

Selected Tinospora Published Scientific Abstracts

Int Immunopharmacol. 2006 Dec 5;6(12):1815-24. Epub 2006 Aug 28.

Mechanism of macrophage activation by (1,4)-alpha-D-glucan isolated from Tinospora cordifolia.

Nair PK, Melnick SJ, Ramachandran R, Escalon E, Ramachandran C.

Research Institute, Miami Children's Hospital, Miami, FL 33155, USA.

The signaling mechanism of the novel (1,4)-alpha-D-glucan (RR1) isolated from the medicinal plant *Tinospora cordifolia* was investigated in macrophages to evaluate its immunostimulating properties. When RAW264.7 macrophages were incubated with RR1 at 4 degrees C, the novel glucan inhibited the phagocytosis of unopsonized zymosan A bioparticles in a dose-dependent manner. RR1 also inhibited the binding and internalization of opsonized zymosan A bioparticles, although at a lower level than laminarin. Incubation of macrophages with anti-CD11b mAb followed by RR1 failed to show any inhibitory effect on RR1-induced TNF-alpha synthesis confirming that complement receptor 3 (CR3) is not involved in the opsonic binding and internalization of RR1 in macrophages unlike zymosan A. The anti-CD11b mAb has significant inhibitory effect on the zymosan A-induced tumor necrosis factor (TNF)-alpha synthesis. RR1 induced TNF-alpha synthesis in macrophages in a dose-dependent manner which can be completely inhibited by the NF-kappaB inhibitor caffeic acid phenethyl ester (CAPE) or curcumin. RR1 activated NF-kappaB in a time- and dose-dependent manner and this modulation of nuclear NF-kappaB activity is associated with the degradation of I-kappaB alpha thus facilitating the translocation of NF-kappaB into the nucleus. RR1-induced NF-kappaB activity peaks at 8 h of RR1 stimulation while I-kappaB alpha degradation occurred within 1 h of stimulation. RR1-induced NF-kappaB activation occurred through TLR6 signaling as evidenced by the synthesis of IL-8 in TLR6-transfected HEK293 cells. These results show that the novel (1,4)-alpha-D-glucan from *Tinospora cordifolia* activates the immune system through the activation of macrophages that occurs through TLR6 signaling, NF-kappaB translocation and cytokine production. PMID: 17052672

Biol Pharm Bull. 2006 Mar;29(3):460-6.

Evaluation of the antineoplastic activity of guduchi (Tinospora cordifolia) in Ehrlich ascites carcinoma bearing mice.

Jagetia GC, Rao SK.

The anticancer activity of dichloromethane extract of guduchi [*Tinospora cordifolia* (Willd.) Miers ex Hook. F. & Thoms. Family: Menispermaceae (TCE)] in the mice transplanted with Ehrlich ascites carcinoma (EAC) was investigated. The EAC mice receiving 25, 30, 40, 50 and 100 mg/kg, TCE showed a dose dependent elevation in tumor-free survival and a highest number of survivors were observed at 50 mg/kg TCE, which was considered as an optimum dose for its neoplastic action. The average survival time (AST) and median survival time (MST) for this dose were approximately 56 and 55 d, respectively when compared with 19 d of non-drug treated controls. Administration of 50 mg/kg TCE resulted in 100% long-term survivors (up to 90 d). An attempt was also made to evaluate the effectiveness of TCE in the various stages of tumor development, where 50 mg/kg TCE was administered intraperitoneally after 1, 3, 6, 9, 12 or 15 d of tumor inoculation and these days have been arbitrarily designated as stage I, II, III, IV or V, respectively for reasons of clarity. The greatest anticancer activity was recorded for stage I, II and III where number of long term survivors (LTS) was approximately 33, 25 and 17%, respectively. However, treatment of mice at stage IV and V did not increase LTS, despite an increase in AST and MST. The EAC mice receiving 50 mg/kg TCE showed a time dependent depletion in the glutathione (GSH) activity up to 12 h post-treatment and marginal elevation thereafter. This depletion in GSH was accompanied by a drastic elevation in lipid peroxidation (LPx) and a maximum elevation in LPx was observed at 6 h that

declined gradually thereafter. TCE exerted cytotoxic effect on tumor cells by reducing the GSH concentration and increase in LPx simultaneously.
PMID: 16508146

Phytomedicine. 2006 Jan;13(1-2):74-84. Epub 2005 Jun 29.

