Reishi Mushroom Extract.Fairy Grass,Ling-Zhi.Mushroom Extract.....

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Ganoderma lucidum:Research update.

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Ganoderma lucidum polysaccharides enhance CD14 endocytosis of LPS and promote TLR4 signal transduction of cytokine expression.:J Cell Physiol. 2007 Aug;212(2):537-50.Hua KF, Hsu HY, Chao LK, Chen ST, Yang WB, Hsu J, Wong CH.Department of Biotechnology and Laboratory Science in Medicine, National Yang-Ming University, Taipei, Taiwan.

We have previously reported that a well-characterized glycoprotein fraction containing fucose residues in an extract of Ganoderma lucidum polysaccharides (EORP) exerts certain immuno-modulation activity by stimulating the expression of inflammatory cytokines via TLR4. Continuing our studies, we have demonstrated that EORP increases the surface expression of CD14 and TLR4 within murine macrophages J774A.1 cells in vitro, and further promotes LPS binding and uptake by J774A.1 cells in a CD14-dependent fashion. Moreover, we observed the co-localization of internalized LPS with lysosome- and Golgi-apparatus markers within 5 min after J774A.1 cells stimulated with LPS. In addition, EORP pretreatment of J774A.1 cells and human blood-derived primary macrophages, followed by LPS stimulation, results in the super-induction of interleukin-1beta (IL-1) expression. Endocytosis inhibitors: such as cytochalasin D and colchicine effectively block EORP-enhanced LPS internalization by J774A.1 cells; yet they fail to decrease the LPS-induced phosphorylation of certain mitogen-activated protein kinases, and IL-1 mRNA and proIL-1 protein expression, indicating that LPS internalization by J774A.1 cells is not associated with LPS-dependent activation. Our current results could provide a potential EORP-associated protection mechanism for bacteria infection by enhancing IL-1 expression and the clearance of contaminated LPS by macrophages. J. Cell. Physiol. 212: 537-550, 2007.

Qualitative and quantitative analyses of nucleosides and nucleobases in Ganoderma spp. by HPLC-DAD-MS.:J Pharm Biomed Anal. 2007 Mar 20;Gao JL, Leung KS, Wang YT, Lai CM, Li SP, Hu LF, Lu GH, Jiang ZH, Yu ZL.Institute of Chinese Medical Sciences, University of Macau, Taipa, Macau, China.

A high-performance liquid chromatography-diode array detector-mass spectrometry (HPLC-DAD-MS) analytical method was developed for detection of the nucleosides and nucleobases in two species of Lingzhi, the dried sporophore of Ganoderma lucidum and G. sinense. The method, combining advantages of both DAD and MS, was successfully used to qualitatively identify for six nucleosides namely, adenosine, cytidine, guanosine, inosine, thymidine, uridine and five nucleobases namely, adenine, guanine, hypoxanthine, thymine and uracil in Lingzhi

samples. Quantitative analyses showed that uridine was the most abundant nucleoside in these Lingzhi samples and the contents of nine target analytes were found to be different in pileus and stipes of the fruiting bodies and among the different species of G. spp. The established method might apply as an alternative approach for the quality assessment of Lingzhi.

Characterization of ganoderma spore lipid by stable carbon isotope analysis: implications for authentication.:Anal Bioanal Chem. 2007 Jun;388(3):723-31. Epub 2007 Apr 20.Liu X, Xu SP, Wang JH, Yuan JP, Guo LX, Li X, Huang XN.State Key Laboratory of Biocontrol/Food Engineering Research Center of State Ministry of Education, College of Life Sciences, Sun Yat-Sen University, Guangzhou, 510275, China, wangjhai@mail.sysu.edu.cn.

The ratios of stable carbon isotopes ((13)C/(12)C) of ganoderma fruiting body, ganoderma spore, ganoderma spore lipid (GSL) and individual fatty acids in GSL were determined by gas chromatography-stable isotope ratio mass spectrometry and elemental analysis-stable isotope ratio mass spectrometry. These values fall into a range from -26.9 to -23.3 per thousand, suggesting that the cut log as the Ganoderma-cultivated substrate in Fujian, China, may belong to C3 plants. Eighteen fatty acids were identified and their abundances measured by gas chromatography-mass spectrometry in the six GSL samples with C(16:0), C(18:0), C(18:1) and C(18:2) as major constituents, and C(16:1) is evidently enriched compared with the other edible vegetable oils. On the basis of the compositions of fatty acids and stable carbon isotopes in GSL, we have developed a novel method to detect the adulteration of GSL products with cheaper edible vegetable oils. An example of ideal blending between GSL and C4 or C3 vegetable oil is further provided to expound the discrimination procedures and corresponding sensitive indicators. Simultaneously, the carbon isotope fractionation in the biosynthesis of individual fatty acids was observed, revealing that the formation of C(18:0) from C(16:0) in ganodema spores had no conspicuous (13)C enrichment of +0.4 per thousand for Ganoderma sinensis spore and +0.1 per thousand for G. lucidum spore; the desaturation of C(18:0) to C(18:1) resulted in a distinct (13)C depletion of -1.4 per thousand for G. sinensis spore and -0.9 per thousand for G. lucidum spore; and the next desaturation from C(18:1) to C(18:2) displayed no evident (13)C fractionation of -0.1 per thousand for G. sinensis spore and -0.2 per thousand for G. lucidum spore. Figure Ganoderma lucidum has been widely used in traditional Chinese medicines. Ganoderma spore lipid (GSL) extracted from the spores of G. lucidum has been approved as a health food supplement. However, because of rarity, GSL has become a target for adulteration with cheaper vegetable oils.

Coprinus comatus and Ganoderma lucidum interfere with androgen receptor function in LNCaP prostate cancer cells.:Mol Biol Rep. 2007 Mar 13;Zaidman BZ, Wasser SP, Nevo E, Mahajna J.Institute of Evolution, University of Haifa, Mount Carmel, Haifa, 31905, Israel.

