis. …The results indicated that cells with higher ERK1/2 activity were more sensitive to hispolon. In addition, hispolon-induced caspase-7 cleavage was inhibited by the ERK1/2 inhibitor, U0126. In conclusion, hispolon ubiquitinates and downregulates MDM2 via MDM2-recruited activated ERK1/2. Therefore, hispolon may be a potential anti-tumor agent in breast and bladder cancers.

Honey

http://onlinelibrary.wiley.com/doi/10.1046/j.0919-8172.2003.00602.x/abstract

Antineoplastic activity of honey in an experimental bladder cancer implantation model: In vivo and in vitro studies

In vitro studies revealed significant inhibition of the proliferation of T24 and MBT-2 cell lines by 1–25% honey and of RT4 and 253J cell lines by 6–25% honey. BrdU labeling index was significantly lower. FCM showed lower S-phase fraction, as well as absence of aneuploidy compared with control cells. In the in vivo studies, intralesional injection of 6 and 12% honey as well as oral ingestion of honey significantly inhibited tumor growth.

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http://cat.inist.fr/?aModele=afficheN&cpsidt=21550819

Bioactivity of Greek honey extracts on breast cancer (MCF-7), prostate cancer (PC-3) and endometrial cancer (Ishikawa) cells

Thyme, pine and fir honey showed both antioestrogenic and a weak oestrogenic effect at low and high concentration, respectively, in MCF-7 cells. Thyme honey reduced the viability of Ishikawa and PC-3 cells, whereas fir honey stimulated the viability of MCF-7 cells. In conclusion, Greek honeys are rich in phenolic compounds, they modulate oestrogenic activity whereas a thyme honey-enriched diet may prevent cancer-related processes in breast, prostate and endometrial cancer cells.

Isoliquiritigenin

(Licorice, Shallots, Bean Sprouts)

https://www.thieme-connect.com/ejournals/abstract/plantamedica/doi/10.1055/s-2001-18361

Apoptosis Induced by Isoliquiritigenin in Human Gastric Cancer MGC-803 Cells

Isoliquiritigenin, which is possibly a principal anti-tumor constituent of licorice, a traditional Chinese herb, was examined for apoptosis-inducing activity in human gastric cancer MGC-803 cells. …These results suggest that isoliquiritigenin induced apoptosis of MGC-803 cells through calcium- and Deltapsi(m)-dependent pathways, indicating that it is potentially useful as a natural anti-cancer agent.

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http://www.aacrmeetingabstracts.org/cgi/content/abstract/2005/1/1222

Isoliquiritigenin induces apoptosis by depolarizing mitochondrial membranes in prostate cancer cells

Isoliquiritigenin (ISL) is a simple chalcone derivative, 4,2',4'-trihydroxychalcone, found in licorice, shallot and bean sprouts. It was reported to have chemoprotective effects; inhibitory effects on murine colonic tumorigenesis, anti-angiogenic effect, and apoptosis-inducing activity. …The present results indicate that ISL inhibits prostate cancer cell growth by decreasing DNA synthesis and inducing apoptosis. The mechanism of apoptosis induction by ISL probably involves a mitochondria / caspase-9-specific pathway for the activation of the caspase cascade.

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http://www.ncbi.nlm.nih.gov/pubmed/15236626

Isoliquiritigenin inhibits the proliferation and induces the apoptosis of human non-small cell lung cancer a549 cells

Isoliquiritigenin (ISL) is a natural pigment with the simple chalcone structure 4,2',4'-trihydroxychalcone. In the present study, we report, for the first time, ISL-induced inhibition of the proliferation of the human non-small cell lung cancer A549 cell line. 2. The results showed that ISL not only inhibited A549 cell proliferation, but also induced apoptosis and blocked cell cycle progression in the G1 phase.

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http://www.ncbi.nlm.nih.gov/pubmed/16399234/

Cyclooxygenase-2 plays a suppressive role for induction of apoptosis in isoliquiritigenin-treated mouse colon cancer cells

Cellular damage induced by chronic inflammation is a well known cause of colon carcinogenesis. Cyclooxygenase-2 (COX-2), the enzyme that converts arachidonic acid to prostanoids, is known to play an important role in inflammation. Herbal flavonoid isoliquiritigenin (ILTG) has previously been reported to be a strong suppresser of the COX-2 pathway as well as an inducer of apoptosis. Here we report that the susceptibility to apoptosis by ILTG is dependent on the level of COX-2 in mouse colon adenocarcinoma Colon 26, which spontaneously expresses COX-2. This dependency was observed to be enhanced by

blockage of the lipoxigenases (LOXs)-mediated metabolic pathway and attenuated by addition of a number of prostaglandins and thromboxanes. Taken together, these findings indicate that ILTG-induced apoptosis is negatively regulated by the COX-2 expression level.

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http://www.ncbi.nlm.nih.gov/pubmed/12589938

Estrogenic and antiproliferative activities of isoliquiritigenin in MCF7 breast cancer cells

Transfection experiments reveal that ISL is able to transactivate the endogenous ER alpha in MCF7 cells and this is supported by the capability to induce down-regulation of ER alpha protein levels and up-regulation of pS2 mRNA. Moreover, by using chimeric proteins consisting of the hormone binding domains of ER alpha and ER beta fused to the Gal4 DNA binding domain, we have determined that ISL is an estrogenic agonist of both ER isoforms. As a biological counterpart, low and intermediate ISL concentrations that induce substantial transcriptional activity stimulate the proliferation of MCF7 cells. However, high levels of ISL become cytotoxic even in steroid-receptor negative HeLa cells. Thus, the activity of ISL and the balance between risk or chemopreventive factor for estrogen-dependent breast cancer may depend on dietary intake.

Kaempferol

(Tea, Broccoli, Grapefruit, Brussel Sprouts, Apples, Witch Hazel)

http://onlinelibrary.wiley.com/doi/10.1002/jcp.10340/abstract

Kaempferol-induced growth inhibition and apoptosis in A549 lung cancer cells is mediated by activation of MEK-MAPK

To elucidate these mechanisms, we challenged human lung cancer cell line A549 with kaempferol and investigated its effects upon cellular growth and signal transduction pathways. Treatment of A549 cells with kaempferol resulted in a dose- and time-dependent reduction in cell viability and DNA synthesis with the rate of apoptosis equivalent to 0.9?±?0.5, 5.2?±?1.5, 16.8?±?2.0, 25.4?±?2.6, and 37.8?±?4.5% on treatment with 0, 17.5, 35.0, 52.5, and 70.0 μM kaempferol, respectively.

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http://www.ncbi.nlm.nih.gov/pubmed/18680719

Kaempferol sensitizes colon cancer cells to TRAIL-induced apoptosis

Kaempferol is a natural compound contained in edible plants, and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is a promising anti-cancer agent. Here, we show for the first time that the combined treatment with kaempferol and TRAIL drastically induced apoptosis in human colon cancer SW480 cells, compared to single treatments. Kaempferol markedly up-regulated TRAIL receptors, DR5 and DR4. DR5 but not DR4 siRNA efficiently blocked apoptosis induced by the co-treatment with kaempferol and TRAIL, indicating that DR5 up-regulation by kaempferol helps to enhance TRAIL actions. Moreover, we examined the combined effect on normal human cells. The co-treatment induced no apoptosis in normal

human peripheral blood mononuclear cells and little apoptosis in normal human hepatocytes. These results suggest that kaempferol is useful for TRAIL-based treatments for cancer.

Limonoids
(Citrus Peels)

http://www.ncbi.nlm.nih.gov/pubmed/11962254

Differential Inhibition of Human Cancer Cell Proliferation by Citrus Limonoids

Limonoids have been shown to inhibit the growth of estrogen receptor-negative and -positive human breast cancer cells in culture. …The human cancer cell lines included leukemia (HL-60), ovary (SKOV-3), cervix (HeLa), stomach (NCI-SNU-1), liver (Hep G2), and breast (MCF-7). The growth-inhibitory effects of the four limonoids and the limonoid glucoside mixture against MCF-7 cells were significant, and the antiproliferative activity of the different citrus limonoids was also dose and time dependent. No significant effects were observed on growth of the other cancer cell lines treated with the four individual limonoids at 100 µg/ml.

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http://jn.nutrition.org/cgi/content/abstract/135/4/870

Citrus Limonoids Induce Apoptosis in Human Neuroblastoma Cells and Have Radical Scavenging Activity

Citrus limonoid glucosides, a family of fruit bioactive compounds, were postulated to have free radical–scavenging and apoptosis-inducing properties against certain types of cancers. Four highly purified limonoid glucosides, limoin 17ß D-glucopypranoside (LG), obacunone 17ß D-glucopyranoside (OG), nomilinic acid 17ß D-glucopyranoside (NAG), and deacetylnomilinic acid 17ß D-glucopyranoside (DNAG) were tested for superoxide radical (O_2^-)-quenching activity and cytotoxic action against undifferentiated human SH-SY5Y neuroblastoma cells in culture. All 4 scavenged O_2^- as measured by inhibition of pyrogallol decomposition in a spectrophotometric assay. …We conclude that citrus limonoid glucosides are toxic to SH-SY5Y cancer cells. Cytotoxicity is exerted through apoptosis by an as yet unknown mechanism of induction. Individual limonoid glucosides differ in efficacy as anticancer agents, and this difference may reside in structural variations in the A ring of the limonoid molecule.

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http://www.ncbi.nlm.nih.gov/pubmed/15749633

Citrus Reticulata blanco induces apoptosis in human gastric cancer cells SNU-668

Citrus fruits have been known to reduce the proliferation of many cancer cells. The antiproliferative effects of Citrus reticulata Blanco (CR) extract, the immature tangerine peel, on human gastric cancer cell line SNU-668 were evaluated using 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide assay, 4,6-diamidineo-2-phenylindole staining, terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling assay, reverse transcription-polymerase chain reaction expressions of BCL-2, BAX and CASP-3 genes, caspase-3 activity, and immunocytochemistry of caspase-3. From the results of the morphological and

biochemical assays, CR (50 microg/ml) increased the apoptosis of human gastric cancer cells with typical apoptotic characteristics, including morphological changes of chromatin condensation and apoptotic body formation.

Luteolin

(Celery, Thyme, Dandelion, Rinds, Clover Blossum, Green Pepper, Chamomile Tea, Olive Oil, Carrots, Sage, Peppermint, Rosemary, Perilla, Oregano)

http://www.ncbi.nlm.nih.gov/pubmed/16469309/

Antioxidant enzymes activity involvement in luteolin-induced human lung squamous carcinoma CH27 cell apoptosis

Luteolin (3',4',5,7-tetrahydroxyflavone) is an active constituent of Lonicera japonica (Caprifoliaceae), and has been reported to produce anti-tumor activities. However, the apoptosis-inducing activity of luteolin still remains unknown. Flavonoids have been found to possess prooxidant and antioxidant action. The biological and pharmacological effect of flavonoid may depend upon its behavior as either an antioxidant or a prooxidant. Our experiments found that luteolin-induced CH27 cell apoptosis was accompanied by activation of antioxidant enzymes, such as superoxide dismutase and catalase, but not through the production of reactive oxygen species and disruption of mitochondrial membrane potential. Therefore, the effects of luteolin on CH27 cell apoptosis were suspected to result from the antioxidant rather than the prooxidant action of luteolin.

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http://www.ncbi.nlm.nih.gov/pubmed/15963948

The combination of TRAIL and luteolin enhances apoptosis in human cervical cancer HeLa cells

Tumor necrosis factor-related apoptosis-inducing ligand (TRAIL) is one of the most promising candidates for cancer therapeutics. However, some tumor cells are resistant to TRAIL-induced apoptosis. Our previous studies have shown that luteolin, a naturally occurring flavonoid, induces the up-regulation of death receptor 5 (DR5), which is a receptor for TRAIL. Here, we show for the first time that luteolin synergistically acts with exogenous soluble recombinant human TRAIL to induce apoptosis in HeLa cells, but not in normal human peripheral blood mononuclear cells. The combined use of luteolin and TRAIL induced Bid cleavage and the activation of caspase-8. Also, human recombinant DR5/Fc chimera protein, caspase inhibitors, and DR5 siRNA efficiently reduced apoptosis induced by co-treatment with luteolin and TRAIL. These results raise the possibility that this combined treatment with luteolin and TRAIL might be promising as a new therapy against cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/12164283

Effects of luteolin on the inhibition of proliferation and induction of apoptosis in human myeloid leukaemia cells

Luteolin, a flavonoid isolated from the fruit of Vitex rotundifolia, has been examined with

regard to the inhibition of proliferation and induction of apoptosis in human myeloid leukaemia HL-60 cells. The concentration required for 50% inhibition of the growth after 96 h was 15 +/- 1.1 microM. The mode of cell death induced by luteolin was found to be apoptosis, as judged by the morphologic alteration of the cells and by the detection of DNA fragmentation using agarose gel electrophoresis. The degree of apoptosis was quantified by a sandwich enzyme immunoassay and flow cytometric analysis. These results suggest that luteolin may be used as potential chemopreventive and chemotherapeutic agents.

