Plantas com efeito na prevenção do câncer

Paula Viñas
José de Felippe Junior

Todas as verduras, legumes e frutas são ricas em antioxidantes e assim protegem os animais que ingerem dos radicais livres. Normalmente produzimos espécies reativas tóxicas de oxigênio, e a quantidade não exagerada desses elementos nos protegem de infeções por bactérias, vírus e fungos. É por intermédio dos radicais livres que o organismo promove a morte celular programada (apoptose) de células defeituosas e de células cancerosas. O problema está no excesso de produção dos radicais livres que poderão lesar o DNA nuclear e provocar o aparecimento de células transformadas ou cancerosas.

Muitas plantas são ricas em antioxidantes e assim funcionam como moduladores nos protegendo do excesso de produção dos radicais livres.

abacate

**Novel nitric oxide and superoxide generation inhibitors, persenone A and B, from avocado fruit.**


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Division of Applied Life Sciences, Graduate School of Agriculture, Kyoto University, Kyoto, Japan.

One known, (2R)-(12Z,15Z)-2-hydroxy-4-oxoheneicosa-12,15-dien+ ++-1-yl acetate (1), and two novel compounds, persenone A (2) and B (3), have been isolated from avocado fruit (Persea americana P. Mill), as inhibitors of superoxide (O(2)(-)) and nitric oxide (NO) generation in cell culture systems. They showed marked inhibitory activities toward NO generation induced by lipopolysaccharide in combination with interferon-gamma in mouse macrophage RAW 264.7 cells. Their inhibitory potencies of NO generation (1, IC(50) = 3.6; 2, IC(50) = 1.2; and 3, IC(50) = 3.5 microM) were comparable to or higher than that of a natural NO generation inhibitor, docosahexaenoic acid (DHA, IC(50) = 4.3 microM). Furthermore, compounds 1-3 and DHA markedly suppressed tumor promoter 12-O-tetradecanoylphorbol-13-acetate-induced O(2)(-)-generation in differentiated human promyelocytic HL-60 cells (1, IC(50) = 33.7; 2, IC(50) = 1.4; 3, IC(50) = 1.8; and DHA, IC(50) = 10.3 microM). It is notable that they were found to be suppressors of both NO- and O(2)(-) -generating biochemical pathways but not to be radical scavengers. The results indicate that these compounds are unique antioxidants, preferentially suppressing radical generation, and thus may be promising as effective chemopreventive agent candidates in inflammation-associated carcinogenesis.

Acerola

**Effect of acerola cherry extract on cell proliferation and activation of ras signal pathway at the promotion stage of lung tumorigenesis in mice.**


Department of Agriculture and Biological Chemistry, College of Bioresource Sciences, Nihon University, Fujisawa, Kanagawa, Japan.

The present study was undertaken to estimate the effect of acerola cherry extract (ACE) pretreatment on cell proliferation and the activation of Ras signal pathway at a promotion stage of lung tumorigenesis in mice treated with 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK). Pretreatment with ACE (dose, 70mg/kg body weight and 700 mg/kg body weight) inhibited increases in the levels of proliferating nuclear cell antigen and ornithine decarboxylase at the promotion stage. This treatment of ACE also suppressed the activation of Ras signal pathway at the same stage. These results suggest that ACE regulates abnormal cell growth at the promotion stage of lung tumorigenesis in mice treated with NNK as a result of suppression of the initiation stage.

Agríno

**A Comparison of Risk and Protective Factors for Colorectal Cancer in the Diet of New Zealand Maori and non-Maori.**


By international standards New Zealand (population 3.8 x 10(6)) has a high rate of colorectal cancer, with approximately 2000 new cases occurring and approximately 1000 deaths each year. But within the New Zealand population, a lower incidence of colorectal cancer is reported for Maori than for non-Maori New Zealanders (22.2 and 43.7 per 100,000 respectively). Information from the New Zealand National Nutrition Survey 1997 shows that in comparison to non-Maori, Maori eat more in total, eat more red meat, drink more alcohol, consume more saturated fat, have a higher prevalence of obesity and have a lower proportion of individuals consuming a given level of fruit and vegetables per day. All these factors would be expected to increase colorectal cancer risk. Puha (sow thistle; Sonchus sp.) and watercress (Nasturtium officinale, N. aquaticum) are foods with plausible cancer protective properties which are components of the Maori, but not the non-Maori diet.