Tinospora cordifolia induces enzymes of carcinogen/drug metabolism and antioxidant system, and inhibits lipid peroxidation in mice.

Singh RP, Banerjee S, Kumar PV, Raveesha KA, Rao AR.

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The present study is an effort to identify a potent chemopreventive agent against various diseases (including cancer) in which oxidative stress plays an important causative role. Here, we investigated the effect of a hydroalcoholic (80% ethanol: 20% distilled water) extract of aerial roots of *Tinospora cordifolia* (50 and 100mg/kg body wt./day for 2 weeks) on carcinogen/drug metabolizing phase-I and phase-II enzymes, antioxidant enzymes, glutathione (GSH) content, lactate dehydrogenase and lipid peroxidation in liver of 8-week-old Swiss albino mice. The modulatory effect of the extract was also examined on extrahepatic organs, i.e., lung, kidney and forestomach, for the activities of GSH S-transferase (GST), DT-diaphorase (DTD), superoxide dismutase (SOD) and catalase. Significant increases in the levels of acid-soluble sulfhydryl (-SH) and cytochrome P(450) contents, and enzyme activities of cytochrome P(450) reductase, cytochrome b(5) reductase, GST, DTD, SOD, catalase, GSH peroxidase (GPX) and GSH reductase (GR) were observed in the liver. Both treated groups showed decreased malondialdehyde (MDA) formation. In lung SOD, catalase and GST; in kidney SOD and catalase; and in forestomach SOD, DTD and GST showed significant increase at both dose levels of treatment. BHA (0.75%, w/w in diet), a pure antioxidant compound, was used as a positive control. This group showed increase in hepatic levels of GSH content, cytochrome b(5), DTD, GST, GR and catalase, whereas MDA formation was inhibited significantly. In the BHA-treated group, the lung and kidney showed increased levels of catalase, DTD and GST, whereas SOD was significantly increased in the kidney and forestomach; the latter also showed an increase in the activities of DTD and GST. The enhanced GSH level and enzyme activities involved in xenobiotic metabolism and maintaining antioxidant status of cells are suggestive of a chemopreventive efficacy of *T. cordifolia* against chemotoxicity, including carcinogenicity, which warrants further investigation of active principle (s) present in the extract responsible for the observed effects employing various carcinogenesis models.
PMID: 16360936

Biol Pharm Bull. 2005 Dec;28(12):2319-22.

Cardioprotective activity of alcoholic extract of *Tinospora cordifolia* in ischemia-reperfusion induced myocardial infarction in rats.

Rao PR, Kumar VK, Viswanath RK, Subbaraju GV.

Pharmacology Division, Department of Pharmaceutical Sciences, Andhra University, Pradesh, India.

It has been suggested that the beneficial effects of reperfusion of the myocardium might be in part reversed by the occurrence of reperfusion injury. Oxidative stress was suggested to be implicating in the pathogenesis of ischemia-reperfusion (I/R) injury. Many antioxidative plants were shown to be cardioprotective in experimental models of myocardial ischemia-reperfusion (I/R) injury. The present study was designed to investigate the effects of pretreatment with alcoholic extract of *Tinospora cordifolia* in an in vivo rat model. The model adopted was that of surgically-induced myocardial ischemia, performed by means of left anterior descending coronary artery occlusion (LAD) for 30 min followed by reperfusion for another 4 h. Infarct size was measured by using the staining agent TTC (2,3,5-triphenyl tetrazolium chloride). Lipid peroxide levels in serum

and in heart tissue were estimated spectrophotometrically by the methods developed by Yagi and Ohkawa et al. respectively. A lead II electrocardiogram was monitored at various intervals throughout the experiment. A dose dependent reduction in infarct size and in lipid peroxide levels of serum and heart tissue were observed with the prior treatment of *T. cordifolia* with various doses for 7 d compared to control animals. Hence, the present study suggests the cardioprotective activity of *T. cordifolia* in limiting ischemia-reperfusion induced myocardial infarction. PMID: 16327173

Fitoterapia. 2006 Jan;77(1):1-11. Epub 2005 Dec 2.

