SELEZIONE BIBLIOGRAFICA SU RHODIOLA ROSEA

1. J Nat Prod. 2012 Apr 27;75(4):531-7. Epub 2012 Apr 6.

Salidroside Protects Human Erythrocytes against Hydrogen Peroxide-Induced Apoptosis.

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Rhodiola rosea is a commonly used folk medicine for the treatment of high altitude sickness, mountain malhypoxia, and anoxia. Its active ingredient, salidroside [2-(4-hydroxyphenyl)ethyl β-d-glucopyranoside (1)], has been reported to have a broad spectrum of biological effects. However, the protective role of 1 in human erythrocytes remains unclear. This study therefore has investigated the effects of 1 on oxidative stress-induced apoptosis in human erythrocytes (also known as eryptosis or erythroptosis). Compound 1 increased cell survival significantly and prevented human erythrocytes from undergoing eryptosis/erythroptosis mediated by H(2)O(2), as confirmed by the decreased expression of phosphatidylserine on the cell surface and reduced leakage of calcein through the damaged membrane. Mechanistically, 1 was found to exert its protective effects through its antioxidative activity and the inhibition of caspase-3 activation and stress-induced intracellular Ca(2+) rise in a dose-dependent manner. Compound 1 is a protective agent in human erythrocytes against oxidative stress and may be a good adaptogen to enhance the body's resistance to stress and fatigue.

PMID: 22483064 [PubMed - in process]

2. Immunopharmacol Immunotoxicol. 2012 Jun;34(3):513-8. Epub 2012 Jan 13.

Anti-cellular and immunomodulatory potential of aqueous extract of Rhodiola imbricata rhizome.

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In the present study, we have evaluated the anti-cellular and immunomodulatory potential of aqueous extract of Rhodiola imbricata rhizome (RAE). Rhodiola extract inhibited the proliferation of human T cell lymphoma cell line EL-4 and erythroleukemic cell line HL-60. Furthermore, treatment of human peripheral blood mononuclear cells (hPBMCs) with lipopolysaccharide (LPS) and RAE suppressed regulated upon activation, normal T cell expressed and secreted (RANTES) production. However, number of TNF-α spots was increased in RAE treated hPBMCs. The reverse transcriptase polymerase chain reaction (RT-PCR) analysis of RAE treated rat splenocytes confirmed the up regulation of TLR-4 mRNA expression. Therefore, the present study concludes that RAE has potent immune boosting activity which might be useful in immunocompromised individuals.

PMID: 22239552 [PubMed - in process]

3. PLoS One. 2012;7(1):e29641. Epub 2012 Jan 3.

Protective effects of a Rhodiola crenulata extract and salidroside on hippocampal neurogenesis against streptozotocin-induced neural injury in the rat.

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Previously we have demonstrated that a Rhodiola crenulata extract (RCE), containing a potent antioxidant salidroside, promotes neurogenesis in the hippocampus of depressive rats. The current study was designed to further investigate the protective effect of the RCE on neurogenesis in a rat model of Alzheimer's disease (AD) induced by an intracerebroventricular injection of streptozotocin (STZ), and to determine whether this neuroprotective effect is induced by the antioxidative activity of salidroside. Our results showed that pretreatment with the RCE significantly improved the impaired neurogenesis and simultaneously reduced the oxidative stress in the hippocampus of AD rats. In vitro studies revealed that (1) exposure of neural stem cells (NSCs) from the hippocampus to STZ strikingly increased intracellular reactive oxygen species (ROS) levels, induced cell death and perturbed cell proliferation and differentiation, (2) hydrogen peroxide induced similar cellular activities as STZ, (3) pre-incubation of STZ-treated NSCs with catalase, an antioxidant, suppressed all these cellular activities induced by STZ, and (4) likewise, pre-incubation of STZ-treated NSCs with salidroside, also an antioxidant, suppressed all these activities as catalase: reduction of ROS levels and NSC death with simultaneous increases in proliferation and differentiation. Our findings indicated that the RCE improved the impaired hippocampal neurogenesis in the rat model of AD through protecting NSCs by its main ingredient salidroside which scavenged intracellular ROS.

PMCID: PMC3250459
PMID: 22235318 [PubMed - indexed for MEDLINE]

4. Phytother Res. 2011 Nov 15. doi: 10.1002/ptr.3662. [Epub ahead of print]

Rhodiola rosea Extract Protects Human Cortical Neurons against Glutamate and Hydrogen Peroxide-induced Cell Death Through Reduction in the Accumulation of Intracellular Calcium.