**Effects of watercress consumption on metabolism of a tobacco-specific lung carcinogen in smokers.**

Cancer Epidemiol Biomarkers Prev. 1995 Dec;4(8):877-84


American Health Foundation, Valhalla, New York 10595, USA.

Epidemiological studies indicate that vegetable consumption protects against lung cancer in humans, but the protective constituents have not been identified. Phenethyl isothiocyanate (PEITC), which is release upon chewing of watercress (nasturtium officinale), is a chemopreventive agent against lung cancer induced by the tobacco-specific lung carcinogen 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanone (NNK) in rats and mice. PEITC inhibits the carcinogenicity of NNK by inhibiting its metabolic activation and thereby increasing the levels of detoxified metabolites excreted in urine. In this study, our goal was to determine whether watercress consumption would modify NNK metabolism in smokers. Eleven smokers maintained constant smoking habits and avoided cruciferous vegetables and other...
sources of isothiocyanates throughout the study. They donated 24-h urine samples on 3 consecutive days (baseline period). One to 3 days later, they consumed 2 ounces (56.8 g) of watercress at each meal for 3 days and donated 24-h urine samples on each of these days (watercress consumption period). One and 2 weeks later; they again donated 24-h urine samples on 2-3 consecutive days (follow-up periods). The samples were analyzed for two metabolites of NNK; 4-(methylthiorosarnino)-1-(3-pyridyl)-1-butanone (NNAL) and [4-(methylthiorosarnino)-1-(3-pyridyl)but-1-yl]-beta-omega-D-glucosiduro nic acid (NNAL-Gluc). NNAL-Gluc is believed to be a detoxification product of NNK. The urine samples were also assayed for PETIT-NAC, a metabolite of PETITC. Minimum exposure to PETITC during the watercress consumption period averaged 19.38 mg/day. Seven of the 11 subjects showed increased levels of total urinary NNAL plus NNAL-Gluc. The percentage of increase in urinary NNAL plus NNAL-Gluc returned to near baseline levels in the follow-up periods. The percentage of increase in urinary NNAL plus NNAL-Gluc during days 2 and 3 of the watercress consumption period correlated with intake of PETITC during this period, as measured by total urinary PETITC-NAC. The results of this study support our hypothesis that PETITC inhibits this oxidative metabolism of NNK in humans, as seen in rodents, and support further development of PETITC as a chemopreventive agent against lung cancer. This is the first study to report an effect of vegetable consumption on metabolism of a lung carcinogen in humans.

**Effects of watercress consumption on metabolism of a tobacco-specific lung carcinogen in smokers.**

Cancer Epidemiol Biomarkers Prev. 1995 Dec;4(8):877-84

Hecht SS, Chung FL, Richie JP Jr, Akerkar SA, Borukhova A, Skowronsik L, Carmella SG.

American Health Foundation, Valhalla, New York 10595, USA.

**Epidemiological studies indicate that vegetable consumption protects against lung cancer in humans, but the protective constituents have not been identified. Phenethyl isothiocyanate (PEITC), which is release upon chewing of watercress (nasturtium officinale), is a chemopreventive agent against lung cancer induced by the tobacco-specific lung carcinogen 4- (methylthiorosarnino)-1-(3-pyridyl)-1-butanone (NNK) in rats and mice. PEITC inhibits the carcinogenicity of NNK by inhibiting its metabolic activation and thereby increasing the levels of detoxified metabolites excreted in urine. In this study, our goal was to determine whether watercress consumption would modify NNK metabolism in smokers. Eleven smokers maintained constant smoking habits and avoided cruciferous vegetables and other sources of isothiocyanates throughout the study. They donated 24-h urine samples on 3 consecutive days (baseline period). One to 3 days later; they consumed 2 ounces (56.8 g) of watercress at each meal for 3 days and donated 24-h urine samples on each of these days (watercress consumption period). One and 2 weeks later; they again donated 24-h urine samples on 2-3 consecutive days (follow-up periods). The samples were analyzed for two metabolites of NNK; 4-(methylthiorosarnino)-1-(3-pyridyl)-1-butanone (NNAL) and [4-(methylthiorosarnino)-1-(3-pyridyl)but-1-yl]-beta-omega-D-glucosiduro nic acid (NNAL-Gluc). NNAL-Gluc is believed to be a detoxification product of NNK. The urine samples were also assayed for PETITC-NAC, a metabolite of PETITC. Minimum exposure to PETITC during the watercress consumption period averaged 19.38 mg/day. Seven of the 11 subjects showed increased levels of urinary NNAL plus NNAL-Gluc during days 2 and 3 of the watercress consumption period correlated with intake of PETITC during this period, as measured by total urinary PETITC-NAC. (r = 0.62; P = 0.04). The results of this study support our hypothesis that PETITC inhibits this oxidative metabolism of NNK in humans, as seen in rodents, and support further development of PETITC as a chemopreventive agent against lung cancer. This is the first study to report an effect of vegetable consumption on metabolism of a lung carcinogen in humans.