Effect of alcoholic extract of Ayurvedic herb *Tinospora cordifolia* on the proliferation and myeloid differentiation of bone marrow precursor cells in a tumor-bearing host.

Singh SM, Singh N, Shrivastava P.

The present study investigates the effect of in vivo administration of alcoholic extract of *Tinospora cordifolia* whole plant (ALTC) on the proliferation and myeloid differentiation of bone marrow hematopoietic precursor cells in mice bearing a transplantable T cell lymphoma of spontaneous origin designated as Dalton's lymphoma (DL). BMC obtained from ALTC administered DL-bearing mice showed an enhanced BMC proliferation and colony forming ability in vitro in response to L929 conditioned medium as a source of colony stimulating factor (CSF). The number of granulocyte-macrophages colony (CFU-GM) was predominantly higher in the cultures of BMC obtained from ALTC administered mice as compared to mice injected with PBS alone. An increase in the count of bone marrow derived macrophages (BMDM) from ALTC administered mice was also observed along with an increase in the count of tumor associated macrophages. The BMDM obtained from ALTC administered mice showed an enhanced response to signal of LPS for activation to produce IL-1 and TNF. This study indicates that the *T. cordifolia* can influence the myeloid differentiation of bone marrow progenitor cells and the recruitment of macrophages in response to tumor growth in situ. PMID: 16326030

Phytomedicine. 2005 Apr;12(4):264-70.

Anti-ulcer and anti-oxidant activity of pepticare, a herbomineral formulation.

Bafna PA, Balaraman R.

Pepticare, a herbomineral formulation of the Ayurveda medicine consisting of the herbal drugs: *Glycyrrhiza glabra*, *Embllica officinalis* and *Tinospora cordifolia*, was tested for its anti-ulcer and anti-oxidant activity in rats. Effects of various doses (125, 250, 500 and 1000mg/kg, p.o.) of Pepticare were studied on gastric secretion and gastric ulcers in pylorus-ligation and on ethanol-induced gastric mucosal injury in rats. The reduction in ulcer index in both the models along with the reduction in volume and total acidity, and an increase in the pH of gastric fluid in pylorus-ligated rats proved the anti-ulcer activity of Pepticare. It was also found that Pepticare was more potent than *G. glabra* alone in protecting against pylorus-ligation and ethanol-induced ulcers. The increase in the levels of superoxide dismutase, catalase, reduced glutathione and membrane bound enzymes like Ca^{2+} ATPase, Mg^{2+} ATPase and Na^{+} K^{+} ATPase and decrease in lipid peroxidation in both the models proved the anti-oxidant activity of the formulation. Thus it can be concluded that Pepticare possesses anti-ulcer activity, which can be attributed to its anti-oxidant mechanism of action. PMID: 15898703

Immunopharmacol Immunotoxicol. 2005;27(1):1-14.

Effect of *Tinospora cordifolia* on the antitumor activity of tumor-associated macrophages-derived dendritic cells.

Singh N, Singh SM, Shrivastava P.