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The aim of this study was to investigate the neuroprotective effects of a titolated extract from Rhodiola rosea L. (RrE) and of salidroside (Sa), one of the major biologically active compounds extracted from this medicinal plant, against oxidative stressor hydrogen peroxide (H(2) O(2)) and glutamate (GLU)-induced cell apoptosis in a human cortical cell line (HCN 1-A) maintained in culture. The results obtained indicate that exposure of differentiated HCN 1-A neurons to GLU or H(2) O(2) resulted in concentration-dependent cell death. A 24 h pre-treatment with RrE significantly increased cell survival and significantly prevented the plasma membrane damage and the morphological disruption caused by GLU or H(2) O(2) , indicating that neurons treated with RrE were protected from the neurotoxicity induced by the oxidative stressor used. In addition, RrE significantly reduced H(2) O(2) or GLU-induced elevation of intracellular free Ca(2+) concentration. The results obtained have also shown that Sa caused similar effects in all experimental models used; however, the potency of the action was lower than that of the extract containing corresponding quantities of Sa. These findings indicate that RrE has a neuroprotective effect in cortical neurons and suggest that the antioxidant activity of the RrE, due to the structural features of the synergic active principles they contain, may be responsible for its ability to stabilize cellular Ca(2+) homeostasis.

PMID: 22086763 [PubMed - as supplied by publisher]

5. Immunopharmacol Immunotoxicol. 2011 Dec;33(4):738-43. Epub 2011 Jun 28.

Adjuvant effects of salidroside from Rhodiola rosea L. on the immune responses to ovalbumin in mice.

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Salidroside, a major component of Rhodiola rosea L., was evaluated for its adjuvant effects on the immune responses in mice by ovalbumin (OVA) stimulation. BALB/c mice were immunized subcutaneously with OVA 100 μg or OVA 100 μg dissolved in saline containing alum (100 μg) or salidroside (12.5, 25, or 50 μg) on Days 1 and 15. Two weeks later (Day 28), blood samples were collected to analyze OVA-specific IgG, IgG1, and IgG2b antibodies. Meanwhile, splenocytes were harvested to assess lymphocyte proliferation, cytokines (IL-2, IL-4, and IFN-γ) production, and CD4(+), CD8(+) lymphocyte subsets. The results indicated that co-administration of salidroside with OVA significantly enhanced the ConA-, LPS-, and OVA-induced splenocyte proliferation, produced more IL-2, IL-4, IFN-γ, and IgG, IgG1, and IgG2b antibody levels, and increased the percentage of CD4(+), CD8(+) lymphocyte subsets than OVA alone. Thus, salidroside possess immunological adjuvant activity by regulating humoral and cellular immune responses in mice.

PMID: 21711135 [PubMed - indexed for MEDLINE]

6. Phytother Res. 2011 Jan;25(1):106-15. doi: 10.1002/ptr.3236.

Rhodiola-induced inhibition of adipogenesis involves antioxidant enzyme response associated with pentose phosphate pathway.

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The aim of this study was to investigate whether Rhodiola crenulata extract and tyrosol, a major bioactive phenolic compound present in Rhodiola, change the activities of endogenous antioxidant enzyme response (AER) and energy pathways linked to proline-mediated pentose phosphate pathway (PPP) during adipogenesis. Treatment with Rhodiola extracts inhibited the activities of proline dehydrogenase (PDH) and glucose-6-phosphate dehydrogenase (G6PDH) as well as lipid accumulation and reactive oxygen species (ROS) production. The inhibition of PDH and G6PDH activities by Rhodiola likely prevented proline oxidation required for critical ATP generation that is coupled to AER via the PPP, leading to inhibition of adipogenesis. Rhodiola extracts dose-dependently increased superoxide dismutase (SOD) activity, resulting in a reduced ROS level during adipogenesis. Moreover, the effects of tyrosol, a major bioactive compound in Rhodiola species, were directly correlated with all observed effects by Rhodiola extracts. These results indicate that the antiadipogenic effects of Rhodiola extracts can be attributed to a phenolic tyrosol that may potentially disrupt proline-mediated energy generation and AER via PPP, resulting in the suppression of adipogenesis and lipid accumulation. This further provides a biochemical rationale to identify the roles of phenolics that modulate the cellular redox environment and therefore have relevance for obesity management.

PMID: 20623718 [PubMed - indexed for MEDLINE]

7. J Sports Med Phys Fitness. 2010 Mar;50(1):57-63.

Effects of chronic Rhodiola Rosea supplementation on sport performance and antioxidant capacity in trained male: preliminary results.