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http://www.ncbi.nlm.nih.gov/pubmed/15710173

Induction apoptosis of luteolin in human hepatoma HepG2 cells

In addition, it showed that c-Jun NH2-terminal kinase (JNK) was activated after the treatment of luteolin for 3-12 h. Further investigation showed that a specific JNK inhibitor, SP600125, reduced the activation of CPP 32, the mitochondrial translocation of Bax, as well as the cytosolic release of cytochrome c that induced by luteolin. Finally, the apoptosis induced by luteolin was suppressed by a pretreatment with SP600125 via evaluating annexin V-FITC binding assay. These data suggest that luteolin induced apoptosis via mechanisms involving mitochondria translocation of Bax/Bak and activation of JNK.

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http://carcin.oxfordjournals.org/cgi/content/abstract/28/3/713

Luteolin inhibits insulin-like growth factor 1 receptor signaling in prostate cancer cells

Luteolin inhibited expression of cyclin D1 and increased expression of p21. As a result, luteolin suppressed proliferation and induced apoptosis of prostate cancer cells. Knockdown of IGF-1R by siRNA led to inhibition of proliferation of prostate cancer cells. Results of in vivo tumor growth assay indicated that luteolin inhibited PC-3 tumor growth. Immunoblotting of the extracts of tumor tissues showed that luteolin inhibited IGF-1R/AKT signaling. Our results provide a new insight into the mechanisms that luteolin is against cancer cells.

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http://ajpgi.physiology.org/cgi/content/abstract/292/1/G66

Induction of cell cycle arrest and apoptosis in HT-29 human colon cancer cells by the dietary compound luteolin

We demonstrate that luteolin promotes both cell cycle arrest and apoptosis in the HT-29 colon cancer cell line, providing insight about the mechanisms underlying its antitumorigenic activities.

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http://jdr.sagepub.com/content/87/4/401.abstract

Luteolin Induces Apoptosis in Oral Squamous Cancer Cells

Results revealed that luteolin reduced the viability of SCC-4 cells and induced apoptosis by

decreasing the expression of cyclin-dependent kinase (CDKs), cyclins, and phosphor-retinoblastoma (p-Rb) anti-apoptotic protein, but increased the expression of pro-apoptotic proteins and activated caspase 9 and 3, with a concomitant increase in the levels of cleaved poly-ADP-ribose polymerase (PARP). Combination treatment of luteolin with paclitaxel enhanced the cytotoxic effect of paclitaxel in SCC-4 cells, and continuous administration of luteolin suppressed the growth of xenograft tumors in nude mice. These results suggest that luteolin could be an effective chemotherapeutic agent for the treatment of oral squamous cell carcinoma.

Lycopene

(Tomato, “Gac” Fruit, Red Carrot, Watermelon, Papaya, Red Algae, Pink Guava, Grapefruit)

http://cancerres.aacrjournals.org/content/63/12/3138.abstract

Lycopene Supplementation Inhibits Lung Squamous Metaplasia and Induces Apoptosis

Higher intake of lycopene is related to a lower risk of lung cancer in human studies. Lung cancer risk is associated with higher plasma levels of insulin-like growth factor I (IGF-I) and/or lower levels of IGF-binding protein 3 (IGFBP-3).

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http://www.ncbi.nlm.nih.gov/pubmed/10798222

Lycopene interferes with mammary cancer cells

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http://ebm.rsmjournals.com/cgi/content/abstract/230/3/171

Concentrations of Lycopene Induce Mitochondrial Apoptosis in LNCaP Human Prostate Cancer Cells

We demonstrated that increasing concentrations of lycopene significantly ($P < 0.05$) reduced mitochondrial transmembrane potential, induced the release of mitochondrial cytochrome c, and increased annexin V binding, confirming induction of apoptosis. Thus, lycopene at physiologically relevant concentrations did not affect cellular proliferation or promote necrosis but clearly altered mitochondrial function and induced apoptosis in LNCaP human prostate cancer cells.

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http://www.ncbi.nlm.nih.gov/pubmed/14680688

A novel cleavage product formed by autoxidation of lycopene induces apoptosis in HL-60 cells

We previously reported that an autoxidation mixture of lycopene induced apoptosis in HL-60 human promyelocytic leukemia cells, but lycopene alone did not. In the present study, bioassay-directed fractionations of autoxidized lycopene led to isolation of a novel cleavage

product of lycopene. Spectral analyses elucidated its structure as (E,E,E)-4-methyl-8-oxo-2,4,6-nonatrienal (MON), suggesting the formation through the oxidative cleavages at the 5, 6- and 13, 14-double bonds of lycopene.

Maitake D-Fraction
(Maitake Mushrooms)

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2840560/

Possible disease remission in patient with invasive bladder cancer with D-fraction regimen

This case study describes an invasive bladder cancer patient at a high risk for disease recurrence who only followed a D-fraction regimen (with vitamin C) refusing other medical interventions. The two-year follow-up yet indicated no clinical evidence of progression of residual disease or recurrence with possible disease remission.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1464-410X.2009.08870.x/abstract

Synergistic potentiation of interferon activity with maitake mushroom d-fraction on bladder cancer cells

The combination of IFN-2b (10 000 IU/mL) and PDF (200 μg/mL) reduced growth by ˜75% in T24 cells. This appears to be due to a synergistic potentiation of these two agents, inducing a G1 arrest with DNA-PK activation. Therefore, the IFN-2b/PDF combination could trigger DNA-PK activation that may act on the cell cycle to cease cancer cell growth.

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http://www.ncbi.nlm.nih.gov/pubmed/15719326

Potential growth inhibitory effect of maitake D-fraction on canine cancer cells

The postulated anticancer effect of D-fraction, the bioactive extract of maitake mushroom, on three types (CF33, CF21, and CL-1) of canine cancer cells was evaluated. The effect of D-fraction on several human cancer cells was also investigated. The effect of other beta-glucan products was likewise examined. D-fraction was highly effective on the canine cancer cells, either potently inhibiting cell growth or directly killing cells. Similar effects were also demonstrated in certain human cancer cells. However, other beta-glucan products relevant to D-fraction had no such effects on canine cancer cells. Therefore, D-fraction is a potent natural agent that could be useful in treating canine cancers as well as other veterinary cancers.

Melatonin

http://www.springerlink.com/content/v37lmn57jq3641gr/

Melatonin and retinoic acid induces apoptosis in MCF-7 human breast cancer cells

These data suggest that the sequential treatment regimen of Mlt and atRA may induce apoptosis by modulation of members of the Bcl-2 family of proteins. Thus, this combinatorial regimen, which reduces the concentration of atRA needed for clinical efficacy while enhancing its anti-tumorigenic activity, could be of great therapeutic benefit, and may, in fact, specifically induce the regression of established breast tumors due to its apoptosis-promoting effects.

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http://www.ncbi.nlm.nih.gov/pubmed/10674014

Decreased toxicity and increased efficacy of cancer chemotherapy using the pineal hormone melatonin in metastatic solid tumour patients with poor clinical status

Melatonin (MLT) has been proven to counteract chemotherapy toxicity, by acting as an anti-oxidant agent, and to promote apoptosis of cancer cells, so enhancing chemotherapy cytotoxicity. The aim of this study was to evaluate the effects of concomitant MLT administration on toxicity and efficacy of several chemotherapeutic combinations in advanced cancer patients with poor clinical status. The study included 250 metastatic solid tumour patients (lung cancer, 104; breast cancer, 77; gastrointestinal tract neoplasms, 42; head and neck cancers, 27), who were randomized to receive MLT (20 mg/day orally every day) plus chemotherapy, or chemotherapy alone. …This study indicates that the pineal hormone MLT may enhance the efficacy of chemotherapy and reduce its toxicity, at least in advanced cancer patients of poor clinical status.

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http://www.ncbi.nlm.nih.gov/pubmed/16879318

Melatonin induces apoptosis in human neuroblastoma cancer cells

Low concentrations (nanomolar) of melatonin had been previously shown to inhibit cell proliferation in several cancer cell lines as well as in experimental animal models. Additionally, cell growth inhibition and differentiation of prostate cancer cell lines by high concentrations (micromolar to millimolar) of melatonin have been recently reported. In the present paper, we show the induction of apoptosis by high doses of melatonin in the human neuroblastoma cell line SK-N-MC. …Treatment with 1 mm melatonin for 6 days induced cell death in 75% of the cells. This novel finding shows that a nontoxic natural indoleamine may be potential therapy for some types of human neuroblastomas.

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http://www.ncbi.nlm.nih.gov/pubmed/11555175

Melatonin and RZR/ROR receptor ligand CGP 52608 induce apoptosis in the murine colonic cancer

The effects of melatonin and the thiazolinidinedione derivative CGP 52608 on apoptosis of Colon 38 cancer cells were investigated. Male mice were implanted subcutaneously with a suspension of Colon 38 cells. Ten days after induction of tumors, the animals were treated with melatonin or CGP 52608. Both substances were given in subcutaneous injections in daily doses of 10 or 100 microg in the evening for 6 days. The control group received solvent. The apoptotic cells were visualized in paraffin sections by means of the transferase-mediated

dUTPnick end-labeling method. Both treatments increased significantly and to the same degree the number of apoptotic cells in tumors. This finding confirms our earlier observation that melatonin exerts a pro-apoptotic effect on murine colonic cancer cells. Moreover, because CGP 52608 is a ligand of RZR/ROR receptors and the latter are considered by some investigators as nuclear binding sites for melatonin, our data suggest the involvement of these receptors in the pro-apoptotic effect of melatonin.

Methylselenocysteine

(Garlic, Onions, Astralagus, Broccoli's, Radishes, Brussel Sprouts, Ramps, Milk Vetch, Indian Mustard, Cabbage)

http://carcin.oxfordjournals.org/cgi/content/abstract/22/4/559

Se-Methylselenocysteine induces apoptosis through caspase activation in HL-60 cells

In our study, we found that Se-methylselenocysteine (MSC) induced apoptosis through caspase activation in human promyelocytic leukemia (HL-60) cells. Measurements of cytotoxicity, DNA fragmentation and apoptotic morphology revealed that MSC was more efficient at inducing apoptosis than selenite, but was less toxic. Moreover, MSC increased both the apoptotic cleavage of poly(ADP-ribose) polymerase (PARP) and caspase-3 activity, whereas selenite did not.

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http://breast-cancer-research.com/content/7/5/R699/abstract

Se-methylselenocysteine inhibits phosphatidylinositol 3-kinase activity of mouse mammary epithelial tumor cells

Se-methylselenocysteine (MSC), a naturally occurring selenium compound, is a promising chemopreventive agent against in vivo and in vitro models of carcinogen-induced mouse and rat mammary tumorigenesis. We have demonstrated previously that MSC induces apoptosis after a cell growth arrest in S phase in a mouse mammary epithelial tumor cell model (TM6 cells) in vitro. The present study was designed to examine the involvement of the phosphatidylinositol 3-kinase (PI3-K) pathway in TM6 tumor model in vitro after treatment with MSC.

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http://pubs.acs.org/doi/abs/10.1021/jf802125t

Selenocystine Induces S-Phase Arrest and Apoptosis in Human Breast Adenocarcinoma MCF-7 Cells by Modulating ERK and Akt Phosphorylation

Selenocystine (SeC) is a nutritionally available selenoamino acid with selective anticancer effects on a number of human cancer cell lines. The present study shows that SeC inhibited the proliferation of human breast adenocarcinoma MCF-7 cells in a time- and dose-dependent manner, through the induction of cell cycle arrest and apoptotic cell death.

Milk Thistle

http://www.reuters.com/article/idUSTRE5BD2XS20091214

Milk thistle may limit liver damage from chemo

An herb used since ancient times to treat liver ailments may help reduce the liver damage caused by some cancer drugs, a study published Monday suggests. In a study of 50 children undergoing chemotherapy for acute lymphoblastic leukemia (ALL), researchers found that an herb called milk thistle appeared to reduce treatment-related liver inflammation.

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http://cancerres.aacrjournals.org/content/65/10/4448.abstract

Milk Thistle and Prostate Cancer

Extracts from the seeds of milk thistle, Silybum marianum, are known commonly as silibinin and silymarin and possess anticancer actions on human prostate carcinoma in vitro and in vivo. Seven distinct flavonolignan compounds and a flavonoid have been isolated from commercial silymarin extracts.

Myricetin

(Walnuts, Red Grapes, Berries, Onions, Bilberry, Southern Bayberry shrub)

http://www.ingentaconnect.com/content/els/00092797/1998/00000116/00000003/art00092

The effect of the flavonoids, quercetin, myricetin and epicatechin on the growth and enzyme activities of MCF7 human breast cancer cells

E and Q inhibited the O-deethylation of ethoxyresorufin (EROD) catalysed by cytochrome P450 CYPIA. In contrast, M increased the EROD reaction 2-fold. Q increased the activity of DT-diaphorase, NADPH cytochrome c reductase and glutathione reductase, while E increased only NADPH cytochrome c reductase activity. The effects on enzyme activities in vitro suggest that there is not only the potential for flavonoids to alter metabolic activation of carcinogens but also of therapeutically administered drugs in vivo. We are at present investigating the synergy between anti-cancer drugs and flavonoids in terms of anti-tumour efficacy.