We and others previously have reported that extract prepared from medicinal plant *Tinospora cordifolia* shows a wide spectrum of immunoaugmentary effects. *Tinospora cordifolia* was shown to upregulate antitumor activity of tumor-associated macrophages (TAM). In this article we present evidence to show that an alcoholic extract of *Tinospora cordifolia* (ALTC) enhances the differentiation of TAM to dendritic cells (DC) in response to granulocyte/macrophage-colony-stimulating factor, interleukin-4, and tumor necrosis factor. DC differentiated *in vitro* from TAM that were harvested from tumor-bearing mice after *i.p.* administration of ALTC (200 mg/kg body weight) 2 days posttumor transplantation shows an enhanced tumor cytotoxicity and production of tumoricidal soluble molecules like TNF, IL-1, and NO. Adoptive transfer of these TAM-derived DC to Dalton's lymphoma-bearing mice resulted in prolongation of survival of tumor-bearing mice. This is the first report regarding the differentiation and antitumor functions of TAM-derived DC obtained from tumor-bearing host administered with ALTC. The possible mechanisms involved also are discussed. PMID: 15803856

J Ethnopharmacol. 2005 Jan 15;96(3):445-9. Epub 2004 Nov 23.

Efficacy of *Tinospora cordifolia* in allergic rhinitis.

Badar VA, Thawani VR, Wakode PT, Shrivastava MP et al.

The efficacy of *Tinospora cordifolia* (TC) extract in patients of allergic rhinitis was assessed in a randomized double blind placebo controlled trial. Seventy-five patients were randomly given either TC or placebo for 8 weeks. They were clinically examined and Hb %, TLC, DLC and nasal smear was done. At the end of trial baseline investigations were repeated, drug decoded and results analyzed. With TC treatment 100% relief was reported from sneezing in 83% patients, in 69% from nasal discharge, in 61% from nasal obstruction and in 71% from nasal pruritus. In placebo group, there was no relief in 79% from sneezing, in 84.8% from nasal discharge, in 83% from nasal obstruction, and in 88% from nasal pruritus. The difference between TC and placebo groups was highly significant. TLC increased in 69% patients in drug treated group and in only 11% with placebo. After TC, eosinophil and neutrophil count decreased and goblet cells were absent in nasal smear. After placebo, decrease in eosinophil and neutrophil count was marginal and goblet cells were present. TC significantly decreased all symptoms of allergic rhinitis. Nasal smear cytology and leukocyte count correlated with clinical findings. TC was well tolerated. PMID: 15619563

Acta Pol Pharm. 2004 Jul-Aug;61(4):283-7.

Restoration of antioxidants by ethanolic *Tinospora cordifolia* in alloxan-induced diabetic Wistar rats.

Prince PS, Kamalakkannan N, Menon VP.

The present study investigates the effect of oral administration of an alcoholic extract of *Tinospora cordifolia* roots on antioxidant defence in alloxan-induced diabetes in rats. A significant increase in the concentration of thiobarbituric acid reactive substances (TBARS) in brain along with a decrease in heart was observed in diabetic rats. Decreased concentration of glutathione (GSH) and decreased activities of superoxide dismutase (SOD), catalase and glutathione peroxidase (GPx) in heart and brain of diabetic rats were also noted. Alcoholic *Tinospora cordifolia* root extract (TCREt) administered at a dose of 100 mg/kg to diabetic rats orally for six weeks normalized the antioxidant status of heart and brain. The effect of *T. cordifolia* root extract was more prominent than glibenclamide (600 microg/kg). Insulin (6 units/kg) restored all the parameters to normal status. PMID: 1557559

Phytother Res. 2004 Sep;18(9):785-7.

Restoration of antioxidant defence by ethanolic *Tinospora cordifolia* root extract in alloxan-induced diabetic liver and kidney.

Prince PS, Padmanabhan M, Menon VP.

The present study investigates the effect of oral administration of an alcoholic extract of *Tinospora cordifolia* roots on antioxidant defence in alloxan-induced diabetes in rats. A significant increase in the concentration of thiobarbituric acid reactive substances (TBARS) in liver and kidney was observed in diabetic rats. Decreased concentration of glutathione (GSH) and decreased activities of superoxide dismutase (SOD), and catalase in liver and kidney of diabetic rats were also noted. Alcoholic *Tinospora cordifolia* root extract (TCREt) administered at a dose of 100 mg/kg body weight to diabetic rats orally for six weeks normalized the antioxidant status of liver and kidney. The effect of *Tinospora cordifolia* root extract was more potent than glibenclamide (600 microg/kg body weight). Insulin (6 units/kg) restored all the parameters to normal status. PMID: 15478189

Int Immunopharmacol. 2004 Dec 15;4(13):1645-59.

