

Research Abstracts

Panax Ginseng

Effect of Panax ginseng extract on tissue glycogen and adrenal cholesterol depletion during prolonged exercise

The acute effect of Panax ginseng (GS), root extract was investigated on the rate of glycogenolysis in white muscle and in liver during prolonged exercise of 3 hours duration in rats. Adrenal cholesterol depletion was also measured. GS inhibited decrease of adrenal cholesterol by 21% after 3 hours of swimming. GS had no effect on hepatic glycogen, but had pronounced inhibitory effects on endogenous glycogen utilization in white skeletal muscle during exercise. These findings indicate that GS has carbohydrate-sparing actions during prolonged exercise, and suggests a possible physiological basis for ginseng's anti-fatigue properties. Avakian EV Jr, Evonuk E. *Planta Med* 1979 May;36(1):43-48.

Effect of Panax ginseng extract on energy metabolism during exercise in rats

We examined the acute effects if ginseng extract (GS) administration on arterial plasma levels of glucose, free fatty acids (FFA), lactic acid (LA) and pyruvic acid (PA) in resting rats, and in animals that swam for 30 or 60 minutes. Compared to vehicle-treated (saline) control animals, GS did not significantly alter these parameters at rest. During exercise, GS-treated animals had higher blood glucose levels than control rats, and markedly lower concentrations of circulating LA and PA. Plasma FFA was also lower in the GS-treated animals at 30 minutes of swimming. These results provide evidence that ginsenosides can significantly alter mechanisms of fuel homeostasis during prolonged exercise, presumably by increasing the biochemical capacity of skeletal muscle to oxidize FFA in preference for cellular energy production. Avakian EV, Sugimoto RB, Taguchi S, Horvath SM. *Planta Med* 1984 Apr;50(2):151-154.

In vitro effects of echinacea and ginseng on natural killer and antibody-dependent cell cytotoxicity in healthy subjects and chronic fatigue syndrome or acquired immunodeficiency syndrome patients

Extracts of *Echinacea purpurea* and Panax ginseng were evaluated for their capacity to stimulate cellular immune function by peripheral blood mononuclear cells (PBMC) from normal individuals and patients with either the chronic fatigue syndrome or the acquired immunodeficiency syndrome. PBMC isolated on a Ficoll-hypaque density gradient were tested in the presence or absence of varying concentrations of each extract for natural killer (NK) cell activity versus K562 cells and antibody-dependent cellular cytotoxicity (ADCC) against human herpesvirus 6 infected H9 cells. Both echinacea and ginseng, at concentrations ≥ 0.1 or 10 micrograms/kg, respectively, significantly enhanced NK-function of all groups. Similarly, the addition of either herb significantly increased ADCC of PBMC from all subject groups. Thus, extracts of *Echinacea purpurea* and Panax ginseng enhance cellular immune function of PBMC both from normal individuals and patients with depressed cellular immunity. See DM, Broumand N, Sahl L, Tilles JG. *Immunopharmacology* 1997 Jan;35(3):229-235.

Antistress and antifatigue properties of Panax ginseng: comparison with piracetam

The antistress and antifatigue properties of a Chinese ginseng preparation were tested on Swiss albino mice, exposed to various experimental models of stress, and were compared with those of piracetam. Both ginseng and piracetam were administered chronically in drinking water for 16-18 days as well as acutely, by injection, 30-60 min prior to the experiments. Reactivity of the mice, loss in body weight, amount of faeces, length of endurance and incidence of mortality were graded and measured. Both piracetam and ginseng treatment provided good protection against electroshock stress when compared to the untreated mice; fighting scores, incidence of tonic convulsion and mortality were significantly less in the treated groups. In the heat stress experiments, both piracetam and ginseng provided significant protection to the treated mice against exposure to heat. In the fatigue stress of forced swim test, ginseng treatment provided effective adaptation to fatigue and increased endurance in both male and female mice; piracetam showed some antifatigue effects on the male mice only. In the locomotor activity tests, ginseng did not depress motility, while piracetam did so in the later part of the tests. Banerjee U, Izquierdo JA. *Acta Physiol Lat Am* 1982;32(4):277-85.