In this study, we screened a total of 201 diethyl ether, ethanol, and ethyl acetate fungal Basidiomycetes extracts for anti-androgenic activity. Based on our screened results in combination with the selective inhibition of prostate cancer LNCaP cells, we selected Coprinus comatus and Ganoderma lucidum for further evaluation. We demonstrated that ethanol and ethyl acetate extracts from C. comatus and G. lucidum, respectively, selectively inhibit dihydrotestosterone-induced LNCaP cell viability, suppress levels of secreted prostate-specific antigen in a dose-dependent manner, and cause a G1 phase arrest in LNCaP, but not in DU 145 and PC-3 cells. For the first time, to the best of our knowledge, we demonstrated that C. comatus and G. lucidum decreased androgen and glucocorticoide receptors transcriptional activity in breast cancer MDA-kb2 cells in a dose-dependent manner, and suppressed androgen receptor (AR) protein level in LNCaP and MDA-kb2 cells. Our findings suggest that AR and non-AR mediated mechanisms underlie the effects of C. comatus and G. lucidum.

Use of whey permeate for cultivating Ganoderma lucidum mycelia.:J Dairy Sci. 2007 May;90(5):2141-6.Song M, Kim N, Lee S, Hwang S.School of Environmental Science and Engineering, Pohang University of Science and Technology, Kyungbuk 790-784, Korea.

A novel approach to utilizing whey permeate, the cultivation of mycelia of the edible mushroom Ganoderma lucidum, is introduced. The major objective of this research was to use whey permeate as an alternative growth medium for the cultivation of mycelia of edible mushroom G. lucidum and to find an optimum condition for solid-state cultivation. Response surface analysis

was applied to determine the combination of substrate concentration (25 to 45 g of lactose/L), pH (3.5 to 5.5), and temperature (25 to 35 degrees C) resulting in a maximal mycelial growth. The radial extension rates, estimated by measuring the diameters of growing colonies on the Petri dishes, were used as the growth of the mycelia at different conditions. In the model, pH and temperature significantly affected mycelial growth, but lactose concentration did not. The condition predicted to maximize the radial extension rate of 17.6 +/- 0.4 mm/d was determined to be pH 4.4 and temperature 29.4 degrees C. Therefore, the results suggest that whey permeate could be utilized as a growth substrate for the cultivation of mycelia from the edible mushroom G. lucidum, enhancing the use of this by-product by the cheese manufacturing industry.

Extract of Ganoderma lucidum potentiates pentobarbital-induced sleep via a GABAergic mechanism.:Pharmacol Biochem Behav. 2007 Apr;86(4):693-8. Epub 2007 Feb 22.Chu QP, Wang LE, Cui XY, Fu HZ, Lin ZB, Lin SQ, Zhang YH.Department of Pharmacology, Peking University, School of Basic Medical Science, 38 Xueyuan Lu, Beijing 100083, China.

Ganoderma lucidum has been used for the treatment of a variety of diseases. For the first time here we report a detailed study on the mechanisms and effects of G. lucidum aqueous extract (GLE) on sleep and its sedative activity. GLE showed no effects on sleep architecture in normal rats at doses of 80 and 120 mg/kg. However, GLE significantly decreased sleep latency, increased sleeping time, non-REM sleep time and light sleep time in pentobarbital-treated rats. Suppression of locomotor activity in normal mice induced by GLE was also observed. Flumazenil, a benzodiazepine receptor antagonist, at a dose of 3.5 mg/kg showed a significant antagonistic effect on the shortening in sleep latency, increase in sleeping time, non-REM sleep time or light sleep time in pentobarbital-treated rat induced by GLE. Significant effect was also observed with GLE on delta activity during non-REM sleep and flumazenil did not block this effect. In conclusion, GLE may be a herb having benzodiazepine-like hypnotic activity at least in part.

Analysis of triterpenoids in ganoderma lucidum using liquid chromatography coupled with electrospray ionization mass spectrometry.:J Am Soc Mass Spectrom. 2007 May;18(5):927-39. Epub 2007 Mar 26.Yang M, Wang X, Guan S, Xia J, Sun J, Guo H, Guo DA.Shanghai Research Center for TCM Modernization, Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai, PR China.

Triterpenoids extracted from Ganoderma lucidum (Leyss. ex Fr.) Karst were separated and characterized using optimized reversed-phase liquid chromatography with diode array detection and electrospray ion trap tandem mass spectrometry (HPLC-DAD-ESI-MS(n)). They could be classified into five types depending on the fragmentation behavior. All triterpenoids gave [M - H](-) and [2M - H](-) ions by electrospray ionization monitored in the negative ion mode; in addition, compounds of types III and IV gave prominent [M - H - H(2)O](-) ions and the unsaturated bond at C-20, 22 would reduce the abundance of [M - H - H(2)O](-) ion. The key fragmentation information was cleavage at C- and D-rings despite the predominant losses of H(2)O and CO(2). Compounds with hydroxyls at C-7 and C-15 would produce a list of b, b - 1, b - 2, and b - 16 ions attributed to cleavage of D-ring; if the second alcohol at C-15 were oxidized to ketone, the prominent cleavage would occur at C-ring and produce a group of ions of a; if C-7 were oxidized to ketone, transference of two hydrogen atoms would occur during the cleavage of rings and a list of ions about a + 2 and/or b + 2 would appear instead. The above fragmentations and regularities in fragmentation pathways were reported for the first time, and were implemented for the analysis of triterpenoids in G. lucidum. The chloroform extract was separated on a Zorbax SB-C(18) column, eluting with an acetonitrile-0.2% acetic acid gradient. A total of 32 triterpenoids, including six new ones, were identified or tentatively characterized based on the tandem mass spectra of the HPLC peaks.

Combined effect of green tea and Ganoderma lucidum on invasive behavior of breast cancer cells.:Int J Oncol. 2007 Apr;30(4):963-9.Thyagarajan A, Zhu J, Sliva D.Cancer Research Laboratory, Methodist Research Institute, E504, Indianapolis, IN 46202, USA.

Epidemiological studies have suggested that consumption of green tea may decrease the risk of a variety of cancers. In addition, mushroom Ganoderma lucidum has been used for the promotion of health, longevity and treatment of cancer in traditional Chinese medicine. In the present study we show that extract from green tea (GTE) increased the anticancer effect of G.

lucidum extract (GLE) on cell proliferation (anchorage-dependent growth) as well as colony formation (anchorage-independent growth) of breast cancer cells. This effect was mediated by the down-regulation of expression of oncogene c-myc in MDA-MB-231 cells. Although individual GTE and GLE independently inhibited adhesion, migration and invasion of MDA-MB-231 cells, their combination demonstrated a synergistic effect, which was mediated by the suppression of secretion of urokinase plasminogen activator (uPA) from breast cancer cells. Our study suggests the potential use of combined green tea and G. lucidum extracts for the suppression of growth and invasiveness of metastatic breast cancers.