Immune stimulating properties of a novel polysaccharide from the medicinal plant *Tinospora cordifolia*.

Nair PK, Rodriguez S, Ramachandran R, Alamo A, Melnick SJ et al.

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An alpha-D-glucan (RR1) composed of (1-->4) linked back bone and (1-->6) linked branches with a molecular mass of >550 kDa and exhibiting unique immune stimulating properties is isolated and characterized from the medicinal plant *Tinospora cordifolia*. This novel polysaccharide is noncytotoxic and nonproliferating to normal lymphocytes as well as tumor cell lines at 0-1000 microg/ml. It activated different subsets of the lymphocytes such as natural killer (NK) cells (331%), T cells (102%), and B cells (39%) at 100 microg/ml concentration. The significant activation of NK cells is associated with the dose-dependent killing of tumor cells by activated normal lymphocytes in a functional assay. Immune activation by RR1 in normal lymphocytes elicited the synthesis of interleukin (IL)-1beta (1080 pg/ml), IL-6 (21,833 pg/ml), IL-12 p70 (50.19 pg/ml), IL-12 p40 (918.23 pg/ml), IL-18 (27.47 pg/ml), IFN- gamma (90.16 pg/ml), tumor necrosis factor (TNF)-alpha (2225 pg/ml) and monocyte chemoattractant protein (MCP)-1 (2307 pg/ml) at 100 microg/ml concentration, while it did not induce the production of IL-2, IL-4, IL-10, interferon (IFN)-alpha and TNF-beta. The cytokine profile clearly demonstrates the Th1 pathway of T helper cell differentiation essential for cell mediated immunity, with a self-regulatory mechanism for the control of its overproduction. RR1 also activated the complements in the alternate pathway, demonstrated by a stepwise increase in C3a des Arg components. Incidentally, RR1 stimulation did not produce any oxidative stress or inducible nitric oxide synthase (iNOS) in the lymphocytes or any significant increase in nitric oxide production. The water solubility, high molecular mass, activation of lymphocytes especially NK cells, complement activation, Th1 pathway-associated cytokine profile, together with a low level of nitric oxide synthesis and absence of oxidative stress confer important immunoprotective potential to this novel alpha-D-glucan. PMID: 15454117

Int Immunopharmacol. 2004 Dec 15;4(13):1569-75.

Effect of *Tinospora cordifolia* on the cytokine profile of angiogenesis-induced animals.

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The antiangiogenic activity of *Tinospora cordifolia* was studied using in vivo as well as in vitro models. In vivo antiangiogenic activity was studied using B16F10 melanoma cell-induced capillary formation in animals. Intraperitoneal administration of the extract at a concentration of 20 mg/kg significantly inhibited the tumour directed capillary formation induced by melanoma cells. Analysis of the serum cytokine profile showed a drastic increase of proinflammatory cytokines such as IL-1beta, IL-6, TNF-alpha, granulocyte monocyte-colony stimulating factor (GM-CSF) and the direct endothelial cell proliferating agent vascular endothelial cell growth factor (VEGF) in the angiogenesis-induced control animals. Administration of *Tinospora* extract could differentially regulate these cytokine's elevation. The differential regulation is further evidenced by the increased production of antiangiogenic agents IL-2 and tissue inhibitor of metalloprotease-1 (TIMP-1) in the B16F10-injected, extract-treated animals. Moreover, using an in vitro rat aortic ring assay, it was observed that the extract at nontoxic concentrations inhibited the production of proangiogenic factors from B16F10 melanoma cells. Direct treatment of the extract also inhibits the microvessel outgrowth from the aortic ring. Hence, the observed antiangiogenic activity of the plant *T. cordifolia* is related, at least in part, to the regulation of the levels of these cytokines and growth factors in the blood of the angiogenesis-induced animal. PMID: 15454110

BMC Complement Altern Med. 2004 Aug 13;4:11.