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http://carcin.oxfordjournals.org/cgi/content/short/28/9/1918

Myricetin is a novel natural inhibitor of neoplastic cell transformation and MEK1

Here we demonstrated that 3,3',4',5,5',7-hexahydroxyflavone (myricetin), one of the major flavonols in red wine, is a novel inhibitor of MEK1 activity and transformation of JB6 P+ mouse epidermal cells. Myricetin (10 μM) inhibited 12-O-tetradecanoylphorbol-13-acetate (TPA) or epidermal growth factor (EGF)-induced cell transformation by 76 or 72%, respectively, compared with respective reductions of 26 or 19% by resveratrol (20 μM). … Overall, these results indicated that myricetin has potent anticancer-promoting activity and

mainly targets MEK signaling, which may contribute to the chemopreventive potential of several foods including red wines.

Nikko Maple Bark

http://www.hort.uconn.edu/plants/a/acenik/acenik1.html

Hot water extract of bark of Nikko maple (Acer nikoense) induces apoptosis in leukemia cells

In screening for antitumor constituents in traditional crude drugs, we used three cultured cell lines: mouse leukemia P388 cells, doxorubicin-resistant P388 cells and leczyme (catalytic lectin)-resistant P388 cells. The hot water extract (HWE) of the bark of Nikko maple (Acer nikoense) showed concentration-dependent inhibitory effects on the growth of these three cell lines. DNA fragmentation and morphological changes, accompanied by condensed and fragmented nuclei, were observed in the leukemia cell lines cultured with HWE of the bark of Nikko maple. Treatment with this HWE increased the expression of sialylated glycoconjugates on the apoptotic cells. These results suggest that HWE induces cell death via apoptosis in vitro.

Olives & Olive Oil

http://www.ncbi.nlm.nih.gov/pubmed/12195161

Epidermal growth factor receptor inhibition is proven to stop many forms and instances of cancer. There are numerous commerical forms of medicine out there, but if you even need such measures is up to professionals. Olive's possess natural EGFR Inhibitors.

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http://www.ncbi.nlm.nih.gov/pubmed/12195161

Cancer chemoprevention by hydroxytyrosol isolated from virgin olive oil through G1 cell cycle arrest and apoptosis

Recent epidemiological evidence and animal studies suggest a relationship between the intake of olive oil and a reduced risk of several malignancies. …The con-centrations of hydroxytyrosol which inhibited 50% of cell proliferation were ~50 and ~750 µmol/l for HL60 and both HT29 and HT29 clone 19A cells, respectively. At concentrations ranging from 50 to 100 µmol/l, hydroxytyrosol induced an appreciable apoptosis in HL60 cells after 24 h of incubation as evidenced by flow cytometry, fluorescence microscopy and internucleosomal DNA fragmentation. … These results support the hypothesis that hydroxytyrosol may exert a protective activity against cancer by arresting the cell cycle and inducing apoptosis in tumour cells, and suggest that hydroxytyrosol, an important component of virgin olive oil, may be responsible for its anticancer activity.

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http://jn.nutrition.org/cgi/content/abstract/136/10/2553

Olive Fruit Extracts Inhibit Proliferation and Induce Apoptosis in HT-29 Human Colon Cancer Cells

We investigated the effect on cell proliferation and apoptosis in HT-29 cells of an extract from the skin of olives composed of pentacyclic triterpenes with the main components maslinic acid (73.25%) and oleanolic acid (25.75%). Studies of the dose-dependent effects showed antiproliferative activity at an EC50 value of 73.96 ± 3.19 µmol/L of maslinic acid and 26.56 ± 2.55 µmol/L of oleanolic acid without displaying necrosis. Apoptosis was confirmed by the microscopic observation of changes in membrane permeability in 40.9 ± 3.9% and detection of DNA fragmentation in 24.5 ± 1.5% of HT-29 cells incubated for 24 h with olive fruit extract containing 150 and 55.5 µmol/L of maslinic and oleanolic acids, respectively.

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http://www.biomedcentral.com/1471-2407/7/80

Olive oils bitter principle reverses acquired autoresistance to trastuzumab (Herceptin™) in HER2-overexpressing breast cancer cells

A low incidence of breast cancer in the Mediterranean basin suggests that a high consumption of Extra Virgin Olive Oil (EVOO) might confer this benefit. …Mechanistically, oleuropein aglycone treatment significantly reduced HER2 ECD cleavage and subsequent HER2 auto-phosphorylation, while it dramatically enhanced Tzb-induced down-regulation of HER2 expression. …Olive oil's bitter principle (i.e., oleuropein aglycone) is among the first examples of how selected nutrients from an EVOO-rich "Mediterranean diet" directly regulate HER2-driven breast cancer disease.

Oridonin

(Rabdosia Rubescens)

http://mct.aacrjournals.org/content/4/4/578.abstract

Oridonin, a diterpenoid purified from Rabdosia rubescens, inhibits the proliferation of cells from lymphoid malignancies

This study found that oridonin, a natural diterpenoid purified from Rabdosia rubescens, inhibited growth of multiple myeloma (MM; U266, RPMI8226), acute lymphoblastic T-cell leukemia (Jurkat), and adult T-cell leukemia (MT-1) cells with an effective dose that inhibited 50% of target cells (ED50) ranging from 0.75 to 2.7 µg/mL.

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http://www.ncbi.nlm.nih.gov/pubmed/17473426

Autophagy preceded apoptosis in oridonin-treated human breast cancer MCF-7 cells

Recent studies have shown that MCF-7 cells undergo autophagy under some conditions, such as tamoxifen treatment and starvation. In this study, we investigated autophagy in MCF-7 cells under oridonin treatment and further examined the relationship between autophagy and apoptosis. After 3-MA (the specific inhibitor of autophagy) pre-culture, MCF-7 cells were

exposed to oridonin, and the growth inhibitory ratio, morphologic changes, DNA fragmentation, proteins expression, autophagic ratio and apoptotic ratio were evaluated. Oridonin inhibited the proliferation of MCF-7 cells and induced autophagy in vitro.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1745-7254.2007.00588.x/abstract

Oridonin-treated MCF-7 human breast cancer cells

Oridonin inhibited cell growth in a time- and dose-dependent manner. Cell cycle was altered through the upregulation of p53 and p21 protein expressions. Pancaspase inhibitor Z-VAD-fmk and calpain inhibitor II both decreased cell death ratio.

Paclitaxel
(Pacific Yew Tree / Taxus brevifolia)

Natural Taxol

Pepino Melon
(Solanum Muricatum)

http://www.ncbi.nlm.nih.gov/pubmed/10226574

Extract of Solanum muricatum (Pepino/CSG) inhibits tumor growth by inducing apoptosis

A lyophilized aqueous fraction extracted from Solanum muricatum (CSG4) was used in this study. The human cell lines tested include: prostate (PC3, DU145), stomach (MKN45), liver (QGY-7721, SK-HEP-1), breast (MDA-MB-435), ovarian (OVCAR), colon (HT29) and lung (NCI-H209) cancer cells; NHP (prostate), HUVEC (umbilical vein endothelial cell), and WI-38 (lung diploid fibroblasts) normal cells. The cell survival was determined by either Cell Titer MTS cell proliferation kit or trypan blue dye exclusion assay. The apoptosis was analyzed by (a) apoptotic morphology by light microscopy; (b) DNA ladder formation; (c) PARP cleavage assay. Taken together, the present study suggests, for the first time, that CSG may represent promising new chemical entity which preferentially targets various tumor cells by triggering apoptosis.

Pinellia
(“Ban Xia” root)

http://en.cnki.com.cn/Article_en/CJFDTOTAL-BXYY200805025.htm

Apoptosis induction effect of Pinellia extract fraction on cell lines of cervical cancer cultured in vitro

We tested the effects of PE on cell proliferation by MTT assay.The effects of PE on

morphology,and cell cycle were studied by phase-contrast microscope and fiowcytometry(FCM).Results: PE could obviously inhibit the proliferation of HeLa and CaSki cells in a time and dose dependent manner.It could induce apoptosis of HeLa and CaSki.Conclusions: PE can suppress proliferation of cervical cancer cells and induce apoptosis.It may be a pure traditional Chinese reagent with non-side effects to prevent and treat cervical cancer effectively.

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http://en.cnki.com.cn/Article_en/CJFDTOTAL-HAIX200909092.htm

Experimental study on Inducing apoptosis effects of the protein of Pinellia pedatisecta Schott on human ovarian cancer cell line SKOV3

OBJECTIVE To investigate the effects of the protein of Pinellia pedatisecta Schott on the proliferation of human ovarian cancer cell line SKOV3 in vitro and to determine whether the protein of Pinellia pedatisecta Schott inhibit the growth of ovarian cancer and its mechanism of action.METHODS CCK-8 was used to detect the effect of the protein of Pinellia pedatisecta Schott on the growth of SKOV3 cells in vitro;using flow cytometry,detected the apoptosis of SKOV3 cells treated with the protein of Pinellia pedatisecta Schott by Anexinn-V.RESULTS The protein of Pinellia pedatisecta Schott had some effect of inhibiting the proliferation and inducing apoptosis of SKOV3 cells,and the mechanism would be further studied.

Polyphenols

(Berries, Tea, Beer, Grapes/Wine, Olive Oil, Chocolate/Cocoa, Coffee, Walnuts, Peanuts, Borojo, Pomegranates, Popcorn, Yerba Mate)

Polysaccharides

(“Turkey Tail” Mushroom / Trametes versicolor, Ginko Biloba plant & seeds, Marine algae Capsosiphon Fulvescens, “loach” fish Misgurnus Anguillicaudatus)

http://www.ncbi.nlm.nih.gov/pubmed/15183847

Protein-bound polysaccharide K induced apoptosis of the human Burkitt lymphoma cell line, Namalwa

Protein-bound polysaccharide K (PSK), which is derived from mushrooms belonging to the Basidiomycetes genus, has been clinically used as a biological response modifier (BRM) for the treatment of epithelial cancer patients in Japan and other Asian countries. There are a large number of studies on the biological activities of PSK as regards the activation of immunocompetent cells and the potential cytotoxic effects on epithelial cancer cells. …These results provide initial evidence of the direct cytotoxic activity of PSK in a hematological malignant cell line, thus encouraging further molecular-level study of PSK-mediated apoptosis in malignant hematological cells.

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http://www.ncbi.nlm.nih.gov/pubmed/15547752/

Gene expression in response to anti-tumour intervention by polysaccharide-K (PSK) in colorectal carcinoma cells

Distant metastasis is one of the major problems in treatment for advanced colorectal cancer. Polysaccharide-K (PSK), or Krestin, a mushroom ingredient, has been used as a chemoimmunotherapeutic agent for the treatment of cancers in Asia for over 30 years. Some studies have reported that PSK prevent distant metastases and improve survival rates by 10-20% in colorectal cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/17344071

A polysaccharide of the marine alga Capsosiphon fulvescens induces apoptosis in AGS gastric cancer cells

Because seaweed extracts have recently been found to have antioxidant and anti-tumor activities, we analyzed a hot-water-soluble polysaccharide (PS) of the marine alga Capsosiphon fulvescens for its potential as a functional foodstuff by determining its effects on cell growth and DNA synthesis. MTS assays showed that the C. fulvescens PS (Cf-PS) significantly inhibited the proliferation of cultured human cancer cells in a dose-dependent manner. Cf-PS-treated AGS cells exhibited a marked increase in caspase-3 activation and a decrease in Bcl-2 expression. In addition, phosphorylation of insulin-like growth factor-I receptor (IGF-IR) was decreased in Cf-PS-treated AGS cells as compared to non-treated control cells, which is consistent with PI3-kinase (PI3K)/Akt activation. Cf-PS also decreased IGF-I-stimulated recruitment of p85 to IGF-IR and IRS-1. These results indicate that Cf-PS inhibits cell proliferation and induces apoptosis by inhibiting IGF-IR signaling and the PI3K/Akt pathway.

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http://www.ncbi.nlm.nih.gov/pubmed/14606069

Therapeutic mechanism of ginkgo biloba exocarp polysaccharides on gastric cancer

Compared with the statement before treatment, GBEP capsules could reduce the area of tumors, and the effective rate was 73.4%. Ultrastructural changes of the cells indicated that GBEP could induce apoptosis and differentiation in tumor cells of patients with gastric cancer. GBEP could inhibit the growth of human gastric cancer SGC-7901 cells following 24-72 h treatment in vitro at 10-320 mg/L, which was dose- and time-dependent. GBEP was able to elevate the apoptosis rate and expression of c-fos gene, but reduce the expression of c-myc and bcl-2 genes also in a dose-dependent manner.

