

## Stimulation of pituitary-adrenocortical system by ginseng saponin

Effects of preparations of saponin mixture and isolated ginsenosides, extracted from the root of *Panax ginseng*, on plasma corticotropin (ACTH) and corticosterone concentrations in rats were determined by the radioimmunoassay and competitive protein binding method. When ginseng saponin mixture was administered to rats intraperitoneally, plasma ACTH and corticosterone increased significantly 30, 60 and 90 min after the treatment. The kinetic pattern of the increase in plasma ACTH was almost parallel to that in plasma corticosterone. Isolated ginsenoside, protopanaxadiol or protopanaxatriol glycoside, also increased plasma corticosterone. The ginseng-induced increase in plasma corticosterone was suppressed by pretreatment with dexamethasone. Thus the ginseng saponin was found to act on the hypothalamus and/or hypophysis primarily, and stimulated ACTH secretion which resulted in increased synthesis of corticosterone in the adrenal cortex. Hiai S, Yokoyama H, Oura H, Yano S. *Endocrinol Jpn* 1979 Dec;26(6):661-665.

## Flow-cytometric studies with eleutherococcus senticosus extract as an immunomodulatory agent

A placebo-controlled study of the effect of an *Eleutherococcus senticosus* extract (Eleukokk) on the immune system was performed with 36 healthy volunteers utilising quantitative multi-parameter flow cytometry with monoclonal antibodies directed against specific surface markers of human lymphocyte subsets. Volunteers in the verum group received 10 ml of an ethanolic (vincamine free) *eleutherococcus senticosus* preparation, 3 times daily for 4 weeks. In the placebo, the *eleutherococcus* extract was substituted by additional wine, resulting in identical final concentrations of ethanol in both preparations. The purpose of the double-blind study was the demonstration of possible effects on the cellular immune status, as determined by quantitative flow cytometry. The most salient feature in the verum group was a drastic increase in the absolute number of immunocompetent cells, with an especially pronounced effect on T lymphocytes, predominantly of the helper/inducer type, but also on cytotoxic and natural killer cells. In addition, a general enhancement of the activation state of T lymphocytes was observed. No side effects were observed during the trial or afterwards (observation period 6 months). Bohn B, Nebe CT, Birr C. *Arzneimittelforschung* 1987 Oct;37(10):1193-1196.

## Effect of Eleutherococcus senticosus extract on human physical working capacity

Ethanol extract of *Eleutherococcus senticosus* Maxim. was discreetly examined as regards its effect on the maximal working capacity of man, using six male adolescents. Single, blind, cross-over studies were conducted where the extract treatment was compared with no treatment and with placebo treatment. Significant increase was noted in all four parameters recorded in the tests due to extract administration. Especially striking was 23.3% increase in total work due to the extract compared with only 7.5% rise due to the placebo. This increase in total work seems to be partially attributable to the improvement of subject's bodily oxygen metabolism that was reflected in the increase in maximal oxygen uptake and that in maximal oxygen pulse. Asano K, et al. *Planta Med* 1986 Jun;3:175-177.

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

We examined the acute effects of 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 to 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 of glucose for cellular energy production. Avakian EV, Sugimoto RB, Taguchi S, Horvath SM. *Planta Med* 1994 Apr; 50(2):151-154.

## Adrenal cortex functional activity in pantothenate deficiency and the administration of the vitamin or its derivatives

Study of the corticosteroid content in the adrenals and blood of rats under pantothenate deficiency has demonstrated a decrease in adrenocortical function. A single administration of pantothenate in a dose of 3.3 mg/kg reduced the influence of hypovitaminosis on the adrenals. The pantothenate derivatives (pantethine, 4'-phosphopantothenate and CoA in particular) injected to intact animals in a single dose equimolar to 3.3 mg/kg calcium pantothenate per kg bw had a marked steroidogenous effect. Tarasov IuA, Sheibak VM, Moiseenok AG. *Vopr Pitan* 1985 Jul;4:51-54.