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AIM: Rhodiola Rosea, is an adaptogen plant which has been reported to promote fatty acids utilisation, to ameliorate antioxidant function, and to improve body resistance to physical strenuous efforts. The purpose of the present study was to investigate the effects on physical performance as well as on the redox status of a chronic Rhodiola Rosea supplementation in a group of competitive athletes during endurance exercise. METHODS: Following a chronic supplementation with Rhodiola Rosea for 4 weeks, 14 trained male athletes underwent a cardio-pulmonary

exhaustion test and blood samples to evaluate their antioxidant status and other biochemical parameters. These data were compared with those coming from the same athletes after an intake of placebo. RESULTS: The evaluation of physical performance parameters showed that HR Max, Borg Scale level, VO(2) max and duration of the test were essentially unaffected by Rhodiola Rosea assumption. On the contrary, Rhodiola Rosea intake reduced, in a statistically significative manner, plasma free fatty acids levels. No effect on blood glucose was found. Blood antioxidant status and inflammatory parameters resulted unaffected by Rhodiola Rosea supplementation. Blood lactate and plasma creatine kinase levels were found significantly lower ($P<0.05$) in Rhodiola Rosea treated subjects when compared to the placebo treated group. CONCLUSION: Chronic Rhodiola Rosea supplementation is able to reduce both lactate levels and parameters of skeletal muscle damage after an exhaustive exercise session. Moreover this supplementation seems to ameliorate fatty acid consumption. Taken together those observation confirm that Rhodiola Rosea may increase the adaptogen ability to physical exercise.

PMID: 20308973 [PubMed - indexed for MEDLINE]

8. Food Chem Toxicol. 2010 Apr;48(4):1019-25. Epub 2010 Jan 15.

Anti-oxidative effect of Rhodiola imbricata root extract in rats during cold, hypoxia and restraint (C-H-R) exposure and post-stress recovery.

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Anti-oxidative potential of Rhodiola imbricata root aqueous extract was examined in rats, administered orally at a dose of 100 mg/kg both in single and multiple doses, 30 min prior to cold (5 degrees C)-hypoxia (428 mmHg)-restraint (C-H-R) exposure. Lipid per-oxidation, anti-oxidant parameters and lactate dehydrogenase (LDH), were studied in blood, liver and muscle of rats on attaining T(rec)23 degrees C during C-H-R exposure and after recovery (T(rec)37 degrees C) from C-H-R induced hypothermia. The results of untreated control rats on attaining T(rec)23 degrees C showed a significant increase in blood, liver and muscle malondialdehyde (MDA) and LDH levels. Hepatic catalase (CAT) and muscle glutathione S-transferase (GST) also increased significantly. Administration of single dose of Rhodiola imbricata root aqueous extract significantly restricted rise in blood MDA, increased blood reduced glutathione (GSH) and superoxide dismutase (SOD) activity with restricted rise in blood, liver and muscle LDH; improved liver and muscle SOD on attaining T(rec)23 degrees C and T(rec)37 degrees C; liver CAT on attaining T(rec)23 degrees C and liver GST during recovery. Multiple doses treatment of the extract further increased blood, liver and muscle GSH and GST levels; restricted increase in LDH on attaining T(rec)23 degrees C and recovery; increased CAT during recovery. Results suggested the anti-oxidant potential of Rhodiola root extract during C-H-R exposure and post-stress recovery and it also maintained cell membrane permeability.

PMID: 20079793 [PubMed - indexed for MEDLINE]

9. J Psychopharmacol. 2011 Mar;25(3):402-10. Epub 2009 Nov 25.

Evaluation of Rhodiola rosea L. extract on affective and physical signs of nicotine withdrawal in mice.

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The aim of the present study was to investigate the effects of a Rhodiola rosea L. extract on the prevention of the development of nicotine dependence and for the reduction of abstinence suffering following nicotine cessation in mice. Dependence was induced in mice by subcutaneous injections of nicotine (2 mg/kg, 4 times/day) for eight days. Spontaneous abstinence syndrome was evaluated 20 h after the last nicotine administration, by analysis of withdrawal

signs, as affective (anxiety-like behaviour) and physical (somatic signs and locomotor activity). Rhodiola rosea L. extract was administered orally during nicotine treatment (10, 15 and 20 mg/kg) or during nicotine withdrawal (20 mg/kg). Results show that both affective and somatic signs (head shaking, paw tremors, body tremors, ptosis, jumping, piloerection and chewing) induced by nicotine withdrawal are abolished by administration of Rhodiola rosea L. extract in a dose-dependent fashion, during both nicotine exposure and nicotine cessation. In conclusion, our data encourage additional studies to define the use of R. rosea L. as a therapeutic approach in the treatment of smoking cessation.

PMID: 19939867 [PubMed - indexed for MEDLINE]

10. Curr Clin Pharmacol. 2009 Sep;4(3):198-219. Epub 2009 Sep 1.

Evidence-based efficacy of adaptogens in fatigue, and molecular mechanisms related to their stress-protective activity.