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http://www.ncbi.nlm.nih.gov/pubmed/12378625

Apoptosis of hepatoma cells SMMC-7721 induced by Ginkgo biloba seed polysaccharide

GBSP product obtained was of high purity with the average molecular weight of 1.86 X 10(5). Quantitative analysis of SMMC-7721 cells in vitro with FCM showed that the percentages of G(2)-M cells without and with GBSP treatment were 17.01+/-1.28 % and 11.77+/-1.50% ($P<0.05$), the debris ratio of the cells were 0.46+/-0.12 % and 0.06+/-0.06 % ($P<0.01$), and the

apoptosis ratio of cells was 3.84+/-0.55 % and 9.13+/-1.48 % (P<0.01) respectively. Following GBSP treatment, microvilli of SMMC-7721 cells appeared thinner and the number of spherical cells increased markedly. Most significantly, the apoptosis bodies were formed on and around the spherical cells treated with GBSP.

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http://www.ncbi.nlm.nih.gov/pubmed/15936790

Mechanism of apoptosis induced by a polysaccharide, from the loach Misgurnus anguillicaudatus (MAP) in human hepatocellular carcinoma cells

The biological activities of the polysaccharide have attracted more and more attention in the biochemical and medical areas due to their anti-cancer effects. To estimate the anti-tumor mechanism of MAP, a novel polysaccharide from the loach, Misgurnus anguillicaudatus, the apoptosis effects of the polysaccharide on the human hepatocellular carcinoma cells (SMMC-7721 cells) were studied. The present studies showed that MAP could induce cell apoptosis which was closely accompanied with an increase of intracellular-free calcium concentration ([Ca2+]i), the enhancement of reactive oxygen species (ROS) level, dissipation of mitochondria membrane potential (MMP), up-regulation of p53 mRNA, increase expression of Bax mRNA, and decrease expression of Bcl-2 mRNA. These results suggested that cell apoptosis induced by MAP mainly was mediated by mitochondrial pathways, not involved death receptors (DRs) pathways. The mechanism possibly is that MAP acts on mitochondria and boosts ROS, ROS mediates a release of Ca2+ from the intracellular Ca2+ pool, increasing [Ca2+]i targets the cells a start-up of the apoptosis program.

Protodioscin

(Fenugreek Seeds / Powder)

http://www.ncbi.nlm.nih.gov/pubmed/12469212

Protodioscin isolated from fenugreek induces cell death and morphological change indicative of apoptosis in leukemic cell line H-60, but not in gastric cancer cell line KATO III.

Protodioscin (PD) was purified from fenugreek (Trigonella foenumgraecum L.) and identified by Mass, and 1H- and 13C-NMR. The effects of PD on cell viability in human leukemia HL-60 and human stomach cancer KATO III cells were investigated. PD displayed strong growth inhibitory effect against HL-60 cells, but weak growth inhibitory effect on KATO III cells.

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http://www.ncbi.nlm.nih.gov/pubmed/16458429/

Methyl protodioscin induces G2/M cell cycle arrest and apoptosis in HepG2 liver cancer cells

Methyl protodioscin (NSC-698790) is one of the main bioactive components in the traditional Chinese medicine Dioscorea collettii var. hypoglauca (Dioscoreaceae). In this study, we investigated the anti-proliferative effect of methyl protodioscin on the HepG2 cells and the mechanism of the induced cytotoxicity. Treatment of methyl protodioscin resulted in G2/M

arrest and apoptosis in HepG2 cells. These effects were attributed to down-regulation of Cyclin B1 and the signaling pathways leading to up-regulation of Bax and down-regulation of BCL2, suggesting that methyl protodioscin may be a novel anti-mitotic agent.

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http://www.ncbi.nlm.nih.gov/pubmed/15914274

Methyl protodioscin induces G2/M arrest and apoptosis in K562 cells

Methyl protodioscin is a furostanol bisglycoside with antitumor properties. The present study investigated its effects on human chronic myelogenous leukemia K562 cells. Cell cycle analysis showed that methyl protodioscin caused distinct G2/M arrest, with the appearance of polyploidy population.

Punicalagin
(Pomegranate)

http://www.plefa.com/article/S0955-2863

In vitro antiproliferative, apoptotic and antioxidant activities of punicalagin, ellagic acid and a total pomegranate tannin extract...

The potent antioxidant and anti-atherosclerotic activities of PJ are attributed to its polyphenols including punicalagin, the major fruit ellagitannin, and ellagic acid (EA). Punicalagin is the major antioxidant polyphenol ingredient in PJ. Punicalagin, EA, a standardized total pomegranate tannin (TPT) extract and PJ were evaluated for in vitro antiproliferative, apoptotic and antioxidant activities. Punicalagin, EA and TPT were evaluated for antiproliferative activity at 12.5–100 μg/ml on human oral (KB, CAL27), colon (HT-29, HCT116, SW480, SW620) and prostate (RWPE-1, 22Rv1) tumor cells. …Pomegranate juice showed greatest antiproliferative activity against all cell lines by inhibiting proliferation from 30% to 100%. At 100 μg/ml, PJ, EA, punicalagin and TPT induced apoptosis in HT-29 colon cells.

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http://pubs.acs.org/doi/abs/10.1021/jf052005r

Pomegranate Juice, Total Pomegranate Ellagitannins, and Punicalagin Suppress Inflammatory Cell Signaling in Colon Cancer Cells

In previous studies, pomegranate juice (PJ) and its ellagitannins inhibited proliferation and induced apoptosis in HT-29 colon cancer cells. The present study examined the effects of PJ on inflammatory cell signaling proteins in the HT-29 human colon cancer cell line. At a concentration of 50 mg/L PJ significantly suppressed TNFa-induced COX-2 protein expression by 79% (SE = 0.042), total pomegranate tannin extract (TPT) 55% (SE = 0.049), and punicalagin 48% (SE = 0.022). Additionally, PJ reduced phosphorylation of the p65 subunit and binding to the NF?B response element 6.4-fold. TPT suppressed NF?B binding 10-fold, punicalagin 3.6-fold, whereas ellagic acid (EA) (another pomegranate polyphenol) was ineffective. PJ also abolished TNFa-induced AKT activation, needed for NF?B activity. Therefore, the polyphenolic phytochemicals in the pomegranate can play an important role in

the modulation of inflammatory cell signaling in colon cancer cells.

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http://www.pnas.org/content/102/41/14813.full

Pomegranate fruit juice for chemoprevention and chemotherapy of prostate cancer

We recently showed that pomegranate fruit extract (PFE) possesses remarkable antitumor-promoting effects in mouse skin. In this study, employing human prostate cancer cells, we evaluated the antiproliferative and proapoptotic properties of PFE. …Oral administration of PFE (0.1% and 0.2%, wt/vol) to athymic nude mice implanted with androgen-sensitive CWR22R?1 cells resulted in a significant inhibition in tumor growth concomitant with a significant decrease in serum prostate-specific antigen levels. We suggest that pomegranate juice may have cancer-chemopreventive as well as cancer-chemotherapeutic effects against prostate cancer in humans.

Quercetin

(Black & Green Tea, Onions, Caper, Lovage, Apples, Red Grapes, Citrus, Tomato, Broccoli, Cherry, Raspberry, Cranberry, Bilberry)

http://www.ncbi.nlm.nih.gov/pubmed/11562764

Induction of cell cycle arrest and apoptosis in human breast cancer cells by quercetin

The present data, therefore, demonstrate that a flavonoid quercetin induces growth inhibition in the human breast carcinoma cell line MCF-7 through at least two different mechanisms; by inhibiting cell cycle progression through transient M phase accumulation and subsequent G2 arrest, and by inducing apoptosis.

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http://www.cancerletters.info/article/S0304-3835

The role of activated MEK-ERK pathway in quercetin-induced growth inhibition and apoptosis in A549 lung cancer cells

Inhibition of caspase activation completely blocked quercetin-induced apoptosis. Expression of constitutively activated MEK1 in A549 cells led to activation of caspase-3 and apoptosis. The results suggest that in addition to inactivation of Akt-1 and alteration in the expression of the Bcl-2 family of proteins, activation of MEK-ERK is required for quercetin-induced apoptosis in A549
lung carcinoma cells.

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http://www.cancerletters.info/article/S0304-3835

Ellagic acid and quercetin interact synergistically with resveratrol in the induction of apoptosis and cause transient cell cycle arrest in human leukemia cells

Results showed a more than additive interaction for the combination of ellagic acid with resveratrol and furthermore, significant alterations in cell cycle kinetics induced by single compounds and combinations were observed. An isobolographic analysis was performed to assess the apparent synergistic interaction for the combinations of ellagic acid with resveratrol and quercetin with resveratrol in the induction of caspase 3 activity, confirming a synergistic interaction with a combination index of 0.64 for the combination of ellagic acid and resveratrol and 0.68 for quercetin and resveratrol. Results indicate that the anticarcinogenic potential of foods containing polyphenols may not be based on the effects of individual compounds, but may involve a synergistic enhancement of the anticancer effects.

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http://www.journals.elsevierhealth.com/periodicals/jnb/article/PIIS0955286304002311/abstract

Quercetin decreases the expression of ErbB2 and ErbB3 proteins in HT-29 human colon cancer cells

Quercetin inhibited HT-29 cell growth in a dose-dependent manner, whereas rutin had no effect on the cell growth. DNA that was isolated from cells treated with 50 µmol/L of quercetin exhibited an oliogonucleosomal laddering pattern characteristic of apoptotic cell death. Western blot analysis of cell lysates revealed that Bcl-2 levels decreased dose-dependently in cells treated with quercetin, but Bax remained unchanged.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.10202/abstract

Food-derived polyphenols inhibit pancreatic cancer growth through mitochondrial cytochrome C release and apoptosis

We measured effects of quercetin on pancreatic cancer in a nude mouse model. We also investigated the effects of quercetin, rutin, trans-resveratrol and genistein on apoptosis and underlying signaling in pancreatic carcinoma cells in vitro. …The inhibition of mitochondrial permeability transition prevented cytochrome c release, caspase-3 activation and apoptosis caused by polyphenols. Nuclear factor-?B activity was inhibited by quercetin and trans-resveratrol, but not genistein, indicating that this transcription factor is not the only mediator of the polyphenols' effects on apoptosis. The results suggest that food-derived polyphenols inhibit pancreatic cancer growth and prevent metastasis by inducing mitochondrial dysfunction, resulting in cytochrome c release, caspase activation and apoptosis.

Raspberries

http://researchnews.osu.edu/archive/canberry.htm

Black Raspberries Show Multiple Defenses In Thwarting Cancer

We chose black raspberries for this study because previous studies had shown that ellagic acid inhibited carcinogen-induced esophageal and colon cancer in animals. He and his colleagues then tested a series of fruits for their ellagic acid content, finding that berries contained the highest amount. "We then decided to take a food-based approach to cancer prevention and began testing the berries' ability to inhibit chemically-induced esophageal and colon cancer,"

Stoner said. “Sure enough, we found that freeze-dried berries were highly protective in the esophagus and colon. But we also found that they were ineffective in protecting against lung cancer. “The protective compounds in berries may not be absorbed into the blood stream and delivered to the lungs in high enough amounts to be protective. We do believe that they protect the esophagus and colon because they are absorbed by these organs as the food moves through the digestive tract.”

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http://www.sciencedaily.com/releases/2008/08/080827163933.htm

Black Raspberries Slow Cancer By Altering Hundreds Of Genes (2008)

The carcinogen affected the activity of some 2,200 genes in the animals’ esophagus in only one week, but 460 of those genes were restored to normal activity in animals that consumed freeze-dried black raspberry powder as part of their diet during the exposure. These findings, published in recent issue of the journal Cancer Research, also helped identify 53 genes that may play a fundamental role in early cancer development and may therefore be important targets for chemoprevention agents.

Resveratrol

(red grapes and blueberries)

http://ar.iiarjournals.org/content/29/10/3733.full

Apoptosis Induced by Capsaicin and Resveratrol in Colon Carcinoma Cells Requires Nitric Oxide Production and Caspase Activation

We examined the role of nitric oxide (NO•) and influence of p53 status during apoptosis induced by these agents in two isogenic HCT116 human colon carcinomas, wild-type p53 (p53-WT) and complete knockout of p53 (p53-null) cells. Capsaicin and resveratrol, alone or in combination, inhibited cell growth and promoted apoptosis by the elevation of NO•; combined treatment in p53-WT cells was most effective. Increased NO• production after treatment uniformly stimulated p53 and Bax expression through Mdm2 down-regulation in p53-WT cells, whereas all were unaffected in p53-null cells. Both cell types underwent a reduction in the levels of anti-apoptotic Bcl-2 protein, cytochrome c loss from mitochondria and activation of caspase 9 together with caspase 3, independently of p53 status.

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http://jcem.endojournals.org/cgi/content/abstract/87/3/1223

Resveratrol Induces Apoptosis in Thyroid Cancer Cell Lines via a MAPK- and p53-Dependent Mechanism

Studies of nucleosome levels estimated by ELISA and of DNA fragmentation showed that RV induced apoptosis in both papillary and follicular thyroid cancer cell lines; these effects were inhibited by pifithrin-{alpha} and by p53 antisense oligonucleotide transfection.