## The cardioprotective and antiadrenergic activity of an extract of *Rhodiola rosea* in stress

The course of administration of *Rhodiola rosea* extract was studied for effects on the pattern of stress-induced cardiac damage which was assessed by <sup>99m</sup>Tc-pyrophosphate accumulation in the heart. *Rhodiola rosea* was found to prevent stress-induced cardiac damage. Simultaneously, myocardial catecholamines and cAMP levels were measured. *Rhodiola rosea* was ascertained to prevent both stress-induced catecholamine release and higher cAMP levels in the myocardium. Moreover, the adaptogen prevented lower adrenal catecholamines during stress. The findings suggest that the antistressor and cardioprotective effects of *Rhodiola rosea* are associated with limited adrenergic effect on the heart. Maslova LV, Kondrat'ev BI, Maslov LN, Lishmanov IB. *Eksp Klin Farmakol* 1994 Nov-Dec;57(6):61-3.

## A double-blind, placebo-controlled pilot study of the stimulating and adaptogenic effect of *Rhodiola rosea* SHR-5 extract on the fatigue of students caused by stress during an examination period with a repeated low-dose regimen

The objective was to investigate the stimulating and normalizing effect of the adaptogen *Rhodiola rosea* extract SHR-5 in foreign students during a stressful examination period. The study was performed as a double-blind, randomized and placebo-controlled with low repeated dose regime. The study drug and the placebo were taken for 20 days by the students during an examination period. The physical and mental performance were assessed before and after the period, based on objective as well as on subjective evaluation. The most significant improvement in the SHR-5 group was seen in physical fitness, mental fatigue and neuro-motoric tests ( $p < 0.01$ ). The self-assessment of the general well-being was also significantly ( $p < 0.05$ ) better in the verum group. No significance was seen in the correction of text tests or a neuro-muscular tapping test. The overall conclusion is that the study drug gave significant results compared to the placebo group but that the dose level probably was suboptimal. Spasov AA, Wikman GK, Mandrikov VB, Mironova IA, Neumoin VV. *Phytomedicine* 2000 Apr;7(2):85-9.

## *Rhodiola rosea* in stress induced fatigue--a double blind cross-over study of a standardized extract SHR-5 with a repeated low-dose regimen on the mental performance of healthy physicians during night duty

The aim of this study was to investigate the effect of repeated low-dose treatment with a standardized extract SHR/5 of rhizome *Rhodiola rosea* L, (RRE) on fatigue during night duty among a group of 56 young, healthy physicians. The effect was measured as total mental performance calculated as Fatigue Index. The tests chosen reflect an overall level of mental fatigue, involving complex perceptive and cognitive cerebral functions, such as associative thinking, short-term memory, calculation and ability of concentration, and speed of audio-visual perception. These parameters were tested before and after night duty during three periods of two weeks each: a) a test period of one RRE/placebo tablet daily, b) a washout period and c) a third period of one placebo/RRE tablet daily, in a double-blind cross-over trial. The perceptive and cognitive cerebral functions mentioned above were investigated using 5 different tests. A statistically significant improvement in these tests was observed in the treatment group (RRE) during the first two weeks period. No side-effects were reported for either treatment noted. These results suggest that RRE can reduce general fatigue under certain stressful conditions. Darbinyan V, Kteyan A, Panossian A, Gabrielian E, Wikman G, Wagner H. *Phytomedicine* 2000 Oct;7(5):365-71.

## Adaptogenic and cardioprotective action of ashwagandha in rats and frogs

Pharmacological and metabolic effects of ashwagandha (*Withania somnifera* L. (Solanaceae)) used in Ayurveda as a herbal tonic and health food were studied. Ashwagandha was shown to increase swimming time in rats in physical working capacity test, i.e. rats swimming endurance test. Significant increase in relative heart weight and glycogen content in myocardium and liver was also observed in ashwagandha treated group. Ashwagandha treatment increased the duration of contractility in functional test for the resistance of frog heart muscle towards the toxic action of strophanthin-K. Ashwagandha treatment also resulted in significant increase in coagulation time which attains normalcy 7 days after cessation of treatment. Ashwagandha possesses no toxicity up to a dose of (100 mg/kg; p.o. for 180 days) and does not cause significant changes in biochemical parameters in the blood serum of rats. Increase in catecholamine content in the heart and aortic tissues and their decrease in adrenal glands are unfavourable effects of high doses of ashwagandha. On the basis of these observations, it was concluded that ashwagandha possesses adaptogenic, cardiotropic, cardioprotective and anticoagulant properties. Dhuley JN. *J Ethnopharmacol* 2000 Apr;70(1):57-63.