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The aim of this review article is to assess the level of scientific evidence presented by clinical trials of adaptogens in fatigue, and to provide a rationale at the molecular level for verified effects. Strong scientific evidence is available for Rhodiola rosea SHR-5 extract, which improved attention, cognitive function and mental performance in fatigue and in chronic fatigue syndrome. Good scientific evidence has been documented in trails in which Schisandra chinensis and Eleutherococcus senticosus increased endurance and mental performance in patients with mild fatigue and weakness. Based on their efficacy in clinical studies, adaptogens can be defined as a pharmacological group of herbal preparations that increase tolerance to mental exhaustion and enhance attention and mental endurance in situations of decreased performance. The beneficial stress-protective effect of adaptogens is related to regulation of homeostasis via several mechanisms of action associated with the hypothalamic-pituitary-adrenal axis and the control of key mediators of stress response such as molecular chaperons (e.g. Hsp70), stress-activated c-Jun N-terminal protein kinase (JNK1), Forkhead Box O transcription factor DAF-16, cortisol and nitric oxide (NO). The key point of action of phytoadaptogens appears to be their up-regulating and stress-mimetic effects on the "stress-sensor" protein Hsp70, which plays an important role in cell survival and apoptosis. Hsp70 inhibits the expression of NO synthase II gene and interacts with glucocorticoid receptors directly and via the JNK pathway, thus affecting the levels of circulating cortisol and NO. Prevention of stress-induced increase in NO, and the associated decrease in ATP production, results in increased performance and endurance. Adaptogen-induced up-regulation of Hsp70 triggers stress-induced JNK-1 and DAF-16-mediated pathways regulating the resistance to stress and resulting in enhanced mental and physical performance and, possibly, increased longevity.

PMID: 19500070 [PubMed - indexed for MEDLINE]

11. Int J Sport Nutr Exerc Metab. 2009 Apr;19(2):186-99.

The influence of supplementation with Rhodiola rosea L. extract on selected redox parameters in professional rowers.

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The aim of this study was to investigate the effect of Rhodiola rosea supplementation on the balance of oxidants and antioxidants in the serum and erythrocytes of competitive rowers. This double-blinded study included 22 members of the Polish Rowing Team who were participating in a preparatory camp. Participants were randomly assigned to the supplemented group (n = 11), who received 100 mg of R. rosea extract twice daily for 4 wk, or the placebo group (n = 11). At the beginning and end of the study, participants performed a 2,000-m maximum test on a rowing ergometer. Blood samples were taken from the antecubital vein before each exercise test, 1 min after completing the test, and

after a 24-hr restitution period. The following redox parameters were assessed in erythrocytes: superoxide dismutase activity, glutathione peroxidase activity, and thiobarbituric-acid-reactive substances concentrations. In addition, creatine kinase activity and total antioxidant capacity were measured in plasma samples, lactate levels were determined in capillary blood samples, and uric acid concentrations were measured in serum. After supplementation, the total plasma antioxidant capacity was significantly higher (p = .0002) in the supplemented group than in the placebo group, and superoxide dismutase activity in erythrocytes directly after and 24 hr after the ergometry was significantly (p = .0461) lower in athletes receiving R. rosea extracts than in the placebo group. In conclusion, supplementation with R. rosea increased antioxidant levels in the plasma of professional rowers but had no effect on oxidative damage induced by exhaustive exercise.

PMID: 19478343 [PubMed - indexed for MEDLINE]

12. Phytother Res. 2009 Aug;23(8):1099-102.

Anti-inflammatory activity of Rhodiola rosea--"a second-generation adaptogen".

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Rhodiola rosea (golden root), a unique phytoadaptogen grown in high-altitude regions has gained attention for its various therapeutic properties. In India, this plant is found in the Himalayan belt and has not been completely explored for its beneficial health effects. The present study was undertaken to evaluate the anti-inflammatory efficacy of the tincture extract of Rhodiola rosea roots (RTE). The anti-inflammatory activity was determined through carrageenan-induced paw oedema, formaldehyde-induced arthritis and nystatin-induced paw oedema in rat model. The tincture extract exhibited inhibitory effect against acute and subacute inflammation at a dose of 250 mg/kg body weight. Inhibition of nystatin-induced oedema was also observed in a dose-dependent manner. The in vitro inhibitory effects of the tincture extract from R. rosea roots was evaluated against the enzymes relating to inflammation. The enzymes include cyclooxygenase-1 (COX-1), cyclooxygenase-2 (COX-2) and Phospholipase A2 (PLA2). The extract showed varying inhibitory activities against these enzymes depending on the concentrations. A potent inhibition was observed against Cox-2 and PLA2. Inhibition of nystatin induced oedema and phospholipase A2 suggested that membrane stabilization could be the most probable mechanism of action of RTE in anti-inflammation. The findings in this study may provide the use of R. rosea root extract in the treatment of inflammatory conditions.