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http://www.fasebj.org/cgi/reprint/17/15/2339.pdf

Resveratrol induces growth inhibition and apoptosis in metastatic breast cancer cells via de novo ceramide signaling

In this study we show that resveratrol has a potent antiproliferative and proapoptotic effect on MDA-MB-231, a highly invasive and metastatic cell line from human breast cancer known to be resistant to several anticancer drugs.

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http://carcin.oxfordjournals.org/cgi/content/short/28/5/922

Resveratrol induces cell death in colon cancer cells by a novel pathway involving lysosomal cathepsin D

In human colorectal cancer cells, the polyphenol resveratrol (RV) activated the caspase-dependent intrinsic pathway of apoptosis. This effect was not mediated via estrogen receptors. Pepstatin A, an inhibitor of lysosomal cathepsin D (CD), not (2S,3S)-trans-epoxysuccinyl-L-leucylamido-3-methylbutane ethyl ester, an inhibitor of cathepsins B and L, prevented RV cytotoxicity. Similar protection was attained by small interference RNA-mediated knockdown of CD protein expression.

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http://carcin.oxfordjournals.org/cgi/content/short/28/5/922

Resveratrol induces apoptosis in human esophageal carcinoma cells

Resveratrol inhibited the growth of esophageal cancer cell line EC-9706 in a dose-and time-dependent manner. Resveratrol induced EC-9706 cells to undergo apoptosis with typically apoptotic characteristics, including morphological changes of chromatin condensation, chromatin crescent formation, nucleus fragmentation and apoptotic body formation.

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http://chesterrep.openrepository.com/cdr/handle/10034/93817

Resveratrol-induced cell death in leukaemia cells

Resveratrol, a natural phytoalexin found in grapes and red wine, displays anti-cancer activities through a variety of mechanisms that include the induction of cancer cell apoptosis. Although high concentrations may be needed for the efficacy of resveratrol alone, the compound shows promise as a potent sensitizer of the apoptotic effect of other anti-cancer agents, including death ligand TRAIL. Intracellular heat shock proteins (Hsps) are frequently up-regulated in cancer cells, conferring resistance to apoptosis. Modulation of these proteins may overcome the resistance and increase efficacy of anticancer therapies. In this study, resveratrol caused significant dose-dependent apoptosis or necrosis in the lymphoid and myeloid leukaemia cell lines Jurkat and U937 at 50μM and above.

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1626081/

Resveratrol interferes with AKT activity and triggers apoptosis in human uterine cancer cells

High-dose of resveratrol triggered apoptosis in five out of six uterine cancer cell lines, as judged from Hoechst nuclear staining and effector caspase cleavage. In accordance, uterine cancer cell proliferation was decreased. Resveratrol also reduced cellular levels of the phosphorylated/active form of anti-apoptotic kinase AKT.

Retinoic Acid & Retinamide

http://mcb.asm.org/cgi/content/abstract/16/3/1138

Retinoic acid receptor beta mediates the growth-inhibitory effect of retinoic acid by promoting apoptosis in human breast cancer cells

Retinoids are known to inhibit the growth of hormone-dependent but not that of hormone-independent breast cancer cells. We investigated the involvement of retinoic acid (RA) receptors (RARs) in the differential growth-inhibitory effects of retinoids and the underlying mechanism. Our data demonstrate that induction of RAR beta by RA correlates with the growth-inhibitory effect of retinoids. The hormone-independent cells acquired RA sensitivity when the RAR beta expression vector was introduced and expressed in the cells.

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http://www.ncbi.nlm.nih.gov/pubmed/8261419

N-(4-hydroxyphenyl)retinamide induces apoptosis of malignant hemopoietic cell lines including those unresponsive to retinoic acid

In conclusion, our study demonstrates that HPR suppresses malignant cell growth and induces apoptosis at pharmacologically relevant doses. The differential responsiveness by a number of cell lines, especially HL-60R and NB306, to HPR and RA indicates that these compounds may act through different receptors. The clinical use of HPR, particularly in retinoic acid-unresponsive acute promyelocytic leukemia patients, is suggested.

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http://clincancerres.aacrjournals.org/content/2/5/855.short

Differential induction of apoptosis by all-trans-retinoic acid and N-(4-hydroxyphenyl)retinamide in human head and neck squamous cell carcinoma cell lines

Retinoids have been shown to act as cytostatic agents against a variety of tumor cell types, including squamous carcinoma cells. Recently it was reported that certain retinoids can induce apoptosis as well. Because we are investigating the potential of retinoids in chemoprevention and therapy for head and neck premalignant and malignant lesions, we compared the effects of all-trans-retinoic acid (ATRA) and N-(4-hydroxyphenyl)retinamide (4HPR) on seven human head and neck squamous cell carcinoma cell lines (17A, 17B, 22A, 22B, 38, SqCC/Y1, and 1483). Six of the seven cell lines showed dramatic morphological changes after treatment with 10 micrometer 4HPR, whereas no such changes were induced by 10 micrometer ATRA. …These results demonstrate that 4HPR causes apoptosis in several head

and neck squamous cell carcinoma cell lines and that it is more potent in this effect than ATRA.

Rhein
(Rhubarb)

http://ar.iiarjournals.org/content/29/1/309.full

Rhein-induced apoptosis in A-549 Human Lung Cancer cells

The Ca2+ chelator BAPTA was added to the cells before rhein treatment, thus blocking the Ca2+ production and inhibiting rhein-induced apoptosis in A-549 cells. Our data demonstrate that rhein induces apoptosis in A-549 cells via a Ca2+-dependent mitochondrial pathway.

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http://www.ncbi.nlm.nih.gov/pubmed/19885952

Rhein lysinate suppresses the growth of tumor cells and increases the anti-tumor activity of Taxol in mice

In previous studies, rhein, one of the major bioactive constituents in the rhizome of rhubarb, inhibited the proliferation of various human cancer cells. However, because of its water insolubility, the anti-tumor efficacy of rhein was limited in vivo. In this study, we observed the anti-tumor activity of rhein lysinate (the salt of rhein and lysine easily dissolves in water) in vivo and investigated its mechanism. …It inhibited tumor growth by both intragastric and intraperitoneal administrations and improved the therapeutic effect of Taxol in H22 hepatocellular carcinoma mice. In conclusion, rhein lysinate offers an anti-tumor activity in vivo and is hopeful to be a chemotherapeutic drug.

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http://www.ncbi.nlm.nih.gov/pubmed/14522581

Rhein induces apoptosis in HL-60 cells

Rhein is an anthraquinone compound enriched in the rhizome of rhubarb, a traditional Chinese medicine herb showing anti-tumor promotion function. In this study, we first reported that rhein could induce apoptosis in human promyelocytic leukemia cells (HL-60), characterized by caspase activation, poly(ADP)ribose polymerase (PARP) cleavage, and DNA fragmentation. …Our data demonstrate that rhein induces apoptosis in HL-60 cells via a ROS-independent mitochondrial death pathway.

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http://www.ncbi.nlm.nih.gov/pubmed/14765286

Rhein Inhibits the Growth and Induces the Apoptosis of Hep G2 Cells

The effects of rhein on the human hepatoblastoma G2 (Hep G2) cell line were investigated in this study. The results showed that rhein not only inhibited Hep G2 cell growth but also

induced apoptosis and blocked cell cycle progression in the G1 phase.

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http://iv.iiarjournals.org/content/23/2/309.abstract

Rhein Induced Apoptosis…in SCC-4 Human Tongue Squamous Cancer Cells

In this study, it was observed that rhein induced S-phase arrest through the inhibition of p53, cyclin A and E and it induced apoptosis through the endoplasmic reticulum stress by the production of reactive oxygen species (ROS) and Ca2+ release, mitochondrial dysfunction, and caspase-8, -9 and -3 activation in human tongue cancer cell line (SCC-4).

Selenium

(Brazil Nuts, Fish, Wheat Flour, Shell Fish, Chicken, Turkey)

http://www.ncbi.nlm.nih.gov/pubmed/8971064

Effects of selenium supplementation for cancer prevention in patients with carcinoma of the skin

Selenium treatment did not protect against development of basal or squamous cell carcinomas of the skin. However, results from secondary end-point analyses support the hypothesis that supplemental selenium may reduce the incidence of, and mortality from, carcinomas of several sites. These effects of selenium require confirmation in an independent trial of appropriate design before new public health recommendations regarding selenium supplementation can be made.

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http://cancerres.aacrjournals.org/content/61/19/7071.abstract

Redox-mediated Effects of Selenium on Apoptosis and Cell Cycle in the LNCaP Human Prostate Cancer

The effects of selenium exposure were studied in LNCaP human prostate cancer cells, and this same cell line adapted to selenium over 6 months to compare acute versus chronic effects of sodium selenite, the latter most closely resembling human clinical trials on the effects of selenium in cancer prevention and therapy. Our results demonstrated that oxidative stress was induced by sodium selenite at high concentrations in both acute and chronic treatments, but outcomes were different. …Our results in selenite-adapted cells suggest that selenium may exert its effects in human prostate cancer cells by altering intracellular redox state, which subsequently results in cell cycle block.

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http://www.ncbi.nlm.nih.gov/pubmed/10569799

Selenium-induced inhibition of angiogenesis in mammary cancer at chemopreventive levels of intake

The trace element nutrient selenium (Se) has been shown to possess cancer-preventive activity in both animal models and humans, but the mechanisms by which this occurs remain to be elucidated. Because angiogenesis is obligatory for the genesis and growth of solid cancers, we investigated, in the study presented here, the hypothesis that Se may exert its cancer-preventive activity, at least in part, by inhibiting cancer-associated angiogenesis. The effects of chemopreventive levels of Se on the intra-tumoral microvessel density and the expression of vascular endothelial growth factor in 1-methyl-1-nitrosourea-induced rat mammary carcinomas and on the proliferation and survival and matrix metalloproteinase activity of human umbilical vein endothelial cells in vitro were examined.

Skullcap
(Scutellaria Baicalensis)

http://www.ncbi.nlm.nih.gov/pubmed/11841797

Wogonin and fisetin induce apoptosis in human promyeloleukemic cells

Seven structurally related flavonoids including luteolin, nobiletin, wogonin, baicalein, apigenin, myricetin and fisetin were used to study their biological activities on the human leukemia cell line, HL-60. On MTT assay, wogonin, baicalein, apigenin, myricetin and fisetin showed obvious cytotoxic effects on HL-60 cells, with wogonin and fisetin being the most-potent apoptotic inducers among them.

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http://www.goldjournal.net/article/S0090-4295

Antitumor effects of Scutellariae radix and its components baicalein, baicalin, and wogonin on bladder cancer cell lines

All the drugs inhibited cell proliferation in a dose-dependent manner, but baicalin exhibited the greatest antiproliferative activity. The concentration of baicalin necessary to obtain 50% inhibition was 3.4 μg/mL for KU-1, 4.4 μg/mL for EJ-1, and 0.93 μg/mL for MBT-2. For KU-1 and MBT-2, the percentage of cell survival significantly decreased ($P < 0.05$) at a baicalin concentration of 1 μg/mL. In an in vivo experiment, antitumor effects of Scutellariae radix on C3H/HeN mice implanted with MBT-2 were investigated. All the control mice showed a progressive increase in tumor volume, reaching 2.81 ± 0.18 cm3 on day 20 and 5.36 ± 0.44 cm3 on day 25. However, when Scutellariae radix was orally administered at a dose of 10 mg per mouse one time daily for 10 days from day 11 to day 20, the tumor volume was 1.99 ± 0.19 cm3 on day 20 and 3.86 ± 0.26 cm3 on day 25, a significant inhibition of tumor growth ($P < 0.05$).

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http://www.cancerletters.info/article/S0304-3835

Induction of apoptosis in prostate cancer cell lines by a flavonoid, baicalin

The flavonoid baicalin (baicalein 7-D-ß-glucuronate), isolated from the dried root of Scutellaria baicalensis Georgi (Huang Qin), is widely used in the traditional Chinese herbal medicine for its anti-inflammatory, anti-pyretic and anti-hypersensitivity effects. In the present

study, we investigated the in vitro effects of baicalin on the growth, viability, and induction of apoptosis in several human prostate cancer cell lines, including DU145, PC-3, LNCaP and CA-HPV-10. The cell viability after treating with baicalin for 2–4 days was quantified by a colorimetric 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium (MTS) assay. The results showed that baicalin could inhibit the proliferation of prostate cancer cells.