**Aipo**

**Chemoprevention of benzo[a]pyrene-induced forestomach cancer in mice by natural phthalides from celery seed oil.**


LKT Laboratories, Minneapolis, MN 55413.

Bioassay-directed fractionation of celery seed oil from the plant Apium graveolens (Umbelliferae) led to the isolation of five natural products, including d-limonene, p-mentha-2,8-dien-1-ol, p-mentha-8(9)-en-1,2-diol, 3-n-butyl phthalide, and sedanolide. Of these compounds, p-mentha-2,8-dien-1-ol, 3-n-butyl phthalide, and sedanolide exhibited high activities to induce the detoxifying enzyme glutathione S-transferase (GST) in the target tissues of female A/J mice. 3-n-Butyl phthalide and sedanolide (20 mg/dose, every two days for a total of 3 doses) increased GST activity 4.5-5.9 and 3.2-5.2 times over the controls in the mouse liver and small intestinal mucosa, respectively. At the same dose, p-mentha-2,8-dien-1-ol induced GST activity about 3.7-fold above that of the controls. Thus, these compounds were further tested for their ability to inhibit benzo[a]pyrene- (BP) induced tumorigenesis in mice. After treatment with 3-n-butyl phthalide and sedanolide, the tumor incidence was reduced from 68% to 30% and 11%, respectively. About 67% and small or no significant reduction of forestomach tumor formation. The data indicating that 3-n-butyl phthalide and sedanolide were both active in tumor inhibition and GST assays suggested a correlation between the inhibitory activity and the GST-inducing ability. The phthalides are known to determine the characteristic odor of celery. The results suggest that phthalides, as a class of bioactive natural products occurring in edible umbelliferous plants, may be effective chemopreventive agents.

**Alicchofa**

**Inhibitory effect of taraxastane-type triterpenes on tumor promotion by 12-O-tetradecanoylphorbol-13-acetate in two-stage carcinogenesis in mouse skin.**


Nestle Research Centre, Lausanne, Switzerland.

Offord EA, Mace K, Ruffieux C, Malnoe A, Pfeifer AM.

American Health Foundation, Valhalla, New York 10595, USA.

Two taraxastane-type hydroxy triterpenes, taxasterol and taxadienol, isolated from the flowers of Composite plants Cynara scolymus (artichoke) and Chrysanthemum morifolium (chrysanthemum), respectively, showed strong inhibitory activity against 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced inflammation in mice. At 2.0 mmol/mouse, these compounds inhibited markedly the tumor-promoting effect of TPA (1 microgram/mouse) on skin tumor formation following initiation with 7,12-dimethylbenz[alpha]anthracene (50 micrograms/mouse).

**Alecrin de Jardim**

**Rosemary components inhibit benzo[a]pyrene-induced genotoxicity in human bronchial cells.**

Carcinogenesis. 1995 Sep;16(9):2057-62.

Zhang J, Kenney PM, Lam LK.

LKT Laboratories, Minneapolis, MN 55413.