***Rubia cordifolia*, *Fagonia cretica* linn and *Tinospora cordifolia* exert neuroprotection by modulating the antioxidant system in rat hippocampal slices subjected to oxygen glucose deprivation.**

Rawal AK, Muddeshwar MG, Biswas SK.

BACKGROUND: The major damaging factor during and after the ischemic/hypoxic insult is the generation of free radicals, which leads to apoptosis, necrosis and ultimately cell death. *Rubia cordifolia* (RC), *Fagonia cretica* linn (FC) and *Tinospora cordifolia* (TC) have been reported to contain a wide variety of antioxidants and have been in use in the eastern system of medicine for various disorders. However, their mechanism of action was largely unknown. We therefore selected these herbs for the present study to test their neuroprotective ability and the associated mechanism in rat hippocampal slices subjected to oxygen-glucose deprivation (OGD). **METHODS:** Hippocampal Slices were subjected to OGD (oxygen glucose deprivation) and divided into 3 groups: control, OGD and OGD + drug treated. Cytosolic Cu-Zn superoxide dismutase (Cu-Zn SOD), reduced glutathione (GSH), glutathione peroxidase (GPx), nitric oxide (NO) was measured as nitrite (NO₂) in the supernatant and protein assays were performed in the respective groups at various time intervals. EPR was used to establish the antioxidant effect of RC, FC and TC with respect to superoxide anion (O₂⁻), hydroxyl radicals (. OH), nitric oxide (NO) radical and peroxynitrite anion (ONOO) generated from pyrogallol, menadione, DETA-NO and Sin-1 respectively. RT-PCR was performed for the three groups for GCLC, iNOS, Cu-Zn SOD and GAPDH gene expression. **RESULTS:** All the three herbs were effective in elevating the GSH levels, expression of the gamma-glutamylcysteine ligase and Cu-Zn SOD genes. The herbs also exhibited strong free radical scavenging properties against reactive oxygen and nitrogen species as studied by electron paramagnetic resonance spectroscopy. In addition all the three herbs significantly diminished the expression of iNOS gene after 48 hours which plays a major role in neuronal injury during hypoxia/ischemia. **CONCLUSIONS:** RC, FC and TC

therefore attenuate oxidative stress mediated cell injury during OGD and exert the above effects at both the cytosolic as well as at gene expression level and may be an effective therapeutic tool against ischemic brain damage. PMID: 15310392

J Radiat Res (Tokyo). 2004 Mar;45(1):61-8.

Radioprotective potential of an herbal extract of *Tinospora cordifolia*.

Goel HC, Prasad J, Singh S, Sagar RK, Agrawala PK, Bala M, Sinha AK, Dogra R. A preparation of *Tinospora cordifolia* (RTc) administered i.p. (200 mg/kg b.w.) to strain "A" male mice 1 h before whole body gamma-irradiation was evaluated for its radioprotective efficacy in terms of whole body survival, spleen colony forming units (CFU), hematological parameters, cell cycle progression, and micronuclei induction. Preirradiation treatment with RTc rendered 76.3% survival (30 days), compared to 100% mortality in irradiated control and prevented radiation induced weight loss. On 10th postirradiation day, the endogenous CFU counts in spleen were decreased with increasing radiation doses 12.0 (5 Gy), 2.16 (7.5 Gy) and 0.33 (10 Gy) but pre-irradiation administration of 200 mg/kg b.w. of RTc increased CFU counts to 31.16, 21.83 and 3.00 respectively. Pre-irradiation RTc treatment could restore total lymphocyte counts (TLC) by the 15th day to normal. It also increased the S-phase cell population that was reduced following 2 Gy irradiation in a time dependent manner. 2 Gy irradiation-induced micronuclei were also decreased by a pre-irradiation administration of RTc from 2.9 to 0.52%. Because the radioprotective manifestation of RTc observed in several systems in experimental animals can be exploited for human applications. PMID: 1513329

Planta Med. 1998 Jun;64(5):393-6.