Ganoderma lucidum: a cause of pseudoparasitosis.:Southeast Asian J Trop Med Public Health. 2006 Nov;37(6):1099-102.Wanachiwanawin D, Piankijagum A, Chaiprasert A, Lertlaituan P, Tungtrongchitr A, Chinabutr P.Department of Parasitology, Faculty of Medicine, Siriraj Hospital, Mahidol University, Bangkok, Thailand. sidwn@mahidol.ac.th

We report a pseudoparasitosis case due to Ganoderma lucidum, (lingzhi or reishi mushroom); we believe this to be a first reported case in Thailand. A 49-year-old male patient with non-Hodgkins lymphoma presented with chronic watery diarrhea. He had a history of consumption of powdered lingzhi extract as a dietary supplement and herbal medicine. Stool examination demonstrated many spores of G. lucidum, which must be differentiated from intestinal helminth ova and coccidia. After discontinuation of mushroom spores ingestion, the diarrheal symptoms improved and fecal examination subsequently showed no Ganoderma spores. Many artifacts in the stool may be confused with parasites. Differentiation of parasites from artifacts depends on characterization of the size, shape, structure, and reactivity with common stains.

Anti-inflammatory and anti-tumor-promoting effects of triterpene acids and sterols from the fungus Ganoderma lucidum.:Chem Biodivers. 2007 Feb;4(2):224-31.

A series of lanostane-type triterpene acids, including eleven lucidenic acids (3, 4, 9, 10, 13-19) and six ganoderic acids (20-22, 24, 26, 27), as well as six sterols (28-33), all isolated from the fruiting bodies of the fungus Ganoderma lucidum, were examined for their inhibitory effects on the induction of Epstein-Barr virus early antigen (EBV-EA) by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells, a known primary screening test for anti-tumor promoters. All of the compounds tested, except for ganolactone (27) and three sterols (29-31), showed potent inhibitory effects on EBV-EA induction, with IC(50) values of 235-370 mol ratio/32 pmol TPA. In addition, nine lucidenic acids (1, 2, 5-8, 11, 12, 18) and four ganoderic acids (20, 23-25) were found to inhibit TPA-induced inflammation (1 microg/ear) in mice, with ID(50) values of 0.07-0.39 mg per ear. Further, 20-hydroxylucidenic acid N (18) exhibited inhibitory effects on skin-tumor promotion in an in vivo two-stage mouse-skin carcinogenesis test based on 7,12-dimethylbenz[a]anthracene (DMBA) as initiator, and with TPA as promoter.

HPLC method for the determination and pharmacokinetic studies of four triterpenoids in rat plasma after oral administration of Ganoderma lucidum extract.:Biomed Chromatogr. 2007 Apr;21(4):389-96.Wang X, Liu R, Sun J, Guan S, Yang M, Bi K, Guo D.Shanghai Research Center for TCM Modernization, Shanghai Institute of Materia Medica, Shanghai Institute for Biological Sciences, Zhangjiang, Shanghai 201203, People's Republic of China.

Four major triterpenoids (ganoderic acids C(2), B, K and H) in rat plasma after oral administration of G. lucidum extract were analyzed quantitatively by high-performance liquid chromatography (HPLC). Plasma samples taken from rats were acidified with hydrochloric acid and extracted with dichloromethane-ethyl acetate (90:10). The chromatographic separation was achieved on an Agilent Zorbax SB-C(18) column (250 x 4.6 mm, 5 microm) at 35 degrees C, with a linear gradient of acetonitrile and 0.03% aqueous phosphoric acid (v/v), at a flow rate of 1.0 mL/min. The four triterpenoids and internal standard (hydrocortisone) were detected at a wavelength 252 nm. All calibration curves showed good linearity (r(2) > 0.99) within test ranges. The relative deviation of this method was less than 10% for intra- and inter-day assays, and the accuracy ranged from 89 to 108%. The extract recovery for the four triterpenoids and internal standard ranged from 95 to 67%, and the QC samples were found to be stable according to the results of the stability study. This is the first report on determination of the major triterpenoids in rat plasma after oral administration of G. lucidum extract and the results provided a firm basis for clarifying the pharmacological effect of G. lucidum and evaluating the clinical applications of this

medicinal fungus.

Ganoderma lucidum polysaccharide peptide reduced the production of proinflammatory cytokines in activated rheumatoid synovial fibroblast.:Mol Cell Biochem. 2007 Jul;301(1-2):173-9. Epub 2007 Jan 12.Ho YW, Yeung JS, Chiu PK, Tang WM, Lin ZB, Man RY, Lau CS.Department of Pharmacology, University of Hong Kong, Hong Kong SAR, Hong Kong.

The aim of the current study was to elucidate the potential therapeutic effect of Ganoderma lucidum polysaccharide peptide (GL-PP) in rheumatoid arthritis (RA). The effects of GL-PP on cell proliferation and cytokine production were studied in RA synovial fibroblasts (RASF). GL-PP significantly inhibited the proliferation of RASF. Following the incubation with GL-PP, production of interleukin (IL)-6 and monocyte chemoattractant protein (MCP)-1 in RASF were significantly increased as expressed as percentage change from basal values. However, the actual effects were minimal due to the low basal values. When RASF were activated by IL-1beta or lipopolysaccharides, IL-8 and MCP-1 production increased many folds. GL-PP significantly suppressed their productions. The inhibitory effects of GL-PP on cytokine production in RASF were at least in part, by inhibiting the nuclear factor-kappa B (NF-kappaB) transcription pathway. Our results demonstrated that GL-PP had the unique ability to modulate cytokine production in RASF and warrants further investigation into its mechanism of action.