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http://www.ncbi.nlm.nih.gov/pubmed/12917023

Effects of wogonin on inducing apoptosis of human ovarian cancer A2780 cells

Wogonin can inhibit proliferation and induce apoptosis of A2780 cells within a certain concentration range(50-250 microg/ml). Anticancer effects of wogonin were associated with the induction of apoptosis and partly with the suppression of telomerase activity.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.22402/abstract

Reversal of inflammation-associated dihydrodiol dehydrogenases (AKR1C1 and AKR1C2) overexpression and drug resistance in nonsmall cell lung cancer cells by wogonin and chrysin

We also showed that IL-6-induced AKR1C1/1C2 expression and drug resistance were inhibited by wogonin and chrysin, which are major flavonoids in Scutellaria baicalensis, a widely used traditional Chinese and Japanese medicine. In conclusion, this study demonstrated novel links of pro-inflammatory signals, AKR1C1/1C2 expression and drug resistance in NSCLC.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.23182/abstract

Anticancer effects of wogonin in both estrogen receptor-positive and -negative human breast cancer cell lines in vitro and in nude mice xenografts

Wogonin feeding to mice showed inhibition of tumor growth of T47D and MDA-MB-231 xenografts by up to 88% without any toxicity after 4 weeks of treatment. As wogonin was effective both in vitro and in vivo, our novel findings open the possibility of wogonin as an effective therapeutic and/or chemopreventive agent against both ER-positive and -negative breast cancers, particularly against the more aggressive and hormonal therapy-resistant ER-negative types.

Sophora

http://academicjournals.org/ajb/abstracts/abs2006/18Sep/Xingming%20et%20al.htm

Ethanolic extracts of Sophora moorcroftiana seeds induce apoptosis of human stomach cancer cell line SGC-7901 in vitro

The seeds of Sophora moorcroftiana are used in Chinese traditional medicine for the treatment of verminosis, infectious diseases, and anti-inflammation. To investigate the antitumor and induction of apoptosis activity of Sophora moorcroftiana seeds, the ethanolic extracts from the seeds was prepared and added into the culture of human stomach cancer cell line SGC-7901 in vitro. The proliferation and apoptosis of cells treated with the ethanolic extracts were assessed by tetrazolium salt reduction (MTT) assay, fluorescence microscopy, transmission electron microscopy, flow cytometry and agarose gel electrophoresis of DNA fragmentation. The results showed that the growth of SGC-7901 cells was strongly inhibited by the ethanolic extracts at the concentration ranging between 0.31-5.00 mg/ml, and the apoptosis of treated cells was induced at the concentration of 1.25, 2.50, and 5.00 mg/ml in vitro. This suggested that the ethanolic extracts from S. moorcroftiana seeds contain potent antitumor fraction(s) on human stomach cancer SGC-7901 cells.

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http://www.ncbi.nlm.nih.gov/pubmed/18434118

A mannose-binding lectin from Sophora flavescens induces apoptosis in HeLa cells

The objective of this study was to investigate the anti-tumor activity of a lectin from Sophora flavescens and explore its potential apoptotic induction mechanism. …In conclusion, all experimental results demonstrated that this lectin seems to be a potent anti-tumor agent for its cytotoxicity and apoptosis effects on HeLa cells. Also, bioinformatics analyses showed that this lectin is speculated to bind a certain mannose-containing receptor on cancer cell surface thereby initiating downstream caspase cascade.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.10414/abstract

Sophoranone, extracted from a traditional Chinese medicine Shan Dou Gen, induces apoptosis in human leukemia U937 cells

Screening of various natural products in a search for novel inducers of apoptosis in human leukemia cells led us to identify the strong apoptosis-inducing activity in a fraction extracted with methanol from the roots of Sophora subprostrata Chun et T. Chen. We purified the compound that induced apoptosis in human leukemia cells and identified it as sophoranone. Sophoranone inhibited cell growth and induced apoptosis in various lines of cells from human solid tumors, with 50% inhibition of growth of human stomach cancer MKN7 cells at 1.2 ± 0.3 μM. The growth-inhibitory and apoptosis-inducing activities of sophoranone for leukemia U937 cells were very much stronger than those of other flavonoids, such as daidzein, genistein and quercetin.

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http://www.ncbi.nlm.nih.gov/pubmed/17134813

Matrine induced gastric cancer MKN45 cells apoptosis via increasing pro-apoptotic molecules of Bcl-2 family

Matrine, one of the main active components from the dry roots of Sophora flavescence, was known to induce apoptosis in a variety of tumor cells in vitro. However, the molecular mechanism of cell apoptosis induced by Matrine remains elusive. Here, we investigated the

apoptosis in Matrine-treated human gastric cancer MKN45 cells. The results showed that Matrine could inhibit cell proliferation and induce apoptosis in a dose-dependent manner. Further immunoblots revealed that in Matrine-treated cells, caspase-3, -7 were activated and the pro-apoptotic molecules Bok, Bak, Bax, Puma, and Bim were also up-regulated. Our results suggested that Matrine induced gastric cancer MKN45 cells apoptosis via increasing pro-apoptotic molecules of Bcl-2 family.

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http://www.ncbi.nlm.nih.gov/pubmed/17379399

Leachianone A as a potential anti-cancer drug by induction of apoptosis in human hepatoma HepG2 cells

The Chinese herbal medicine Radix Sophorae is widely applied as an anti-carcinogenic/ anti-metastatic agent against liver cancer. In this study, Leachianone A, isolated from Radix Sophorae, possessed a profound cytotoxic activity against human hepatoma cell line HepG2 in vitro, with an IC(50) value of 3.4microg/ml post-48-h treatment. Its action mechanism via induction of apoptosis involved both extrinsic and intrinsic pathways. Its anti-tumor effect was further demonstrated in vivo by 17-54% reduction of tumor size in HepG2-bearing nude mice, in which no toxicity to the heart and liver tissues was observed. In conclusion, this is the first report describing the isolation of Leachianone A from Radix Sophorae and the molecular mechanism of its anti-proliferative effect on HepG2 cells.

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http://ar.iiarjournals.org/content/25/3B/2055.abstract

Tumor-specificity and Apoptosis-inducing Activity of Stilbenes and Flavonoids

A total of eleven stilbenes [1-6] and flavonoids [7-11] were investigated for their tumor-specific cytotoxicity and apoptosis-inducing activity, using four human tumor cell lines (squamous cell carcinoma HSC-2, HSC-3, submandibular gland carcinoma HSG and promyelocytic leukemia HL-60) and three normal human oral cells (gingival fibroblast HGF, pulp cell HPC, periodontal ligament fibroblast HPLF). All of the compounds, especially sophorastilbene A [1], (+)-a-viniferin [2], piceatannol [5], quercetin [9] and isoliquiritigenin [10], showed higher cytotoxicity against the tumor cell lines than normal cells, yielding tumor-specific indices of 3.6, 4.7, >3.5, >3.3 and 4.0, respectively. Among the seven cell lines, HSC-2 and HL-60 cells were the most sensitive to the cytotoxic action of these compounds. Sophorastilbene A [1], piceatannol [5], quercetin [9] and isoliquiritigenin [10] induced internucleosomal DNA fragmentation and activation of caspases -3, -8 and -9 dose-dependently in HL-60 cells. (+)-a-Viniferin [2] showed similar activity, but only at higher concentrations. All the compounds failed to induce DNA fragmentation and activated caspases to much lesser extents in HSC-2 cells. Western blot analysis showed that sophorastilbene A [1], piceatannol [5] and quercetin [9] did not induce any consistent changes in the expression of pro-apoptotic proteins (Bax, Bad) and anti-apoptotic protein (Bcl-2) in HL-60 and HSC-2 cells. An undetectable expression of Bcl-2 protein in control and drug-treated HSC-2 cells may explain the relatively higher sensitivity of this cell line to stilbenes and flavonoids.

Spikemoss

(Selaginella Tamariscina)

http://www.ncbi.nlm.nih.gov/pubmed/16822197

Selaginella tamariscina induces apoptosis via a caspase-3-mediated mechanism in human promyelocytic leukemia cells

ST-induced apoptosis is accompanied by the activation of caspase-3 and the specific proteolytic cleavage of PARP. Concomitantly, ST treatments led to an increase in the proapoptotic Bax levels, while Bcl-2 expression was decreased. Moreover, this effect was attenuated by SOD and catalase. These results suggest that oxidative stress may be involved in the cytotoxicity of ST, and that ST-induced apoptosis of HL-60 cells is primarily mediated by the caspase activation pathway.

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http://www.ncbi.nlm.nih.gov/pubmed/10503882

Effects of Selaginella tamariscina on in vitro tumor cell growth, p53 expression, G1 arrest and in vivo gastric cell proliferation

The 1% Selaginella tamariscina feeding caused a significant reduction ($P < 0.05$) in the proliferating cell nuclear antigen-(PCNA) labeling index of the glandular stomach epithelium as compared with the MNNG-alone group value although 5% Selaginella tamariscina feeding was only associated with a tendency for decrease. These results suggest that Selaginella tamariscina could be a candidate chemopreventive agent against gastric cancer.

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http://en.cnki.com.cn/Article_en/CJFDTOTAL-MYXZ200802014.htm

Radioprotective effects of the water-soluble part of Selaginella Tamariscina on thymus and spleen in irradiated mice

Conclusion The water-soluble part of Selaginella tamariscina can protect mice from rays by inhibiting of apoptosis,adjusting of cell cycle progression of thymus and spleen cells in irradiated mice.

Stonebreaker

(Phyllanthus Niruri)

http://www.ncbi.nlm.nih.gov/pubmed/12559392

Phyllanthus urinaria triggers the apoptosis and Bcl-2 down-regulation in Lewis lung carcinoma cells

Phyllanthus urinaria (P. urinaria), a widely used herb medicine, was tested for the anticancer effect in its water extract for the first time. The water extract of P. urinaria significantly decreased the number of Lewis lung carcinoma cells in a dose-and time-dependent manner as determined by MTT assay. However, the water extract of P. urinaria did not exert any cytotoxic effect on normal cells such as endothelial cells and liver cells. Result from flow

cytometry revealed a dose-dependent increase of dead cells 24 hours after treating Lewis lung carcinoma cells with P. urinaria extract.

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http://en.cnki.com.cn/Article_en/CJFDTOTAL-ZYXY200703004.htm

In-vitro Inhibitory Effect of Phyllanthus Urinaria L Compound on Proliferation of Human liver Cancer Cell HePG_2 and Its Apoptosis Induction

Within a certain limit of concentrations,the higher the concentration and the longer the acting time,the stronger the inhibition.Co-cultured with 500 μ g/mL Phyllanthus Urinaria L compound for 72 h,the inhibitory rate reached 93.58 % and IC50 was 240 μ g/mL.Phyllanthus Urinaria L compound at different concentrations had an certain effect on inducing cell apoptosis.Conclusion Phyllanthus Urinaria L compound can inhibit the proliferation of hepatoma cell,and its mechanism may be related with the induction of hepatoma cell HePG2 apoptosis.

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http://ict.sagepub.com/content/early/2009/02/17/1534735408330713.abstract

Phyllanthus Amarus Inhibits Cell Growth and Induces Apoptosis in Daltons Lymphoma Ascites Cells

The authors found in an earlier study that Phyllanthus amarus extract could significantly inhibit the solid and ascites tumor development in mice induced by Dalton's lymphoma ascites (DLA) cells. In the present study, the apoptotic effects of P.amarus against DLA cells in culture was evaluated. P.amarus produced significant reduction in cell viability as determined by the MTT assay.

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http://en.cnki.com.cn/Article_en/CJFDTOTAL-NJZY201001008.htm

Inhibiting Effect of Phyllanthus Urinaria Alcohol Extract on Human Stomach Cancer Cell MKN28

MTT method determination showed that the extract had inhibiting effect on the multiplication of MKN28 cells and the inhibiting effect was dependent on concentration and time.The result of flow cytometry suggested that the extract could induce MKN28 apoptosis.CONCLUSION The alcohol extract of phyllanthus ruinaria can inhibit the growth of human stomach cell MKN28,and apoptosis is one of its mechanisms.

Styrylpyrone

(Goniothalamus Umbrosus)

http://www.cancerci.com/content/3/1/16

Styrylpyrone Derivative (SPD) induces apoptosis in a caspase-7-dependent manner in the human breast cancer cell line MCF-7

Styrylpyrone derivative (SPD) is a plant-derived pharmacologically active compound extracted from Goniothalamus sp. Previously, we have reported that SPD inhibited the proliferation of MCF-7 human breast cancer cells by inducing apoptotic cell death, while having minimal effects on non-malignant cells.

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http://docsdrive.com/pdfs/medwelljournals/rjbsci/2009/209-215.pdf

Oncolysis of Breast, Liver and Leukemia Cancer Cells Using Ethyl Acetate and Methanol Extracts of Goniothalamus umbrosus

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THC
(Cannabis)

http://www.ncbi.nlm.nih.gov/pubmed/17583570

The cannabinoid delta(9)-tetrahydrocannabinol inhibits RAS-MAPK and PI3K-AKT survival signalling and induces BAD-mediated apoptosis in colorectal cancer cells

The inhibition of ERK and AKT activity by THC was accompanied by activation of the proapoptotic BCL-2 family member BAD. Reduction of BAD protein expression by RNA interference rescued colorectal cancer cells from THC-induced apoptosis. These data suggest an important role for CB1 receptors and BAD in the regulation of apoptosis in colorectal cancer cells. The use of THC, or selective targeting of the CB1 receptor, may represent a novel strategy for colorectal cancer therapy.