Anti-proliferating effects of ginsenoside Rh2 on MCF-7 human breast cancer cells

Ginsenoside Rh2 (G-Rh2) isolated from the root of *Panax ginseng* has been shown to have anti-cancer proliferation, differentiation and chemopreventive effects in certain cancer cell types. We investigated the mechanism of G-Rh2-induced growth inhibition in MCF-7 human breast carcinoma cells. G-Rh2 significantly inhibited the cell growth in a concentration-dependent manner, which effect was reversible, and induced a G1 arrest in cell cycle progression. G-Rh2 treatment down-regulated the protein level of cyclin D3 but upregulated the expression of cyclin-dependent kinase (Cdk) inhibitor p21WAF1/CIP1. The increased levels of p21 were associated with increased binding of p21 and Cdk2 concomitant with marked decrease in Cdk2 and cyclin E-dependent kinase activities with no changes in Cdk2 and cyclin E expression. G-Rh2 markedly reduced the phosphorylated retinoblastoma protein (pRb) and enhanced association of unphosphorylated pRb and the transcription factor E2F-1. These data suggest that G-Rh2 inhibited the growth of MCF-7 cells, by inducing protein expression of p21 and reducing the protein levels of cyclin D which resulted in the down-regulation of cyclin/Cdk complex kinase activity, decreasing phosphorylation of pRb, and inhibiting E2F release. Oh M, Choi YH, Choi S, Chung H, Kim K, Kim SI, Kim DK, Kim ND. *Int J Oncol* 1999 May;14(5):869-75.

Non-organ specific cancer prevention of ginseng: a prospective study in Korea

BACKGROUND: A number of studies have reported that increased consumption of natural products reduced the risk of cancer. Our previous case-control studies have shown a significant reduction in the risk of cancer development among those who regularly consumed ginseng. We conducted a prospective cohort study to evaluate the preventive effect of ginseng against cancer on a population residing in a ginseng cultivation area on the basis of the result of case-control studies. **METHODS:** This study was conducted in Kangwha-eup from August 1987 to December 1992. We studied 4634 people over 40 years old who completed a questionnaire on ginseng intake. In an attempt to obtain detailed information about ginseng intake, we asked them to specify their age at initial intake, their frequency and duration of ginseng intake, the kind of ginseng, etc. Multiple logistic regression was used to estimate relative risks (RR) when controlling simultaneously for covariates. **RESULTS:** Ginseng consumers had a decreased risk (RR = 0.40, 95% confidence interval [CI] : 0.28-0.56) compared with non-consumers. On the type of ginseng, the RR was 0.31 (95% CI: 0.13-0.74) for fresh ginseng extract consumers and 0.34 (95% CI: 0.20-0.53) for consumers of multiple combinations. There was no cancer death among 24 red ginseng consumers. There was a decreased risk with a rise in the frequency of ginseng intake, showing a dose-response relationship. The RR of ginseng consumers were 0.33 (95% CI: 0.18-0.57) in gastric cancer and 0.30 (95% CI : 0.14-0.65) in lung cancer. Among ginseng preparations, fresh ginseng extract consumers were significantly associated with a decreased risk of gastric cancer (RR = 0.33, 95% CI: 0.12-0.88). **CONCLUSIONS:** These results strongly suggest that *Panax ginseng* C.A. Meyer has non-organ specific preventive effect against cancer, providing support for the previous case-control studies. Yun TK, Choi SY. *Int J Epidemiol* 1998 Jun;27(3):359-64.

Ginsenoside-induced relaxation of human bronchial smooth muscle via release of nitric oxide

Ginsenoside, an extract of *Panax ginseng*, is an essential constituent of anti-asthmatic Chinese herbal medicine. To elucidate whether ginsenoside affects airway smooth muscle tone and, if so, what the mechanism of action is, we studied relaxant responses of human bronchial strips under isometric condition in vitro, and directly measured the release of nitric oxide (NO) by an amperometric sensor for this molecule. Addition of ginsenoside relaxed the tissues precontracted with acetylcholine in a dose-dependent manner, the maximal relaxation and the ginsenoside concentration required to produce 50% relaxation being 67±8% and 210±29 µg/ml, respectively. The relaxant responses to ginsenoside were inhibited by N(G)-nitro-L-arginine methylester (L-NAME) and removal of the epithelium, but not by N(G)-nitro-D-arginine methylester (D-NAME) or tetrodotoxin. This inhibitory effect of L-NAME was reversed by L-arginine but not by D-arginine. Addition of ginsenoside to the medium containing bronchial tissues dose-dependently increased NO-selective electrical current, and this effect was greatly attenuated by the epithelial removal or Ca²⁺-free medium. Ginsenoside also increased tissue cyclic GMP contents, an effect that was abolished in the presence of L-NAME. It is concluded that ginsenoside induces relaxation of human bronchial smooth muscle via stimulation of NO generation predominantly from airway epithelium and cyclic GMP synthesis. This action might account for the anti-asthmatic effect of *Panax ginseng*. Tamaoki J, Nakata J, Kawatani K, Tagaya E, Nagai A. *Br J Pharmacol*. 2000 Aug;130(8):1859-64.