Effects of ganoderma lucidum spores on cytochrome C and mitochondrial calcium in the testis of NIDDM rats.:Zhonghua Nan Ke Xue. 2006 Dec;12(12):1072-5.Wang BX, Wang SQ, Qin WB, Wang SX, Ma XR, Zhang T.Department of Pathology and Physiology, College of Basic Medical Sciences, China.

OBJECTIVE: To observe the effects of Ganoderma lucidum spores on Cytochrome C (Cyt-C) and mitochondrial calcium in the testis of NIDDM rats. METHODS: Fifty male Wistar rats were divided randomly into three groups: model, ganoderma and normal control, the first two groups injected with 2% STZ through vena caudalis, and the last one with half-and-half sodium citrate/citrate buffer solution. Two weeks after normal diet, glucose tolerance tests were performed and the rats with abnormal glucose tolerance from the model and ganoderma groups received high-fat and high-carbohydrate food, the ganoderma group given Ganoderma lucidum spores (250mg/[kg x d]) in addition, both for 10 weeks. Glucose tolerance tests were repeated 1 day before the end of the experiment and the rats were castrated and relevant indexes measured. RESULTS: The NIDDM model was successfully constructed. In the model group, the levels of mitochondrial Cyt-C and mitochondrial calcium were significantly lower (P <0. 05) while that of the plasma Cyt-C was significantly higher than in the ganoderma and the control groups. CONCLUSION: Cyt-C and calcium ion are involved in the damage of the testis. Ganoderma lucidum spores can protect the testis of NIDDM rats.

Ganoderma lucidum polysaccharides enhance the function of immunological effector cells in immunosuppressed mice.:J Ethnopharmacol. 2007 May 4;111(2):219-26. Epub 2006 Nov 21.Zhu XL, Chen AF, Lin ZB.Department of Pharmacology, School of Basic Medical Science, Peking University Health Science Center, 38 Xueyuan Road, Beijing 100083, PR China. xiaolingzhu88yahoo.com.cn

The present study was designed to determine in vivo efficacy of Ganoderma lucidum polysaccharides (Gl-PS) for enhancing the activity of immunological effector cells in immunosuppressed mice. Mice were injected intraperitoneally (i.p.) once daily with low-dose (2.5mg/kg), intermediate-dose (25mg/kg), and high-dose (250 mg/kg) of Gl-PS, respectively, for 7 consecutive days 24h after i.p. injection of a immunosuppressing anti-tumor agent cyclophosphamide (Cy, 300 mg/kg). In Cy-treated mice, compared to vehicle, low-dose Gl-PS accelerated recovery of bone marrow cells, red blood cells and white blood cells, as well as splenic natural killer cells and natural killer T cells, and enhanced T and B cell proliferation responses on day 8, cytotoxic T lymphocyte activity on day 5, as well as NK cell and lymphokine activated killer cell activity on days 7-9. Furthermore, it promoted phagocytosis and cytotoxicity of macrophages on day 12. The above beneficial effects induced by the low-dose Gl-PS treatment did not result in any side effects. These results demonstrate the efficacious effects of low-dose Gl-PS treatment for enhancing the activity of immunological effector cells in immunosuppressed mice, and may provide a basis for applying this herb as an efficacious adjacent

immunopotentiating therapy against cancer chemotherapy-induced immunosuppression.

Antitumor activity of extracts of Ganoderma lucidum and their protective effects on damaged HL-7702 cells induced by radiotherapy and chemotherapy.:Zhongguo Zhong Yao Za Zhi. 2006 Oct;31(19):1618-22.Wang DH, Weng XC.School of Life Sciences, Shanghai University, Shanghai 200444, China.

OBJECTIVE: To study the inhibitory effect of Ganoderma lucidum, the extract of chloroform, the extract of ethyl acetate and the remains after two-time extraction on BEL-7402 and MGC-803 cells and their protective effects on HL-7702 cells pre-and post-exposed to cisplatin (DDP) and various doses of 60Co gamma irradiation. METHOD: The antitumor activity and protective effects on damaged HL-7702 cells induced by radiotherapy and chemotherapy of ganoderma lucidum were determined by MTT technique. RESULT: The anticancer activity of the extract of chloroform Ganoderma lucidum was the best: at the concentration of 0.125 mg x mL(-1), the inhibitory rate was over 50%. To the HL-7702 cells damaged by DDP, four kinds of extracts didn't exert restoring effect, but the pretreatment with the extract of chloroform reduced the damaged degree significantly. To the 60Co gamma irradiated HL-7702 cells, only the extract of chloroform exerted restoring effect to some extent when exposed to middle or high dose of irradiation. The pre-administration of four kinds of extracts reduced the damaged degree by radiation. CONCLUSION: The extract of chloroform exerts notable antitumor effects on cancer cells and protective effects on damaged normal cells induced by radiotherapy and chemotherapy.

Effect of polysaccharides from Ganoderma lucidum on streptozotocin-induced diabetic nephropathy in mice.:J Asian Nat Prod Res. 2006 Dec;8(8):705-11.He CY, Li WD, Guo SX, Lin SQ, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Centre, Beijing, 100094, China.

The effects of Ganoderma lucidum polysaccharides (GL-PS) on renal complication in streptozotocin-induced diabetic mice have been investigated in the present study. C57BL/6J mice were made diabetic by injection of streptozotocin and GL-PS (125 and 250 mg kg-1) was administered for 8 weeks. Body weight was monitored every week. Serum glucose, creatinine (Cr), blood urea nitrogen (BUN), triglyceride (TG) and urinary albumin excretion (UAE) were measured after 8 weeks of treatment. Glomerular size and mesangial matrix index were assayed by morphometric analysis. Renal expression of transforming growth factor-beta1 (TGF-beta1) were determined by immunochemistry. Renal malondialdehyde (MDA) level and superoxide dismutase (SOD) activities were also evaluated. GL-PS was able to reduce the serum Cr and BUN levels and UAE compared with diabetic model mice in a dose-dependent manner. Increasing serum glucose and triglyceride levels in diabetic mice could also be lowered by GL-PS. Moreover, GL-PS had the capacity to improve the renal morphometric changes and oxidative stress state of diabetic mice. In summary, GL-PS can improve the metabolic abnormalities of diabetic mice and prevent or delay the progression of diabetic renal complications.