## Anxiolytic-antidepressant activity of *Withania somnifera* glycowithanolides: an experimental study

The roots of *Withania somnifera* (WS) are used extensively in Ayurveda, the classical Indian system of medicine, and WS is categorized as a rasayana, which are used to promote physical and mental health, to provide defence against disease and adverse environmental factors and to arrest the aging process. WS has been used to stabilize mood in patients with behavioural disturbances. The present study investigated the anxiolytic and antidepressant actions of the bioactive glycowithanolides (WSG), isolated from WS roots, in rats. WSG (20 and 50 mg/kg) was administered orally once daily for 5 days and the results were compared by those elicited by the benzodiazepine lorazepam (0.5 mg/kg, i.p.) for anxiolytic studies, and by the tricyclic anti-depressant, imipramine (10 mg/kg, i.p.), for the antidepressant investigations. Both these standard drugs were administered once, 30 min prior to the tests. WSG induced an anxiolytic effect, comparable to that produced by lorazepam, in the elevated plus-maze, social interaction and feeding latency in an unfamiliar environment, tests. Further, both WSG and lorazepam, reduced rat brain levels of tribulin, an endocoid marker of clinical anxiety, when the levels were increased following administration of the anxiogenic agent, pentylenetetrazole. WSG also exhibited an antidepressant effect, comparable with that induced by imipramine, in the forced swim-induced 'behavioural despair' and 'learned helplessness' tests. The investigations support the use of WS as a mood stabilizer in clinical conditions of anxiety and depression in Ayurveda. Bhattacharya SK, Bhattacharya A, Sairam K, Ghosal S. *Phytomedicine* 2000 Dec;7(6):463-9.

## Changes in thyroid hormone concentrations after administration of ashwagandha root extract to adult male mice

The importance of ashwagandha root extract in the regulation of thyroid function with special reference to type-I iodothyronine 5'-monodeiodinase activity in mice liver has been investigated. Although the root extract (1.4 g kg<sup>-1</sup>) administered daily for 20 days by gastric intubation increased serum 3,3',5-triiodothyronine (T3) and tetraiodothyronine (T4) concentrations and hepatic glucose-6-phosphatase activity, hepatic iodothyronine 5'-monodeiodinase activity did not change significantly. Furthermore, ashwagandha root extract significantly reduced hepatic lipid peroxidation, whereas the activity of antioxidant enzymes such as superoxide dismutase and catalase were increased. These findings reveal that the ashwagandha root extract stimulates thyroidal activity and also enhances the antiperoxidation of hepatic tissue. Panda S, Kar A. *J Pharm Pharmacol* 1998 Sep;50(9):1065-8.

## Studies on the immunomodulatory effects of Ashwagandha

The immunomodulatory activity of an Indian Ayurvedic medicinal preparation, Ashwagandha (*Withania somnifera* (L. Dunal)) was studied in mice with myelosuppression induced by one or more of the following three compounds: cyclophosphamide, azathioprin, or prednisolone. The assessment of immunomodulatory activity was carried out by hematological and serological tests. A significant modulation of immune reactivity was observed in all the three animal models used. Ashwagandha prevented myelosuppression in mice treated with all three immunosuppressive drugs tested. A significant increase in hemoglobin concentration ( $P < 0.01$ ), red blood cell count ( $P < 0.01$ ), white blood cell count ( $P < 0.05$ ), platelet count ( $P < 0.01$ ), and body weight ( $P < 0.05$ ) was observed in Ashwagandha-treated mice as compared with untreated (control) mice. We also report an immunostimulatory activity: treatment with Ashwagandha was accompanied by significant increases in hemolytic antibody responses towards human erythrocytes. Ziauddin M, Phansalkar N, Patki P, Diwanay S, Patwardhan B. *J Ethnopharmacol* 1996 Feb;50(2):69-76.

## Enhancement of the immune response in mice by *Astragalus membranaceus* extracts

*Astragalus membranaceus* extracts injected into normal mice or mice immunodepressed by cyclophosphamide or radiation treatment or by aging are able to enhance the antibody response to a T-dependent antigen. Optimal conditions for maximum effect have been established in normal C3H/HeJ and (C57B1/10 x DBA/2)F1 mice. Enhancement of the antibody response was associated with increase of Th cell activity in normal and immunodepressed mice. The biological activity of endotoxin-free extracts is dependent on the carbohydrate content. Zhao KS, Mancini C, Doria G. *Immunopharmacology* 1990 Nov;20(3):225-233.