Effects of ginsenosides from *Panax ginseng* on cell-to-cell communication function mediated by gap junctions

Gap junctions have been shown or are believed to be involved in the pathogenesis of many inherited and acquired human diseases. Agents that regulate the gap junction-mediated intercellular communication (GJIC) function may facilitate prevention and treatment of GJIC-involved diseases. In the present study we examined the effects of 27 ginsenosides isolated from *Panax ginseng* on GJIC. The results show that compounds 1 (oleanolic acid), 2 (ginsenoside-R0), 3 (ginsenoside-Rb1), 5 (ginsenoside-Rb2), 7 (ginsenoside-Rd), 8 (ginsenoside-Rg3), 12 (panaxadiol), 13 (notoginsenoside-R4), 17 [ginsenoside-Rg2 (20S)], 18 (ginsenoside-Rf), and 26 (ginsenoside-F3) did not obviously affect GJIC, whereas compounds 4 (ginsenoside-Rc), 6 (ginsenoside-Rb3), 9 (ginsenoside-Rd2), 10 (notoginsenoside-Fe), 11 (ginsenoside-Rh2), 14 (ginsenoside-Ra1), 15 (ginsenoside-Re), 16 [ginsenoside-Rg2 (20R)], 19 (ginsenoside-Ia), 20 [ginsenoside-Rh1 (20S)], 21 [ginsenoside-Rh1 (20R)], 22 (ginsenoside-F1), 23 (protopanaxatriol), 24 (panaxatriol), 25 (ginsenoside-Rg1), and 27 (chikusetsaponin-L8) induced GJIC reductions at various degrees. Compounds 2, 7, and 8 protected against the tyrosine phosphatase inhibitor vanadate-induced GJIC reduction, while compounds 1, 5, 7, and 17 inhibited the cytokine interleukin 1 alpha (IL-1alpha)-induced reduction in GJIC. Nevertheless, no compounds protected against the protein kinase C (PKC) activator 12-O-tetradecanoylphorbol-13-acetate (TPA)-induced GJIC inhibition. On the other hand, GJIC reductions induced by compounds 6, 9, 10, 20, 21, 22, 24, and 25 were inhibited by the tyrosine kinase (TK) inhibitor genistein, while GJIC reductions induced by compounds 6, 9, 14, 16, 19, 21, and 24 were attenuated in the presence of the PKC inhibitor calphostin C. However, GJIC reductions induced by compounds 4, 23, and 27 were not inhibited either by genistein or by calphostin C. These data indicate that various mechanisms are responsible for effects of ginsenosides on GJIC. Zhang YW, Dou DQ, Zhang L, Chen YJ, Yao XS.

Extracts of *Ginkgo biloba* and *Panax ginseng* protect brain proteins from free radical induced oxidative damage in vitro

Oxidative damage to normal human brain tissue was induced following exposure to hydroxyl (OH \cdot) or superoxide (O $_2^{\cdot-}$) free radical species generated by CO60 irradiation in vitro. Both enzymic and cytoskeletal proteins showed substantial (dose dependent) oxidative damage following exposure to OH \cdot or O $_2^{\cdot-}$, as quantified by SDS-polyacrylamide gel electrophoretic analysis. Extracts of *Ginkgo biloba* or *Panax ginseng* showed a remarkable capacity to protect brain tissue proteins from oxidative damage in vitro, even at extreme (2000 kRads) dosage levels of OH \cdot or O $_2^{\cdot-}$. We suggest, therefore, that the beneficial effect of these plant extracts in preventing brain tissue damage in vivo (e.g. following ischemia-reperfusion) may result from their action in protecting brain proteins from oxidative damage, in addition to their previously reported capacity to reduce free radical induced lipid peroxidation. Siddique MS, Eddeb F, Mantle D, Mendelow AD. *Acta Neurochir Suppl* 2000;76:87-90.