On-line hyphenation of supercritical fluid extraction and two-dimensional high performance liquid chromatography-atmospheric pressure chemical ionization tandem mass spectrometer for the analysis of Ganoderma lucidum.:J Sep Sci. 2006 Nov;29(16):2514-22.Zhang J, Zhang L, Duan J, Liang Z, Zhang W, Huo Y, Zhang Y.National Chromatographic Research & Analysis Center, Dalian Institute of Chemical Physics, Chinese Academy of Sciences, Dalian, P. R. China.

A novel on-line system combining supercritical fluid extraction (SFE) and two-dimensional high performance liquid chromatography (2D-HPLC) was developed. A trap column and two three-port valves were employed to couple SFE and 2D-HPLC system, which was composed of a CN column and a monolithic silica column, connected by a 10-port dual-position valve. The analytes extracted by supercritical CO2 were completely transferred to the 2D-HPLC system. After separation in two orthogonal modes, the eluents were delivered to APCI-tandem-MS for identification of the samples. In this way, sample preparation, separation, detection, and identification were integrated into an on-line system permitting analysis of the fruiting bodies of Ganoderma lucidum, and at least 73 components in the extract were resolved with calculated peak capacity of up to 1643.

Enhancement of polysaccharides production in Ganoderma lucidum by the addition of ethyl acetate extracts from Eupolyphaga sinensis and Catharsius molossus.:Appl Microbiol Biotechnol. 2007 Mar;74(3):572-7. Epub 2006 Nov 14.Liu GQ, Zhang KC.Key Laboratory of Industrial Biotechnology, Ministry of Education, Southern Yangtze University, 170 Huihe Road, Wuxi, 214036, People's Republic of China.

To screen stimulators from Chinese medicinal insects for mycelial growth and polysaccharides production of Ganoderma lucidum, G. lucidum was inoculated into the media with and without supplementation of medicinal insect extracts. The ethyl acetate extract of Eupolyphaga sinensis at 55 mg l(-1) lead to significant increase in both biomass and intracellular polysaccharides (IPS) concentration from 8.53 +/- 0.41 to 14.16 +/- 0.43 and 1.28 +/- 0.09 to 2.13 +/- 0.11 g l(-1), respectively. In addition, the ethyl acetate extract of Catharsius molossus at 55 mg l(-1) significantly enhanced extracellular polysaccharides (EPS) production; the EPS yield increased from 350.9 +/- 14.1 to 475.1 +/- 15.3 mg l(-1). There were no new components in the two types of polysaccharides obtained by the addition of the insect extracts.

HPLC determination of four triterpenoids in rat urine after oral administration of total triterpenoids from Ganoderma lucidum.:J Pharm Biomed Anal. 2007 Feb 19;43(3):1185-90. Epub 2006 Nov 20.Wang XM, Guan SH, Liu RX, Sun JH, Liang Y, Yang M, Wang W, Bi KS, Guo DA.Shanghai Research Center for TCM Modernization, Shanghai Institute of Materia Medica, Shanghai Institute for Biological Sciences, Guo Shoujing Road 199, Zhangjiang, Shanghai, PR China.

A sensitive and simple high-performance liquid chromatography (HPLC) method was applied for the quantitative determination of four major triterpenoids (ganoderic acids C(2), B, K and H) in rat urine after oral administration of total triterpenoids from Ganoderma lucidum. The urine sample was extracted with dichloromethane-ethyl acetate (90:10) after acidification by hydrochloric acid (0.2 mol/ml). Chromatographic separation was achieved on a Zorbax SB-C(18) column (250 mm x 4.6 mm, 5 microm) at 35 degrees C, with a linear gradient of acetonitrile and 0.03% aqueous phosphoric acid (v/v), at a flow rate of 1.2 ml/min. The four triterpenoids and internal standard (hydrocortisone) were detected at a wavelength 252 nm. The within- and between-day assay coefficients of variation for the four triterpenoids in urine were less than 9% and the extraction recovery of this method was higher than 90%. Using this method, the excretion profile of the triterpenoids in rat urine after oral administration of total triterpenoids of G. lucidum was revealed for the first time.

Antiproliferative ability of a combination regimen of crocodile egg extract, wild radix ginseng and natural Ganoderma lucidum on acute myelogenous leukemia.:Oncol Rep. 2006 Dec;16(6):1313-6.Chui CH, Wong RS, Cheng GY, Lau FY, Kok SH, Cheng CH, Cheung F, Tang WK, Teo IT, Chan AS, Tang JC.Central Laboratory of the Institute of Molecular Technology for Drug Discovery and Synthesis, State Key Laboratory of Chinese Medicine and Molecular Pharmacology, The Hong Kong Polytechnic University, Kowloon, Hong Kong, P.R. China.

Chinese practitioners have employed the use of traditional Chinese medicine as an anti-cancer agent since the ancient period. Different combinations have been formulated for various purposes. Some have been claimed for post-chemotherapy use but their direct actions on cancer cells may not be significantly reported. In the present study, we have tested the possible anti-leukemia potential of a combination regimen including crocodile egg extract, wild radix ginseng and natural Ganoderma lucidum (CGG extract) on acute myelogenous leukemia (AML) in vitro. A water soluble CGG extract was prepared and its antiproliferative activity was tested on the KG1a AML cell line and two freshly prepared bone marrow aspirate samples isolated from patients with de novo AML during presentation by a MTS/PMS assay. Furthermore, the possible activity of the CGG extract on the regeneration potential of KG1a cells was also investigated using a semi-solid methyl-cellulose colony formation assay. Lastly, the acute toxicity of CGG extract was further examined by a single high-dose oral feeding to rats. We found that the CGG extract could possess significant antiproliferative activity on AML cells. A strong colony formation inhibition was further demonstrated on KG1a cells. After feeding the rats with an excessive dose of CGG extract, we observed no development of acute toxicity. We concluded that the CGG extract has growth inhibitory potential on KG1a cells and AML bone marrow samples in vitro. An in vivo toxicity test revealed that no acute toxicity was observed after feeding the rats a high dosage of

the CGG extract. Further animal model tests are necessary to investigate the possible chronic toxicity of the CGG extract.

Inhibitory effect of a water-soluble extract from the culture medium of Ganoderma lucidum (Rei-shi) mycelia on the development of pulmonary adenocarcinoma induced by N-nitrosobis (2-hydroxypropyl) amine in Wistar rats.:Oncol Rep. 2006 Dec;16(6):1181-7.