Antioxidant and Lipophilic Constituents of *Tinospora crispa*.

Cavin A, Hostettmann K, Dyatmyko W, Potterat O.

Institut de Pharmacognosie et Phytochimie, Universite de Lausanne, Switzerland. TLC autographic assays revealed in the CH (2)Cl (2) extract of *TINOSPORA CRISPA* Miens (Menispermaceae) the presence of three compounds exhibiting antioxidant and radical scavenging properties towards beta-carotene and 2,2-diphenyl-1-picrylhydrazyl (DPPH) radical. They were isolated and identified as N-CIS-feruloyltyramine (4), (N-TRANS-feruloyltyramine (6) and secoisolariciresinol (5). When tested in dilution assays on the reduction of the DPPH radical, these 3 compounds proved to be more active than the synthetic antioxidant butylhydroxytoluene (BHT). Further investigation of the CH (2)Cl (2) extract led to the isolation of vanillin, syringin, the alkaloid N-formylnorcuciferin and the diterpene derivatives borapetosides B and C. In addition, a LC/UV/MS analysis enabled the on-line identification of borapetoside F and N-formylannonain. PMID: 17253260

Phytother Res. 2003 May;17(5):552-4.

Alteration of lethal effects of gamma rays in Swiss albino mice by *Tinospora cordifolia*.

Pahadiya S, Sharma J.

Tinospora cordifolia is widely used in Ayurvedic medicines. It is known for its immunomodulatory, antihepatotoxic, antistress and antioxidant properties. It has been used in combination with other plant products to prepare a number of Ayurvedic preparations. The present study was undertaken to evaluate the radioprotective effect of an aqueous extract of *Tinospora cordifolia* (TC) against (60)Co gamma radiation. Oral administration of TC 5 mg/kg body wt to Swiss albino mice 1 h and 15 days prior to whole body radiation exposure (8 Gy) produced a significant protection in terms of survival percentage. After oral

administration of TC 10 mg/kg body wt/day to mice 7 days prior to whole body irradiation (8 Gy) there was no mortality until day 13 and 50% of the animals survived until day 30. Mice exposed to radiation (8 Gy) without TC pretreatment exhibited signs of radiation sickness such as anorexia, lethargy, ruffled hair, diarrhoea and these animals died within 14 days of irradiation. The results from the present study suggest that *Tinospora cordifolia* has a radioprotective effect in Swiss albino mice, thereby enhancing the survival of mice against a sublethal dose of gamma radiation. PMID: 12748997

Indian J Exp Biol. 2002 Jun;40(6):727-34.

Free radical scavenging and metal chelation by *Tinospora cordifolia*, a possible role in radioprotection.

Goel HC, Prem Kumar I, Rana SV.

Aqueous extract of *T. cordifolia* inhibited Fenton (FeSO_4) reaction and radiation mediated 2-deoxyribose degradation in a dose dependent fashion with an IC_{50} value of 700 microg/ml for both Fenton and radiation mediated 2-DR degradation. Similarly, it showed a moderate but dose dependent inhibition of chemically generated superoxide anion at 500 microg/ml concentration and above with an IC_{50} value of 2000 microg/ml. Aqueous extract inhibited the formation of Fe^{2+} -bipyridyl complex and formation of comet tail by chelating Fe^{2+} ions in a dose dependent manner with an IC_{50} value of 150 microg/ml for Fe^{2+} -bipyridyl formation and maximally 200 microg/ml for comet tail formation, respectively. The extract inhibited ferrous sulphate mediated lipid peroxidation in a dose-dependent manner with an IC_{50} value of 1300 microg/ml and maximally (70%) at 2000 microg/ml. The results reveal that the direct and indirect antioxidant actions of *T. cordifolia* probably act in corroboration to manifest the overall radioprotective effects. PMID: 1258772

J Toxicol Sci. 2002 Aug;27(3):139-46.