PMID: 19152369 [PubMed - indexed for MEDLINE]

13. Planta Med. 2010 Mar;76(4):331-8. Epub 2009 Sep 29.

Potent in vitro inhibition of CYP3A4 and P-glycoprotein by Rhodiola rosea.

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Six clones of RHODIOLA ROSEA, obtained from plants originating from widely different areas in Norway, were investigated for their IN VITRO inhibitory potential on CYP3A4-mediated metabolism and P-gp efflux transport activity. Presumed active constituents in the ethanol extracts of the different clones were quantified. C-DNA baculovirus expressed CYP3A4 and Caco-2 cells were used for inhibitory assays, and as positive control inhibitors ketoconazole and verapamil were applied, respectively. A validated HPLC methodology was used to quantify the formation of 6-beta-OH-testosterone and scintillation counting was used to quantify the transport of (3)H-digoxin in Caco-2 cells. All clones showed potent inhibition of CYP3A4 and P-gp activities, with IC (50) values ranging from 1.7 to 3.1 microg/mL and

from 16.7 to 51.7 microg/mL, respectively, being below that reported for other herbs and some known classic drug inhibitors, such as St. John's wort and fluoxetine. RHODIOLA ROSEA might thus be a candidate for clinically relevant drug interactions. The concentration of presumed biologically active constituents in the different clones varied considerably, but this variation was not related to the clones' inhibitory potential on CYP3A4 or P-gp activities. Other constituents might thus be responsible for the observed inhibitory properties. The place of origin seemed to be of minor importance for CYP3A4 or P-gp inhibition.

PMID: 19790032 [PubMed - indexed for MEDLINE]

14. Arch Dermatol Res. 2010 Apr;302(3):191-200. Epub 2009 Aug 25.

Rhodiola rosea ability to enrich cellular antioxidant defences of cultured human keratinocytes.

Calcabrini C, De Bellis R, Mancini U, Cucchiarini L, Potenza L, De Sanctis R, Patrone V, Scesa C, Dachà M.

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Keratinocytes are cells strongly exposed to oxidative stress, but normally good equipped for antioxidant responses. However, it has long been suggested that exogenous antioxidants could play a useful role in minimizing the adverse skin responses associated with such oxidant species. In this work it was paid attention to the extract of Rhodiola rosea L. roots by using the phytocomplex as a whole because of the important activity of its composition and mutual distribution of its components. We have measured the protection afforded by the extract to reduced glutathione levels, glyceraldehyde-3-phosphate dehydrogenase activity, and thiobarbituric acid reactive substances levels in cultured human keratinocytes (NCTC 2544) exposed to different oxidative insults: Fe(II)/ascorbate, Fe(II)/H(2)O(2), and tert-butyl-hydroperoxide. We also have investigated the influence of the R. rosea extract on the production of intracellular reactive oxygen species and on the activity of antioxidant enzymes (catalase, superoxide dismutase, glutathione peroxidase, and glutathione reductase). Furthermore, we have demonstrated that R. rosea extract was able to increase in a time- and dose-dependent manner the activity of the trans plasma membrane oxido reductase activity as an indirect evaluation of the intracellular redox status and this effect was already evident with small concentration of the extract and in a long time. As a result, NCTC 2544 are able to better counteract to several oxidative insults if incubated with R. rosea extract demonstrating a very good antioxidant activity of this phytocomplex.

PMID: 19705137 [PubMed - indexed for MEDLINE]

15. Am J Chin Med. 2009;37(3):557-72.

Chronic Rhodiola rosea extract supplementation enforces exhaustive swimming tolerance.

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We explored the effects and mechanisms of Rhodiola rosea extract supplementation on swimming-induced fatigue in rats. The concentrations of active components in Rhodiola rosea have been determined by high performance liquid chromatography-mass spectrometer. The Rhodiola rosea extract supplementation in water for 2-4 weeks was evaluated in male Wistar rats with 90-min unloaded swimming exercise and 5% body weight loaded swimming up to fatigue. We measured the fatigue biomarkers, including blood urea nitrogen (BUN), glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT), lactate dehydrogenase (LDH), hepatic glycogen content, the activity of fat metabolism enzymes, sterol regulatory element-binding protein-1 (SREBP-1) and fatty acid synthase (FAS), the tissue oxygen content and ratio of red and white skeletal muscle fibers in rats. Rhodiola rosea significantly increased liver glycogen, SREBP-1, FAS, heat shock protein 70 expression, Bcl-2/Bax ratio and oxygen content before swimming. Rhodiola rosea supplementation significantly increased the swimming time in a dose-dependent manner and reduced

swimming-enhanced serum BUN, GOT and GPT levels. The ratio of red and white muscle fibers was not altered after chronic Rhodiola rosea extract supplementation. Chronic Rhodiola rosea supplementation significantly improved exhaustive swimming-induced fatigue by the increased glycogen content, energy supply of lipogenic enzyme expressions and protective defense mechanisms.