Bioassay-directed fractionation of celery seed oil from the plant Apium graveolens (Umbelliferae) led to the isolation of five natural products, including d-limonene, p-mentha-2,8-dien-1-ol, p-mentha-8(9)-en-1,2-diol, 3-n-butyl phthalide, and sedanolide. Of these compounds, p-mentha-2,8-dien-1-ol, 3-n-butyl phthalide, and sedanolide exhibited high activities to induce the detoxifying enzyme glutathione S-transferase (GST) in the target tissues of female A/J mice. 3-n-Butyl phthalide and sedanolide (20 mg/dose, every two days for a total of 3 doses) increased GST activity 4.5-5.9 and 3.2-5.2 times over the controls in the mouse liver and small intestinal mucosa, respectively. At the same dose, p-mentha-2,8-dien-1-ol induced GST activity about 3.7-fold above that of the controls. Thus, these compounds were further tested for their ability to inhibit benzo[a]pyrene- (BP) induced tumorigenesis in mice. After treatment with 3-n-butyl phthalide and sedanolide, the tumor incidence was reduced from 68% to 30% and 11%, respectively. About 67% and small or no significant reduction of forestomach tumor formation. The data indicating that 3-n-butyl phthalide and sedanolide were both active in tumor inhibition and GST assays suggested a correlation between the inhibitory activity and the GST-inducing ability. The phthalides are known to determine the characteristic odor of celery. The results suggest that phthalides, as a class of bioactive natural products occurring in edible umbelliferous plants, may be effective chemopreventive agents.
The commonly used spice and flavouring agent, rosemary, derived from the leaves of the plant Rosmarinus officinalis L., displays antioxidant properties in foods and in biological systems. Moreover, in animal models rosemary components were found to inhibit the initiation and tumour promotion phases of carcinogenesis. In this work, we studied the mechanisms by which rosemary components block initiation of carcinogenesis by the procarcinogen benzo[a]pyrene (B[a]P) in human bronchial epithelial cells (BEAS-2B). Whole rosemary extract (6 micrograms/ml) or an equivalent concentration of its most potent antioxidant constituents, carnosol or carnosic acid, inhibited DNA adduct formation by 80% after 6 h co-incubation with 1.5 μM B[a]P. Under similar conditions, cytochrome P450 (CYP) 1A1 mRNA expression was 50% lower in the presence of rosemary components, and CYP1A1 activity was inhibited 70-90%. The observed reduction of DNA adduct formation by rosemary components may mostly result from the inhibition of the activation of benzo[a]pyrene to its ultimate metabolites. Carnosol also affected expression of the phase II enzyme glutathione-S-transferase which is known to detoxify the proximate carcinogenic metabolite of B[a]P. Treatment of BEAS-2B cells with carnosol (1 microgram/ml) for 24 h resulted in a 3- to 4-fold induction of GST pi mRNA. Moreover, expression of a second important phase II enzyme, NAD(P)H:quinone reductase, was induced by carnosol in parallel with GST pi. Therefore, rosemary components have the potential to decrease activation and increase detoxification of an important human carcinogen, identifying them as promising candidates for chemopreventive programs.

Angelica

Antimutagenic properties of Angelica archangelica L
Salkhova RA, Poroshenko GG.

The antimutagenic activity of Angelica archangelica L. aqueous and alcohol extracts of thio-TEPA against mutagenicity was examined by the micronucleus test in murine bone marrow cells. The reduction of Thio-TEPA's mutagenic activity was more profound when the extracts were injected 2 hours before thio-TEPA treatment, as seen during simultaneous treatment. The observed reduction of micronuclear frequencies was as high as 77%.

Study of the antimutagenic properties of Angelica archangelica by the micronucleus test
Salkhova RA, Dulatova ShN, Poroshenko GG.

The antimutagenic activity of Angelica archangelica L. water and alcohol extracts thio-tepa against mutagenicity was investigated by the micronucleus test in mouse bone marrow and peripheral blood cells. The reduction of thio-tepa mutagenic activity was more prominent when the extracts were injected 2-hours before thio-tepa treatment as it could be seen at the simultaneous treatment. The observed reduction of micronuclear frequencies was up to 77%. No genotoxic effects of Angelica extracts had been seen at the concentrations 50-100 mg/kg.

Herbals, cancer prevention and health

Resumo: The use of herbs for medical benefit has played an important role in nearly every culture on earth. Herbal medicine was practiced by ancient cultures in Asia, Africa, Europe and the Americas. The recent popularity in use of herbals can be tied to the belief that herbs can provide some benefit over and above allopathic medicine and allow users to feel that they have some control in their choice of medications. The widespread use of herbs, either directly or as dietary supplements, has raised many scientific questions. Are herbal preparations safe? Do herbs interact with pharmaceutical medications to enhance or reduce their efficacy? The first interaction can be shown by the effects of St. John's Wort, a mild herbal antidepressant, and many commonly used medicines. St. John's Wort can induce the CYP3A family of activation enzymes through which approximately 50% of drugs are metabolized. This poses some risk of inadvertently reducing the half-life of such drugs as indinavir, cyclosporin and cyclophosphamide. On the other hand, herbal products may act in a pathway similar to pharmaceuticals yet without side effects. Natural anti-inflammatory compounds abound in the herbal world and are found in green tea, the spices turmeric and rosemary, feverfew and others. Because the use of nonsteroidal anti-inflammatory drugs (NSAID) is associated with a reduced risk for several cancers, it is at least plausible that natural NSAID should be explored for possible use as cancer preventives.