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http://cancerres.aacrjournals.org/content/66/13/6615.abstract

Tetrahydrocannabinol Inhibits Cell Cycle Progression in Human Breast Cancer Cells

Here, we show that Delta-9-tetrahydrocannabinol (THC), through activation of CB2 cannabinoid receptors, reduces human breast cancer cell proliferation by blocking the progression of the cell cycle and by inducing apoptosis.

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http://www.ncbi.nlm.nih.gov/pubmed/10570948

Delta9-tetrahydrocannabinol induces apoptosis in human prostate PC-3 cells

The effect of delta9-tetrahydrocannabinol (THC), the major psycho-active component of marijuana, in human prostate cancer cells PC-3 was investigated. THC caused apoptosis in a dose-dependent manner. Morphological and biochemical changes induced by THC in prostate PC-3 cells shared the characteristics of an apoptotic phenomenon. First, loss of plasma membrane asymmetry determined by fluorescent anexin V binding. Second, presence of apoptotic bodies and nuclear fragmentation observed by DNA staining with 4',6-diamino-2-phenylindole (DAPI). Third, presence of typical ‘ladder-patterned’ DNA fragmentation. Central cannabinoid receptor expression was observed in PC-3 cells by immunofluorescence

studies. However, several results indicated that the apoptotic effect was cannabinoid receptor-independent, such as lack of an effect of the potent cannabinoid agonist WIN 55,212-2, inability of cannabinoid antagonist AM 251 to prevent cellular death caused by THC and absence of an effect of pertussis toxin pre-treatment.

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http://www.nature.com/onc/journal/v27/n3/full/1210641a.html

Delta-9-Tetrahydrocannabinol inhibits epithelial growth factor-induced lung cancer cell migration in vitro as well as its growth and metastasis in vivoTHC inhibits NSCLC metastasis and growth

Delta-9-Tetrahydrocannabinol (THC) is the primary cannabinoid of marijuana and has been shown to either potentiate or inhibit tumor growth, depending on the type of cancer and its pathogenesis. Little is known about the activity of cannabinoids like THC on epidermal growth factor receptor-overexpressing lung cancers, which are often highly aggressive and resistant to chemotherapy. In this study, we characterized the effects of THC on the EGF-induced growth and metastasis of human non-small cell lung cancer using the cell lines A549 and SW-1573 as in vitro models. We found that these cells express the cannabinoid receptors CB1 and CB2, known targets for THC action, and that THC inhibited EGF-induced growth, chemotaxis and chemoinvasion.

Theaflavin
(Green & Black Tea)

http://www.ncbi.nlm.nih.gov/pubmed/16253767

Induction of apoptosis in human leukemia cells by black tea and its polyphenol theaflavin

Treatment of human leukemic cell lines HL-60 and K-562 with extracts of green and black tea and their polyphenols epigallocatechin gallate and theaflavins, respectively, showed a dose dependent inhibition of growth as a result of cytotoxicity and suppression of cell proliferation.

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http://www.ncbi.nlm.nih.gov/pubmed/9852288

Black tea theaflavins induce programmed cell death in cultured human stomach cancer cells

The exposure of human stomach cancer KATO III cells to black tea theaflavin extract, free theaflavin, and theaflavin digallate that are main components of the extract, led to both growth inhibition and the induction of programmed cell death (apoptosis). Morphological changes showing apoptotic bodies were observed in the cells treated with black tea theaflavin extract, theaflavin and theaflavin digallate. The fragmentations by these theaflavin compounds of DNA to oligonucleosomal-sized fragments that are characteristics of apoptosis were observed to be concentration- and time-dependent. These data suggest that drinking of black tea in large amounts is recommended to protect humans from stomach cancer.

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http://www.ncbi.nlm.nih.gov/pubmed/17499812

Theaflavins induced apoptosis of LNCaP cells

Prostate cancer (PCA), the most frequently diagnosed malignancy in men, represents an excellent candidate disease for chemoprevention studies because of its particularly long latency period, high rate of mortality and morbidity. Infusion of black tea and its polyphenolic constituents have been shown to possess antineoplastic effects in androgen dependent PCA in both in vivo and in vitro models including transgenic animals.

Thymoquinone
(Nigella Sativa / Black Cumin Seeds & Oil)

http://www.biomedcentral.com/content/pdf/1756-9966-29-87.pdf

Thymoquinone and cisplatin as a therapeutic combination in lung cancer: Invitro and in vivo

TQ was able to inhibit cell proliferation, reduce cell viability and induce apoptosis. TQ at 100 μM and CDDP at 5 μM inhibited cell proliferation by nearly 90%and the combination showed synergism. TQ was able to induced apoptosis in both NCI-H460 and NCI-H146 cell lines. TQ also appears to affect the extracellular environmentinhibiting invasion and reducing the production of two cytokines ENA-78 and Gro-alphawhich are involved in neo-angiogenesis.

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http://www.ncbi.nlm.nih.gov/pubmed/12881014

Chemopreventive potential of volatile oil from black cumin (Nigella sativa L.) seeds against rat colon carcinogenesis

These findings demonstrate that the volatile oil of N. sativa has the ability to inhibit colon carcinogenesis of rats in the postinitiation stage, with no evident adverse side effects, and that the inhibition may be associated, in part, with suppression of cell proliferation in the colonic mucosa.

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http://www.ncbi.nlm.nih.gov/pubmed/15906362/

Thymoquinone induces apoptosis through activation of caspase-8 and mitochondrial events in p53-null myeloblastic leukemia HL-60 cells

Here, we report that TQ exhibits antiproliferative effect, induces apoptosis, disrupts mitochondrial membrane potential and triggers the activation of caspases 8, 9 and 3 in myeloblastic leukemia HL-60 cells. The apoptosis induced by TQ was inhibited by a general caspase inhibitor, z-VAD-FMK; a caspase-3-specific inhibitor, z-DEVD-FMK; as well as a caspase-8-specific inhibitor, z-IETD-FMK.

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http://www.springerlink.com/content/l84x8772v751373u/

Structure-Activity Studies on Therapeutic Potential of Thymoquinone Analogs in Pancreatic Cancer

Pancreatic cancer (PC) is one of the deadliest of all tumors. Previously, we were the first to show that Thymoquinone (TQ) derived from black seed (Nigella sativa) oil has anti-tumor activity against PC. However, the concentration of TQ required was considered to be high to show this efficacy. Therefore, novel analogs of TQ with lower IC50 are highly desirable.

Uncaria
("Cat's Claw")

http://www.ncbi.nlm.nih.gov/pubmed/15649507

Ethnobotany, phytochemistry and pharmacology of Uncaria (Rubiaceae)

The Uncaria genus is an important source of medicinal natural products, particularly alkaloids and triterpenes. The collected information is an attempt to cover the more recent developments in the ethnobotany, pharmacology and phytochemistry of this genus. During the past 20 years, alkaloids, terpenes, quinovic acid glycosides, flavonoids and coumarins have been isolated from Uncaria. Fifty-three novel structures are reported in this review. The species in which the largest number of compounds has been identified is the Peruvian Uncaria tomentosa or 'cat's claw.' Pharmacological studies are described according to cytotoxicity, anti-inflammatory, antiviral, immunostimulation, antioxidant, CNS-related response, vascular, hypotensive, mutagenicity and antibacterial properties. The potential for development of leads from Uncaria continues to grow, particularly in the area of immunomodulatory, anti-inflammatory and vascular-related conditions.

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http://onlinelibrary.wiley.com/doi/10.1111/j.1365-2141.2005.05907.x/abstract

Oxindole alkaloids from Uncaria tomentosa induce apoptosis in proliferating, G0/G1-arrested and bcl-2-expressing acute lymphoblastic leukaemia cells

Natural products are still an untapped source of promising lead compounds for the generation of antineoplastic drugs. Here, we investigated for the first time the antiproliferative and apoptotic effects of highly purified oxindole alkaloids, namely isopteropodine (A1), pteropodine (A2), isomitraphylline (A3), uncarine F (A4) and mitraphylline (A5) obtained from Uncaria tomentosa, a South American Rubiaceae, on human lymphoblastic leukaemia T cells (CCRF-CEM-C7H2). Four of the five tested alkaloids inhibited proliferation of acute lymphoblastic leukaemia cells. Furthermore, the antiproliferative effect of the most potent alkaloids pteropodine (A2) and uncarine F (A4) correlated with induction of apoptosis. After 48 h, 100 μmol/l A2 or A4 increased apoptotic cells by 57%. CEM-C7H2 sublines with tetracycline-regulated expression of bcl-2, p16ink4A or constitutively expressing the cowpox virus protein crm-A were used for further studies of the apoptosis-inducing properties of these alkaloids. Neither overexpression of bcl-2 or crm-A nor cell-cycle arrest in G0/G1 phase by tetracycline-regulated expression of p16INK4A could prevent alkaloid-induced apoptosis. Our results show the strong apoptotic effects of pteropodine and uncarine F on acute leukaemic

lymphoblasts and recommend the alkaloids for further studies in xenograft models.

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http://www.springerlink.com/content/d1638h2q68559044/

Methanolic Extracts of Uncaria rhynchophylla Induce Cytotoxicity and Apoptosis in HT-29 Human Colon Carcinoma Cells

In this paper, we report the anticancer activities of Uncaria rhynchophylla extracts, a Rubiaceae plant native to China. Traditionally, Uncaria rhynchophylla has been used in the prevention and treatment of neurotoxicity. However, the cytotoxic activity of Uncaria rhynchophylla against human colon carcinoma cells has not, until now, been elucidated. We found that the methanolic extract of Uncaria rhynchophylla (URE) have cytotoxic effects on HT-29 cells. The URE showed highly cytotoxic effects via the MTT reduction assay, LDH release assay, and colony formation assay. As expected, URE inhibited the growth of HT-29 cells in a dose-dependent manner. In particular, the methanolic URE of the 500 μg/ml showed 15.8% inhibition against growth of HT-29 cells. It induced characteristic apoptotic effects in HT-29 cells, including chromatin condensation and sharking occurring 24 h when the cells were treated at a concentration of the 500 μg/ml.

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http://ar.iiarjournals.org/content/29/11/4519.abstract

Antiproliferative and Pro-apoptotic Effects of Uncaria tomentosa in Human Medullary Thyroid Carcinoma Cells

Medullary thyroid carcinoma (MTC), a rare calcitonin-producing tumor, is derived from parafollicular C-cells of the thyroid and is characterized by constitutive Bcl-2 overexpression. The tumor is relatively insensitive to radiation therapy as well as conventional chemotherapy. To date, the only curative treatment is the early and complete surgical removal of all neoplastic tissue. In this study, the antiproliferative and pro-apoptotic effects of fractions obtained from Uncaria tomentosa (Willd.) DC, commonly known as uña de gato or cat's claw were investigated. Cell growth of MTC cells as well as enzymatic activity of mitochondrial dehydrogenase was markedly inhibited after treatment with different fractions of the plant. Furthermore, there was an increase in the expressions of caspase-3 and -7 and poly(ADP-ribose) polymerase (PARP) fraction, while bcl-2 overexpression remained constant. In particular, the alkaloids isopterpodine and pteropodine of U. tomentosa exhibited a significant pro-apoptotic effect on MTC cells, whereas the alkaloid-poor fraction inhibited cell proliferation but did not show any pro-apoptotic effects. These promising results indicate the growth-restraining and apoptotic potential of plant extracts against neuroendocrine tumors, which may add to existing therapies for cancer.

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http://journals.indexcopernicus.com/abstracted.php?icid=865894

An ethanolic extract of Uncaria tomentosa reduces inflammation and B16-BL6 melanoma growth in C57BL/6 mice

Extracts of the bark of Uncaria tomentosa (Cat's Claw – Uña de Gato) have been used traditionally for their anti-inflammatory and anticancer properties. We investigated the effect

of a hydroethanolic extract (UT) of U. tomentosa on a) the viability of primary and tumor cells, b) the inflammatory response (tumor necrosis factor alpha [TNF-a], interleukin-6 [IL-6] and nitric oxide [NO]) both in vitro and in vivo, c) B16/BL6 melanoma cell growth and metastasis in the C57BL/6 mouse, and d) nuclear factor ?B (NF-?B) activity in LPS-stimulated HeLa cells. UT did not show an important cytotoxic effect in vitro at the doses up to 300 µg/ml, but did inhibit tumor growth and metastasis in vivo. UT inhibited TNF-a, IL-6 and NO production in vitro. NF-?B activity was also inhibited. Our studies show that UT merits further study for its effects on processes common to inflammation and cancer.

Vanillin
(Vanilla Beans)

http://www.ncbi.nlm.nih.gov/pubmed/15854801

Vanillin suppresses in vitro invasion and in vivo metastasis of mouse breast cancer cells

Vanillin, a food flavoring agent, has been reported to show anti-mutagenic activity and to inhibit chemical carcinogenesis. In this study, we examined the effect of vanillin on the growth and metastasis of 4T1 mammary adenocarcinoma cells in BALB/c mice. Mice orally administered with vanillin showed significantly reduced numbers of lung metastasized colonies compared to controls. In vitro studies revealed that vanillin, at concentrations that were not cytotoxic, inhibited invasion and migration of cancer cells and inhibited enzymatic activity of MMP-9 secreted by the cancer cells.