A water-soluble extract from the culture medium of Ganoderma lucidum (Rei-shi) mycelia (MAK) has been shown to exert a potent chemopreventive effect. The present study was designed to investigate the effects of dietary MAK supplementation on the development of lung tumors initiated by N-nitrosobis (2-hydroxypropyl) amine (BHP) in male Slc:Wistar rats. A total of 77 animals, 6 weeks of age, were divided into 5 groups and given BHP (2,000 ppm) in their drinking water for 10 weeks. The normal controls were not supplied with BHP. After treatment with the carcinogen, the rats were fed a normal control MF solid diet, or the same diet containing MAK (1.25%, 2.5% or 5%) for 12 weeks. Macroscopically, all the doses of MAK reduced the number of nodules, and the effect of 5% MAK was found to be especially significant. Microscopically, an increase in the number of proliferating cell nuclear antigen (PCNA)-negative tumors and a decrease in the number of tumors strongly positive for PCNA were observed in the tissue sections from the rats that had received all the doses of MAK. The present results thus indicate that dietary supplementation with MAK inhibits the development of lung tumors, suggesting that MAK may be a potent chemopreventive agent against lung carcinogenesis.

Cloning and sequence analysis of a glyceraldehyde-3-phosphate dehydrogenase gene from Ganoderma lucidum.:J Microbiol. 2006 Oct;44(5):515-22.Fei X, Zhao MW, Li YX.College of Life Sciences, Nanjing Agricultural University, PR China.

A cDNA library of Ganoderma lucidum has been constructed using a Zap Express cloning vector. A glyceraldehyde-3-phosphate dehydrogenase gene (gpd) was isolated from this library by hybridization of the recombinant phage clones with a gpd-specific gene probe generated by PCR. By comparison of the cDNA and the genomic DNA sequences, it was found that the complete nucleotide sequence encodes a putative polypeptide chain of 338 amino acids interrupted by 6 introns. The predicted amino acid sequence of this gene shows a high degree of sequence similarity to the GPD proteins from yeast and filamentous fungi. The promoter region contains a CT-rich stretch, two CAAT boxes, and a consensus TATA box. The possibility of using the gpd promoter in the construction of new transformation vectors is discussed.

New ganoderic acids, bioactive triterpenoid metabolites from the mushroom Ganoderma lucidum.:Nat Prod Res. 2006 Sep;20(11):985-91.Li C, Li Y, Sun HH.Pharmanex Shanghai R&D, Building 11, Bi Po Rd, Shanghai 201203, China.

Two new lanostanoids, 7-oxo-ganoderic acid Z (1) and 15-hydroxy-ganoderic acid S (2), were isolated from a lipophilic extract of the fruiting body of Ganoderma lucidum. The structures of both compounds were established by interpretation of their spectroscopic data. Compounds 1 and 2 both exhibited inhibitory activities against the HMG-CoA reductase and acyl CoA acyltransferase.

Comparative studies of various ganoderma species and their different parts with regard to their antitumor and immunomodulating activities in vitro.:J Altern Complement Med. 2006 Oct;12(8):777-89.Yue GG, Fung KP, Tse GM, Leung PC, Lau CB.Institute of Chinese Medicine, The Chinese University of Hong Kong, Shatin, Hong Kong, China.

OBJECTIVES: Ganoderma lucidum (Lingzhi or Reishi) has been commonly suggested in East Asia as a potential candidate for prevention and treatment of different diseases, including cancer. Ganoderma extracts, in particular Ganoderma lucidum (extracts or isolated components), have previously been shown to possess antitumor activities. The present study aimed at comparing three different species of Ganoderma, wildly grown versus cultivated, as well as the different parts of the fruiting body (whole fruiting body, pileus, and stipe), with regard to their antitumor effects in human breast cancer cells and immunomodulatory activities in mouse splenic

lymphocytes in vitro. METHODS: The aqueous extracts (12.5-400 microg/mL) of G. lucidum, G. sinense, and G. tsugae were examined for their antiproliferative activities in human breast cancer cell lines, MCF-7 and MDA-MB-231, as well as in normal human mammary epithelial cells (primary culture). The immunomodulatory effects of the extracts were evaluated in mouse splenic lymphocytes. The proliferative responses of the mentioned cell types were determined by MTT [3-(4,5-dimethylthiazolyl)-2,5-diphenyl-tetrazolium bromide] assay. RESULTS: The present results demonstrated that the extracts of all tested Ganoderma samples could significantly inhibit cell proliferation in human breast cancer cell lines MCF-7 and MDA-MB-231, with G. tsugae being the most potent. The extracts, however, did not exert any significant cytotoxic effect on human normal mammary epithelial cells. Within the species G. sinense, the inhibitory effects of wildly grown samples were not significantly different from those of the cultivated samples, except at 400 microg/mL. Most of the tested extracts of Ganoderma stimulated mouse splenic lymphocytes proliferation. The extracts from the stipes of the G. tsugae and wildly grown G. sinense showed much stronger inhibitory effects than the other parts of the fruiting body in both cancer cell lines, whereas the extracts from the stipes of G. lucidum and wildly grown G. sinense showed stronger immunopotentiating activities in mouse splenic lymphocytes. CONCLUSIONS: These results indicate that the aqueous extracts of these commonly available Ganoderma fruiting bodies, G. lucidum, G. sinense, and G. tsugae have antitumor activities in human breast cancer cells and immunomodulatory activities in murine lymphocytes. In addition, the present findings also suggest that the stipes of fruiting bodies of Ganoderma species should be included in the preparation of extract of these fungi in order to obtain the most comprehensive active ingredients. To the best of the authors' knowledge, this is the first detailed comparison among the different parts of the fruiting bodies of Ganoderma.

Ganoderic acid T from Ganoderma lucidum mycelia induces mitochondria mediated apoptosis in lung cancer cells.:Life Sci. 2006 Dec 23;80(3):205-11. Epub 2006 Sep 6.Tang W, Liu JW, Zhao WM, Wei DZ, Zhong JJ.State Key Laboratory of Bioreactor Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China.