PMID: 19606515 [PubMed - indexed for MEDLINE]

16. Food Chem Toxicol. 2009 Jun;47(6):1239-45. Epub 2009 Feb 25.

Mechanism of action of Rhodiola imbricata Edgew during exposure to cold, hypoxia and restraint (C-H-R) stress induced hypothermia and post stress recovery in rats.

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Mechanism of rhodiola root extract adaptogenic activity was studied in rats. The extract was orally administered in rats (100mg/kg body weight), 30 min prior to cold (5 degrees C)-hypoxia (428 mmHg)-restraint (C-H-R) exposure up to fall of T(rec)23 degrees C and recovery (T(rec)37 degrees C) from hypothermia. In untreated control rats serum lactate and non-esterified fatty acids (NEFA) increased on attaining T(rec)23 degrees C with decreased blood enzyme activities hexokinase (HK), phosphofructokinase (PFK), citrate synthase (CS) and glucose-6-phosphate dehydrogenase (G-6-PD), on attaining T(rec)23 degrees C and T(rec)37 degrees C. Decreases were also observed in liver and muscle tissues HK and G-6-PD enzyme activities and liver glycogen and CS on attaining T(rec)23 degrees C and recovery; muscle PFK during recovery; muscle CS on attaining T(rec)23 degrees C. Single and five doses of extract administration restricted increase in serum lactate values of rats on attaining T(rec)23 degrees C and maintained blood NEFA in single dose extract treated animals, indicating improved utilization of NEFA as energy fuel. The single and five doses extract treatment decreased or better maintained tissue glycogen and enzyme activities, viz. HK, PFK, CS and G-6-PD, in blood, liver and muscle, on attaining T(rec)23 degrees C and recovery. The results suggest that rhodiola extract treatment in rats shifted anaerobic metabolism to aerobic, during C-H-R exposure and post stress recovery.

PMID: 19248814 [PubMed - indexed for MEDLINE]

17. J Ethnopharmacol. 2009 Mar 18;122(2):397-401. Epub 2009 Jan 9.

Monoamine oxidase inhibition by Rhodiola rosea L. roots.

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AIM OF THE STUDY: Rhodiola rosea L. (Crassulaceae) is traditionally used in Eastern Europe and Asia to stimulate the nervous system, enhance physical and mental performance, treat fatigue, psychological stress and depression. In order to investigate the influence of Rhodiola rosea L. roots on mood disorders, three extracts were tested against monoamine oxidases (MAOs A and B) in a microtitre plate bioassay. MATERIALS AND METHODS: Methanol and water extracts gave the highest inhibitory activity against MAOs. Twelve compounds were then isolated by bioassay-guided fractionation using chromatographic methods. The structures were determined by 1H, 13C NMR and HR-MS. RESULTS: The methanol and water extracts exhibited respectively inhibitions of 92.5% and 84.3% on MAO A and 81.8% and 88.9% on MAO B, at a concentration of 100 microg/ml. The most active compound (rosiridin) presented an inhibition over 80% on MAO B at a concentration of 10(-5) M (pIC50=5.38+/-0.05). CONCLUSIONS: The present investigation demonstrates that Rhodiola rosea L. roots have potent anti-depressant activity by inhibiting MAO A and may also find application in the control of senile dementia by their inhibition of MAO B.

PMID: 19168123 [PubMed - indexed for MEDLINE]

18. J Psychopharmacol. 2009 Mar;23(2):130-42. Epub 2008 May 30.

Effects of Rhodiola rosea L. extract on behavioural and physiological alterations induced by chronic mild stress in female rats.