Hepatoprotective and immunomodulatory properties of *Tinospora cordifolia* in CCl_4 intoxicated mature albino rats.

Bishayi B, Roychowdhury S, Ghosh S, Sengupta M.

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Effect of *Tinospora cordifolia* extract on modulation of hepatoprotective and immunostimulatory functions in carbon tetrachloride (CCl_4) intoxicated mature rats is reported here. Administration of CCl_4 (0.7 ml/kg body weight for 7 days) produces damage in the liver as evident by estimation of enzymes such as serum glutamate oxaloacetate transaminase (SGOT), serum glutamate pyruvate transaminase (SGPT) and alkaline phosphatase (ALP) as well as serum bilirubin level. CCl_4 administration also causes immunosuppressive effects as indicated by phagocytic capacity, chemotactic migration and cell adhesiveness of rat peritoneal macrophages. However, treatment with *T. cordifolia* extract (100 mg/kg body weight for 15 days) in CCl_4 intoxicated rats was found to protect the liver, as indicated by enzyme level in serum. A significant reduction in serum levels of SGOT, SGPT, ALP, bilirubin were observed following *T. cordifolia* treatment during CCl_4 intoxication. Treatment with *T. cordifolia* extract also deleted the immunosuppressive effect of CCl_4 , since a significant increment in the functional capacities of rat peritoneal macrophages (PM phi) was observed following *T. cordifolia* treatment. The results of our experiment suggest that treatment by *T. cordifolia* extract may be the critical remedy for the adverse effect of CCl_4 in liver function as well as immune functions.

PMID: 12238138

Redox Rep. 2002;7(3):137-43.

Antioxidant properties of a *Tinospora cordifolia* polysaccharide against iron-mediated lipid damage and gamma-ray induced protein damage.

Subramanian M, Chintalwar GJ, Chattopadhyay S.

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The antioxidant activity of an arabinogalactan polysaccharide (TSP) isolated from *Tinospora cordifolia*, an Indian medicinal plant, was studied. The polysaccharide showed good protection against iron-mediated lipid peroxidation of rat brain homogenate as revealed by the thiobarbituric acid reactive substances (TBARS) and lipid hydroperoxide (LOOH) assays. TSP also provided significant protection to protein against gamma-ray induced damage. The protective action can possibly be explained by its very high reactivity towards DPPH, superoxide radicals and the most damaging of radicals, the hydroxyl radical. PMID: 12189043

Indian J Exp Biol. 1992 Jul;30(7):592-6.

Mechanism of anti-stress activity of *Ocimum sanctum* Linn, eugenol and *Tinospora malabarica* in experimental animals.

Sen P, Maiti PC, Puri S, Ray A, Audulov NA, Valdman AV.

Department of Pharmacology, University College of Medical Sciences, Delhi, India.

Effects of restraint stress (RS) and its modulation by *O. sanctum* (Os), eugenol and *T. malabarica* (Tm) were evaluated on some biochemical and biophysical parameters in rats. RS induced elevations in blood glucose and urea levels, were unaffected by either Os, eugenol or Tm pretreatment. However, both Os and eugenol lowered RS-induced cholesterol levels. RS also caused a generalized increase in enzyme activity and Os, eugenol or Tm effectively lowered the RS-induced elevations in lactate dehydrogenase (LDH) and alkaline phosphatase. RS also induced (a) increased membrane protein clusterization, (b) increased membrane fluidity and (c) reduced membrane thickness--in RBC membrane, whereas, the effects on the synaptosomal membrane were less marked. The RS-induced changes in RBC membrane dynamics were attenuated/reversed by Os, eugenol or Tm, in a differential manner. These biochemical and membrane changes during Rs and their modulation by the adaptogens are discussed in light of the possible mechanisms of action of these agents, during such aversive stimuli. PMID: 1459632