Ganoderma lucidum is a well-known traditional Chinese medicinal herb containing many bioactive compounds. Ganoderic acid T (GA-T), which is a lanostane triterpenoid purified from methanol extract of G. lucidum mycelia, was found to exert cytotoxicity on various human carcinoma cell lines in a dose-dependent manner, while it was less toxic to normal human cell lines. Animal experiments in vivo also showed that GA-T suppressed the growth of human solid tumor in athymic mice. It markedly inhibited the proliferation of a highly metastatic lung cancer cell line (95-D) by apoptosis induction and cell cycle arrest at G(1) phase. Moreover, reduction of mitochondria membrane potential (Delta psi(m)) and release of cytochrome c were observed during the induced apoptosis. Our data further indicate that the expression of proteins p53 and Bax in 95-D cells was increased in a time-dependent manner, whereas the expression of Bcl-2 was not significantly changed; thus the ratio of Bcl-2/Bax was decreased. The results show that the apoptosis induction of GA-T was mediated by mitochondrial dysfunctions. Furthermore, stimulation of the activity of caspase-3 but not caspase-8 was observed during apoptosis. The experiments using inhibitors of caspases (Z-VAD-FMK, Z-DEVD-FMK and Z-IETD-FMK) confirmed that caspase-3 was involved in the apoptosis. All our findings demonstrate that GA-T induced apoptosis of metastatic lung tumor cells through intrinsic pathway related to mitochondrial dysfunction and p53 expression, and it may be a potentially useful chemotherapeutic agent.

Inhibition of oxidative stress-induced invasiveness of cancer cells by Ganoderma lucidum is mediated through the suppression of interleukin-8 secretion.:Int J Mol Med. 2006 Oct;18(4):657-64.Thyagarajan A, Jiang J, Hopf A, Adamec J, Sliva D.Cancer Research Laboratory, Methodist Research Institute, Indianapolis, IN 46202, USA.

Epidemiological studies suggest that the intake of natural/nutrient products is inversely related to cancer risk. While oxidative stress, generating reactive oxygen species, has been linked to cancer initiation and progression, dietary antioxidants have reduced the risk of certain cancers. Experimental studies have demonstrated that antioxidants and phytochemicals could prevent cancer metastasis, and antioxidants were suggested as adjuvants in cancer therapy. Ganoderma lucidum is an Asian medicinal mushroom that has been used for the past two thousand years for the treatment of various diseases, including cancer. G. lucidum is currently popular as a dietary supplement in the form of tea, powder or extract. We have previously demonstrated that G. lucidum suppresses growth, angiogenesis and invasiveness of highly invasive and metastatic

breast cancer cells. The present study was undertaken to evaluate the effect of G. lucidum on oxidative stress-induced metastatic behavior of poorly-invasive MCF-7 breast cancer cells. We show that G. lucidum inhibits oxidative stress-induced migration of MCF-7 cells by the down-regulation of MAPK signaling. G. lucidum suppressed oxidative stress stimulated phosphorylation of extracellular signal-regulated protein kinases (Erk1/2), which resulted in the down-regulation of expression of c-fos, and in the inhibition of transcription factors AP-1 and NF-kappaB. The biological effect of G. lucidum on cell migration was mediated by the suppression of secretion of interleukin-8 from MCF-7 cells exposed to oxidative stress. In summary, our results suggest that G. lucidum inhibits the oxidative stress-induced invasive behavior of breast cancer cells by modulating Erk1/2 signaling and can be potentially considered as an antioxidant in adjuvant cancer therapy.

Ganoderma lucidum extract stimulates glucose uptake in L6 rat skeletal muscle cells.:Acta Biochim Pol. 2006;53(3):597-601. Epub 2006 Sep 10.Jung KH, Ha E, Kim MJ, Uhm YK, Kim HK, Hong SJ, Chung JH, Yim SV.Department of Pharmacology, College of Medicine, Kyung Hee University, Seoul, Republic of Korea.

The effect of Ganoderma lucidum extract on glucose uptake was studied in L6 rat skeletal muscle cells. G. lucidum extract increased glucose uptake about 2-fold compared to control. The extract stimulated the activity of phosphatidylinositol (PI) 3-kinase which is a major regulatory molecule in the glucose uptake pathway. About 7-fold increased activity of a PI 3-kinase was observed after treatment with G. lucidum extract, whereas PI 3-kinase inhibitor, LY294002, blocked the G. lucidum extract-stimulated PI 3-kinase activity in L6 skeletal muscle cells. Protein kinase B, a downstream mediator of PI 3-kinase, was also activated by G. lucidum extract. We then assessed the activity of AMP-activated protein kinase (AMPK), another regulatory molecule in the glucose uptake pathway. G. lucidum extract increased the phosphorylation level of both AMPK alpha1 and alpha2. Activity of p38 MAPK, a downstream mediator of AMPK, was also increased by G. lucidum extract. Taken together, these results suggest that G. lucidum extract may stimulate glucose uptake, through both PI 3-kinase and AMPK in L6 skeletal muscle cells thereby contributing to glucose homeostasis.

Structure-activity relationship for inhibition of 5alpha-reductase by triterpenoids isolated from Ganoderma lucidum.:Bioorg Med Chem. 2006 Dec 15;14(24):8654-60. Epub 2006 Sep 8.

In humans, 5alpha-reductase is involved in the development of benign prostatic hyperplasia. Triterpenoids isolated from ethanol extracts of Ganoderma lucidum (Fr.) Krast (Ganodermataceae) inhibited 5alpha-reductase activity. The presence of the C-3 carbonyl group and of the C-26-alpha,beta-unsaturated carbonyl group was characteristic of almost all inhibitors isolated from G. lucidum.

Anti-tumor activities of the antlered form of Ganoderma lucidum in allogeneic and syngeneic tumor-bearing mice.:Biosci Biotechnol Biochem. 2006 Sep;70(9):2028-34. Epub 2006 Sep 7.