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http://www.ncbi.nlm.nih.gov/pubmed/19679064

Apoptosis and cell cycle arrest of human colorectal cancer cell line HT-29 induced by vanillin

Results showed that apoptosis was induced by vanillin and the IC(50) for HT-29 and NIH/3T3 normal cell lines were 400 microg/ml and 1000 microg/ml, respectively. Different concentrations of vanillin arrest cell cycle at different checkpoints. 5-Bromo-2-deoxyuridine-labeling cell proliferation assay showed that G0/G1 arrest was achieved at lower concentration of vanillin (200 microg/ml) while cell cycle analysis by flow cytometer showed that G2/M arrest occurs at higher concentration of vanillin (1000 microg/ml).

Vitamin D3
(Salmon, Catfish, Tuna, Eggs, Milk, Yogurt, Margarine, Bread)

http://www.ncbi.nlm.nih.gov/pubmed/12888897

Vitamin D3 inhibits Thioredoxin

Thioredoxin, a Gene Found Overexpressed in Human Cancer, Inhibits Apoptosis. The redox protein thioredoxin plays an important role in controlling cancer cell growth through regulation of DNA synthesis and transcription factor activity. Thioredoxin is overexpressed by a number of human primary cancers and its expression is decreased during dexamethasone-

induced apoptosis of mouse WEHI7.2 thymoma cells. We examined the ability of WEHI7.2 cells stably transfected with human thioredoxin cDNA showing increased levels of cytoplasmic thioredoxin to undergo apoptosis in vitro and in vivo. The cells were protected from apoptosis induced by dexamethasone, staurosporine, etoposide, and thapsigargin, but not by N-acetyl-sphingosine.

Vitamin K2

(“Natto”, Chicken, Beef, Egg Yolks, Cheese, and Salami. Only about 10% of dietary vitamin K intake is in the K2 form, the other 90% being the more common K1. Other foods that contain Vitamin K: Peas, Spinach, Swiss Chard, Brussel Sproats, Broccoli, Carrots, Kale, Asparagus, Mustard Greens and Green Beans)

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http://www.ncbi.nlm.nih.gov/pubmed/12888897

Apoptosis induction of vitamin K2 in lung carcinoma cell lines: the possibility of vitamin K2 therapy for lung cancer

Morphologic features of the cells treated with VK2 were typical for apoptosis along with caspase-3 activation and becoming positive for APO2.7 monoclonal antibody, an antibody which specifically detects the cell undergoing apoptosis. In addition to the leukemia cell line, LU-139 cells accumulated into G0/G1 phase during 72-h exposure to VK2. Combined treatment of cisplatin plus VK2 resulted in enhanced cytocidal effect compared to the cells treated with either cisplatin or VK2 alone. Since VK2 is a safe medicine without prominent adverse effects including bone marrow suppression, our data strongly suggest the therapeutic possibility of using VK2 for the treatment of patients with lung carcinoma.

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http://www.ncbi.nlm.nih.gov/pubmed/17088989

Apoptosis of liver cancer cells by vitamin K2 and enhancement by MEK inhibition

These data demonstrated that VK2 induced apoptosis and activated the MEK/ERK1/2 signaling pathway in a cell-type specific manner, and a MEK inhibitor could augment the cell death in these cells.

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http://www.ncbi.nlm.nih.gov/pubmed/16391821

Vitamin K2-induced antitumor effects via cell-cycle arrest and apoptosis in gastric cancer cell lines

Vitamin K2 (VK2) has a growth inhibitory effect on various types of cancer cells in vitro, and its efficacy has been demonstrated in clinical applications in a number of patients with leukemia and hepatocellular carcinoma. In this study, the effect of cell growth inhibition and apoptosis induction and the concomitant use of an anticancer agent by VK2 (menaquinone: MK4), on gastric cancer cell lines were examined. When 4 kinds of gastric cancer cells (KATO III, MKN7, MKN74 and FU97) were exposed to MK4, the cell growth was inhibited

in an MK4 dose-dependent manner. Morphologically, apoptosis induced by MK4 was recognized in FU97, but only a slight number of apoptotic images was recognized in other cell lines.

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http://www.springerlink.com/content/r0507273724l4xpq/

Production of superoxide and dissipation of mitochondrial transmembrane potential by vitamin K2 trigger apoptosis in human ovarian cancer TYK-nu cells

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Watercress

http://www.medicalnewstoday.com/articles/30696.php

Compounds in broccoli, cauliflower, and watercress block lung cancer progression

A family of compounds found in cruciferous vegetables, such as broccoli, cauliflower, and watercress, blocked lung cancer progression in both animal studies and in tests with human lung cancer cells, report researchers from Georgetown University Medical Center and the Institute for Cancer Prevention. They say the results, published in a set of papers in the September 15 issue of Cancer Research, suggest that these chemicals — put into a veggie pill of sorts — might some day be used to help current and former smokers ward off development of lung cancer, the leading cause of cancer death in Americans.

Willow

http://www.ncbi.nlm.nih.gov/pubmed/17418981

Willow bark extract (BNO1455) and its fractions suppress growth and induce apoptosis in human colon and lung cancer cells

We showed that willow bark extract BNO 1455 an its fractions inhibit the cell growth and promote apoptosis in human colon and lung cancer cell lines irrespective of their COX-selectivity.

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http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1779808/

Willow Leaves Extracts Contain Anti-Tumor Agents Effective against Three Cell Types

In vivo Ehrlich Ascites Carcinoma Cells (EACC) were injected into the intraperitoneal cavity of mice. The willow extract was fed via stomach tube. The (EACC) derived tumor growth was reduced by the willow extract and death was delayed (for 35 days). In vitro the willow extract could kill the majority (75%–80%) of abnormal cells among primary cells harvested from seven patients with acute lymphoblastic leukemia (ALL) and 13 with AML (acute myeloid leukemia). DNA fragmentation patterns within treated cells inferred targeted cell death by apoptosis had occurred. The metabolites within the willow extract may act as tumor inhibitors

that promote apoptosis, cause DNA damage, and affect cell membranes and/or denature proteins.

White Button Mushroom
(Agaricus mushrooms)

http://www.ncbi.nlm.nih.gov/pubmed/19020714

Blazein of a new steroid isolated from Agaricus blazei Murrill (himematsutake) induces cell death and morphological change indicative of apoptotic chromatin condensation in human lung cancer LU99 and stomach cancer KATO III cells.

Blazein was isolated from mushroom (Agaricus blazei Murrill) and identified by Mass and 1H-NMR as blazein. The effect of blazein on the DNA of human various cancer cells was investigated. DNA fragmentations by blazein to oligonucreosomal-sized fragments, a characteristic of apoptosis, were observed in the human lung LU99 and stomach KATO III cancer cells. The DNA fragmentations by blazein were observed from day 2 (KATO III cells) or day 3 (LU99 cells) after the addition of blazein to the culture cells. These findings suggest that growth inhibition by blazein results from the induction of apoptosis by the compound.

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http://www.ncbi.nlm.nih.gov/pubmed/19005974

White Button Mushroom (Agaricus Bisporus) Exhibits Antiproliferative and Proapoptotic Properties and Inhibits Prostate Tumor Growth in Athymic Mice

White button mushrooms are a widely consumed food containing phytochemicals beneficial to cancer prevention. The purpose of this research was to evaluate the effects of white button mushroom extract and its major component, conjugated linoleic acid (CLA) on prostate cancer cell lines in vitro and mushroom extract in vivo. In all cell lines tested, mushroom inhibited cell proliferation in a dose-dependent manner and induced apoptosis within 72 h of treatment.

Xanthohumol
(Hops, Ashataba Extracts)

http://www.ncbi.nlm.nih.gov/pubmed/16563612

Xanthohumol induces apoptosis in cultured 40-16 human colon cancer cells by activation of the death receptor- and mitochondrial pathway

In this study, we investigated the cell growth inhibitory potential of XN on cultured human colon cancer cells. Cell proliferation was measured by sulforhodamine B staining. Poly(ADP-ribose)polymerase (PARP) cleavage, activation of caspases-3, -7, -8, and -9, and Bcl-2 family protein expression were detected by Western blot analyses. XN significantly reduced proliferation of the HCT116-derived colon cancer cell line 40-16. …We conclude that induction of apoptosis by downregulation of Bcl-2 and activation of the caspase cascade may contribute to the chemopreventive or therapeutic potential of XN.

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http://www.ncbi.nlm.nih.gov/pubmed/16563612

Xanthohumol, a prenylflavonoid derived from hops induces apoptosis and inhibits NF-kappaB activation in prostate epithelial cells

Limited in vitro studies indicate that several prenylated flavonoids present in the hop plant (Humulus lupulus) possess anticarcinogenic properties. The purpose of this study was to investigate the anti-tumorigenic effects of xanthohumol (XN), the major prenylflavonoid in hops, on prostate cancer and benign prostate hyperplasia. …XN and its oxygenated derivative also induced cell cycle changes in both cells lines, seen in an elevated sub G1 peak at 48h treatment. Western blot analysis was performed to confirm the activation of proapoptotic proteins, Bax and p53. XN and its derivative caused decreased activation of NFkappaB. This work suggests that XN and its oxidation product, XAL, may be potentially useful as a chemopreventive agent during prostate hyperplasia and prostate carcinogenesis, acting via induction of apoptosis and down-regulation of NFkappaB activation in BPH-1 cells.

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http://onlinelibrary.wiley.com/doi/10.1002/jcb.21738/abstract

Xanthohumol inhibits inflammatory factor production and angiogenesis in breast cancer xenografts

Xanthohumol (XN), a natural polyphenol present in beer, is known to exert anti-cancer effects. However, its precise mechanisms are not yet clearly defined. The aim of this study was to investigate the effect of oral administration of XN in breast cancer xenografts in nude mice. …Oral administration of XN to nude mice inoculated with MCF7 cells resulted in central necrosis within tumours, reduced inflammatory cell number, focal proliferation areas, increased percentage of apoptotic cells and decreased microvessel density. Anti-angiogenic effects of XN were further confirmed by immunoblotting for factor VIII expression in XN-treated tumours as compared to controls. Decreased immunostaining for NF?B, phosphorylated-inhibitor of kappa B and interleukin-1ß were also observed as well as a significant decrease in NF?B activity to 60% of control values. These novel findings indicate that XN is able to target both breast cancer and host cells, namely inflammatory and endothelial cells, suggesting its potential use as a double-edge anti-cancer agent.

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http://onlinelibrary.wiley.com/doi/10.1002/mnfr.200500045/abstract

Xanthohumol kills B-chronic lymphocytic leukemia cells by an apoptotic mechanism

Based on these observations, lymphocytes from patients with B-CLL were cultured in the presence of XA in vitro. XA induced a dose-dependent killing of B-CLL cells at an LD50(24 h) of 24.4 ± 6.6 μM, independent of known adverse prognostic factors including functional loss of p53. Cell death was associated with poly (ADP)-ribose polymerase cleavage and annexin V positivity, suggestive of an apoptotic mechanism. Surprisingly, p70S6K phosphorylation was stimulated upon XA treatment. In conclusion, XA has an antitumor activity on B-CLL cells in vitro. The molecular mechanisms behind this pro-apoptotic effect deserve further investigation.

Zerumbone

(Shampoo Ginger Plant -- Zingiber Zerumbet)

http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1852295/

Zerumbone induced apoptosis in liver cancer cells via modulation of Bax/Bcl-2 ratio

Zerumbone is a cytotoxic component isolated from Zingiber zerumbet Smith, a herbal plant which is also known as lempoyang. …zerumbone was found to induce the apoptotic process in HepG2 cells through the up and down regulation of Bax/Bcl-2 protein independently of functional p53 activity.

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http://www.ncbi.nlm.nih.gov/pubmed/17129359

Zerumbone, a bioactive sesquiterpene, induces G2/M cell cycle arrest and apoptosis in leukemia cells via a Fas- and mitochondria-mediated pathway

We demonstrated here for the first time that zerumbone (ZER), a natural cyclic sesquiterpene, significantly suppressed the proliferation of promyelocytic leukemia NB4 cells among several leukemia cell lines, but not human umbilical vein endothelial cells (HUVECs), by inducing G2/M cell cycle arrest followed by apoptosis with 10 microM of IC50.

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http://onlinelibrary.wiley.com/doi/10.1002/ijc.23923/abstract

Zerumbone, a tropical ginger sesquiterpene, inhibits colon and lung carcinogenesis in mice

Our findings suggest that dietary administration of ZER effectively suppresses mouse colon and lung carcinogenesis through multiple modulatory mechanisms of growth, apoptosis, inflammation and expression of NF?B and HO-1 that are involved in carcinogenesis in the colon and lung.

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