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Rhodiola rosea L. is one of the most popular adaptogen and an antistress plant in European and Asiatic traditional medicine. Our previous studies have confirmed the adaptogenic and antistress properties of a single administration of R. rosea L. extract in rats exposed to acute stress. There is increasing evidence that prolonged exposure to stressful life events and depression are both related to significant behavioural, endocrinological and neurobiological changes in human and animal subjects. The aim of this study was to determine whether chronic treatment with a hydroalcoholic R. rosea extract (RHO) standardized in 3% rosavin and 1% salidroside can prevent alterations induced in female rats following 6 weeks of a chronic mild stress (CMS) procedure. This was analysed through the behavioural and physiological parameters of consumption of 1% sucrose solution, locomotor and exploratory activities, body weight gain and oestrous cycle length. After the first 3 weeks of stress, RHO was administered daily by gavage at doses of 10, 15 and 20 mg/kg for the remaining 3 weeks. In addition, the antidepressant drug fluoxetine (10 mg/kg os), which has been shown to reverse CMS-induced disruptions, was used as the reference treatment. Rats subjected to the CMS procedure demonstrated decreased sucrose intake, reduced moving behaviour, minimized weight gain and dysregulation of their oestrous cycle. Treatment with RHO completely reverted all of these changes. The effects of RHO were comparable to those of fluoxetine. Interestingly, neither RHO nor fluoxetine influence the behavioural and physiological parameters tested in non-stressed animals. These findings strongly showed that chronic administration of RHO results in potent inhibition of the behavioural and physiological changes induced by chronic exposure to mild stressors.

PMID: 18515456 [PubMed - indexed for MEDLINE]

19: J Altern Complement Med. 2008 Mar;14(2):175-80.

A pilot study of Rhodiola rosea (Rhodax) for generalized anxiety disorder (GAD).

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BACKGROUND: Rhodiola rosea is an herbal supplement that many in the general population in Russia and elsewhere in the world have used for decades to alleviate everyday anxiety, depression, and insomnia. Whether R. rosea is effective in reducing similar symptoms in clinical samples is unknown. The goal of this pilot study was to evaluate whether R. rosea is effective in reducing symptoms of generalized anxiety disorder (GAD). METHOD: Ten (10) participants with a DSM-IV diagnosis of GAD, recruited from the UCLA Anxiety Disorders Program and between the ages of 34 and 55, were enrolled in this study from November 2005 to May 2006. Participants received a total daily dose of 340 mg of R. rosea extract for 10 weeks. Assessments included the Hamilton Anxiety Rating Scale (HARS), the Four-Dimensional Anxiety and Depression Scale, and the Clinical Global Impressions of Severity/Improvement Scale. RESULTS: Individuals treated with R. rosea showed significant decreases in mean HARS scores at endpoint ($t=3.27$, $p=0.01$). Adverse events were generally mild or moderate in severity, the most common being dizziness and dry mouth. CONCLUSIONS: Significant improvement in GAD symptoms was found with R. rosea, with a reduction in HARS scores similar to that found in clinical trials. These preliminary findings warrant further exploration of treatment with R. rosea in clinical samples.

20: Adv Ther. 2007 Jul-Aug;24(4):929-39.

Efficacy and tolerability of a Rhodiola rosea extract in adults with physical and cognitive deficiencies.

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During a 12-wk drug monitoring study, the efficacy and safety of a Rhodiola rosea extract given in combination with vitamins and minerals (vigodana(R)) were tested in 120 adults (83 women and 37 men, ages 50-89 y) with physical and cognitive deficiencies. Two different dosage regimens were chosen. One group of 60 patients (group 1) took 2 capsules orally in the morning after breakfast, and the other group (group 2) took 1 capsule after breakfast and 1 after lunch. Three medical examinations were performed during the course of the study (at baseline, after 6 wk, and after 12 wk). The evaluated symptoms were divided into physical disturbances such as exhaustion, decreased motivation, daytime sleepiness, decreased libido, sleep disturbances, and cognitive complaints (eg, concentration deficiencies, forgetfulness, decreased memory, susceptibility to stress, irritability). A statistically highly significant improvement (P<.001) in physical and cognitive deficiencies was observed in the overall group, as well as in the separately evaluated groups 1 and 2. In addition, the time needed to complete a digit connection test decreased significantly in all groups (P<.001). Improvements in group 1 were more pronounced than in group 2, however, indicating that the intake of 2 capsules after breakfast is more effective than the intake of 1 capsule after breakfast and 1 after lunch. Global assessment of efficacy revealed that treatment was "very good" or "good" for 81% of patients, as reported by physicians, and for 80%, as reported by patients. Ninety-nine percent of patients and physicians rated safety as "good" or "very good." No adverse events occurred during the course of the study. The results of this drug monitoring study are very promising, but they still need to be corroborated by future placebo-controlled clinical trials.

21: Phytother Res. 2005 Oct;19(10):819-38.

Stimulating effect of adaptogens: an overview with particular reference to their efficacy following single dose administration.

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Plant adaptogens are compounds that increase the ability of an organism to adapt to environmental factors and to avoid damage from such factors. The beneficial effects of multi-dose administration of adaptogens are mainly associated with the hypothalamic-pituitary-adrenal (HPA) axis, a part of the stress-system that is believed to play a primary role in the reactions of the body to repeated stress and adaptation. In contrast, the single dose application of adaptogens is important in situations that require a rapid response to tension or to a stressful situation. In this case, the effects of the adaptogens are associated with another part of the stress-system, namely, the sympatho-adrenal-system (SAS), that provides a rapid response mechanism mainly to control the acute reaction of the organism to a stressor. This review focuses primarily on the SAS-mediated stimulating effects of single doses of adaptogens derived from Rhodiola rosea, Schizandra chinensis and Eleutherococcus senticosus. The use of these drugs typically generates no side effects, unlike traditional stimulants that possess addiction, tolerance and abuse potential, produce a negative effect on sleep structure, and cause rebound hypersomnolence or 'come down' effects. Furthermore, single administration of these adaptogens effectively increases mental performance and physical working capacity in humans. R. rosea is the most active of the three plant adaptogens producing, within 30 min of administration, a stimulating effect that continues for at least 4-6 h. The active principles of the three plants that exhibit single dose stimulating effects are glycosides of phenylpropane- and phenylethane-based phenolic compounds such as salidroside, rosavin, syringin and triandrin, the latter being the most active.

22: Int J Sport Nutr Exerc Metab. 2004 Jun;14(3):298-307.

Acute Rhodiola rosea intake can improve endurance exercise performance.

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PURPOSE: The purpose of this study was to investigate the effect of acute and 4-week Rhodiola rosea intake on physical capacity, muscle strength, speed of limb movement, reaction time, and attention. METHODS: PHASE I: A double blind placebo-controlled randomized study (n= 24) was performed, consisting of 2 sessions (2 days per session). Day 1: One hour after acute Rhodiola rosea intake (R, 200-mg Rhodiola rosea extract containing 3% rosavin + 1% salidroside plus 500 mg starch) or placebo (P, 700 mg starch) speed of limb movement (plate tapping test), aural and visual reaction time, and the ability to sustain attention (Fepsy Vigilance test) were assessed. Day 2: Following the same intake procedure as on day 1, maximal isometric knee-extension torque and endurance exercise capacity were tested. Following a 5-day washout period, the experimental procedure was repeated, with the treatment regimens being switched between groups (session 2). PHASE II: A double blind placebo-controlled study (n = 12) was performed. Subjects underwent sessions 3 and 4, identical to Phase I, separated by a 4-week R/P intake, during which subjects ingested 200 mg R/P per day. RESULTS: PHASE I: Compared with P, acute R intake in Phase I increased (p <.05) time to exhaustion from 16.8 +/- 0.7 min to 17.2+/- 0.8 min. Accordingly, VO2peak (p <.05) and VCO2peak (p<.05) increased during R compared to P from 50.9 +/- 1.8 ml x min(-1) x kg(-)1 to 52.9 +/- 2.7 ml x min(-10) x kg(-1) (VO2peak) and from 60.0 +/- 2.3 ml x min(-1) x kg(-1) to 63.5+/- 2.7 ml x min(-1) x kg(-1) (VCO2peak). Pulmonary ventilation (p =.07) tended to increase more during R than during P (P: 115.9+/- 7.7 L/min; R: 124.8 +/- 7.7 L/min). All other parameters remained unchanged. PHASE II: Four-week R intake did not alter any of the variables measured. CONCLUSION: Acute Rhodiola rosea intake can improve endurance exercise capacity in young healthy volunteers. This response was not altered by prior daily 4-week Rhodiola intake.

23: Phytomedicine. 2003 Mar;10(2-3):95-105.

A randomized trial of two different doses of a SHR-5 Rhodiola rosea extract versus placebo and control of capacity for mental work.

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A randomized, double-blind, placebo-controlled, parallel-group clinical study with an extra non-treatment group was performed to measure the effect of a single dose of standardized SHR-5 Rhodiola rosea extract on capacity for mental work against a background of fatigue and stress. An additional objective was to investigate a possible difference between two doses, one dose being chosen as the standard mean dose in accordance with well-established medicinal use as a psychostimulant/adaptogen, the other dose being 50% higher. Some physiological parameters, e.g. pulse rate, systolic and diastolic blood pressure, were also measured. The study was carried out on a highly uniform population comprising 161 cadets aged from 19 to 21 years. All groups were found to have very similar initial data, with no significant difference with regard to any parameter. The study showed a pronounced antifatigue effect reflected in an antifatigue index defined as a ratio called AFI. The verum groups had AFI mean values of 1.0385 and 1.0195, 2 and 3 capsules respectively, whilst the figure for the placebo group was 0.9046. This was statistically highly significant (p < 0.001) for both doses (verum groups), whilst no significant difference between the two dosage groups was observed. There was a possible trend in favour of the lower dose in the psychometric tests. No such trend was found in the physiological tests.