We investigated the anti-tumor effects of a dry powder preparation of the antlered form of Ganoderma lucidum (G. lucidum AF, rokkaku-reishi in Japanese), a variant type of G. lucidum, not only in allogeneic Sarcoma 180-bearing ddY mice, but also in syngeneic MM 46-bearing C3H/He mice. G. lucidum AF inhibited tumor growth and elongated the life span when orally administered to mice by free-feeding of a 2.5% G. lucidum AF-containing diet. It also showed anti-tumor activity in spite of post-feeding after tumor inoculation. G. lucidum AF significantly countered the depression of splenic CD8+ cells and protected the decrease in interferon-gamma (IFN-gamma) production in regional lymph nodes of MM 46-bearing mice, indicating that the anti-tumor activity of G. lucidum AF might be caused by its immunostimulating action. These results suggest that the ingestion of G. lucidum AF can be useful for the prevention and curing of cancer.

Culture pH affects exopolysaccharide production in submerged mycelial culture of Ganoderma lucidum.:Appl Biochem Biotechnol. 2006 Sep;134(3):249-62.Kim HM, Park MK, Yun JW.Department of Biotechnology, Daegu University, Kyungsan, Kyungbuk 712-714, Korea.

In submerged culture of Ganoderma lucidum, the pH optimum for cell growth has been shown to be lower than that for exopolysaccharides (EPS) formation. Therefore, in the present study, a two-stage pH-control strategy was employed to maximize the productions of mycelial biomass and EPS. When compared, a batch culture without pH control had a maximum concentration of EPS and endopolysaccharides, which was much lower than those with pH control. Maximum mycelial growth (12.5 g/L) and EPS production (4.7 g/L) were achieved by shifting the controlled pH from 3.0 to 6.0 after day 4. The contrast between the controlled-pH process and uncontrolled pH was marked. By using various two-stage culture processes, it was also observed that culture pH has a significant affect on the yield of product, mycelial morphology, chemical composition, and molecular weight of EPS. A detailed observation of mycelial morphology revealed that the productive morphological form for EPS production was a dispersed pellet (controlled pH shifting from 3.0 to 6.0) rather than a compact pellet with a dense core area (controlled pH 4.5) or a feather-like pellet (controlled pH shifting from 6.0 to 3.0). Three different polysaccharides were obtained from each pH conditions, and their molecular weights and chemical compositions were significantly different.

Determination of ergosterol in ganoderma spore lipid from the germinating spores of Ganoderma lucidum by high-performance liquid chromatography.:J Agric Food Chem. 2006 Aug 23;54(17):6172-6.Yuan JP, Wang JH, Liu X, Kuang HC, Huang XN.Food Engineering Research Center of State Education Ministry, College of Life Sciences, Sun Yat-Sen University, Guangzhou 510275, People's Republic of China. yuanjp@mail.sysu.edu.cn

A gradient reversed-phase high-performance liquid chromatography (HPLC) method was developed for the separation and determination of free ergosterol in ganoderma spore lipid (GSL) extracted from the sporoderm-broken germinating spores of Ganoderma lucidum. Sodium hydroxide in methanol was added for the hydrolysis of ergosteryl esters to determine the total content of ergosterol in GSL by HPLC. A 0.04 M concentration of sodium hydroxide in reaction mixtures was appropriate for the complete hydrolysis of ergosteryl esters without a significant loss of ergosterol during saponification. In addition, the ergosterol content in four commercial GSL softgel supplements from four different firms was determined. The results showed that the ergosterol content in these samples had significant differences. Ergosterol content may be a suitable marker for evaluating the quality of GSL products.

Ganoderma - a therapeutic fungal biofactory.:Phytochemistry. 2006 Sep;67(18):1985-2001. Epub 2006 Aug 14.Paterson RR.Micoteca da Universidade do Minho, Centro de Engenharia Biol¨®gica, Campus de Gualtar, 4710-057 Braga, Portugal. russell.paterson@deb.uminho.pt

Ganoderma is a basidiomycete white rot fungus which has been used for medicinal purposes for centuries particularly in China, Japan and Korea. A great deal of work has been carried out on Ganoderma lucidum. The common names for preparations include Lingzhi, Munnertake, Sachitake, Reishi and Youngzhi. This review collates the publications detailing activities and compounds by representative species whilst considering the most valid claims of effectiveness. The biological activities reported of preparations from Ganoderma are remarkable and given most emphasis herein as distinct from structure/activity information. The metabolites consist of mainly polysaccharides and terpenoids. Many are activities against the major diseases of our time and so the present review is of great importance. The list of effects is huge ranging from anti-cancer to relieving blockages of the bladder. However, the reports have not all been tested scientifically with the convincing evidence is reserved for assays of pure compounds. It is a prime example of an ancient remedy being of great relevance to the modern era. There does appear to be an assumption that the therapeutic effects attributed to the fungus have been proven. The next step is to produce some effective medicines which may be hampered by problems of mass production.

Immunomodulatory effects of lingzhi and san-miao-san supplementation on patients with rheumatoid arthritis.:Immunopharmacol Immunotoxicol. 2006;28(2):197-200.Xi Bao Y, Kwok Wong C, Kwok Ming Li E, Shan Tam L, Chung Leung P, Bing Yin Y, Wai Kei Lam C.Chinese University of Hong Kong, Prince of Wales Hospital, Shatin, NT, Hong Kong.

Rheumatoid arthritis (RA) is an autoimmune joint disease. We evaluated a standard preparation

of Lingzhi (Ganoderma lucidum) and San-Miao-San (Rhizoma atractylodis, Cortex phellodendri, Radix achyranthes bidentatae) capsules (TCM group) for its supplementary treatment efficacy for RA. There was no significant difference in the absolute count, percentage, and ratios of CD4(+)/CD8(+)/natural killer/B lymphocytes between the TCM and placebo groups after taking the capsules (all $p > 0.05$). There was no significant change in concentrations of plasma cytokines of interferon-gamma-induced protein-10 (IP-10), monocyte chemoattractant protein-1, monokine induced by IFN-gamma, regulated upon activation normal T-cell expressed and secreted, interleukin (IL)-8, and IL-18 after taking the capsules for 8 and 24 weeks (all $p > 0.05$). The percentage change in ex vivo-induced level of inflammatory cytokine IL-18 was significantly lower in the TCM group than in the placebo group after taking the capsules for 24 weeks ($p < 0.05$). Therefore, Lingzhi and San-Miao-San capsules might exert a beneficial immunomodulatory effect in patients with rheumatoid arthritis.

Ganoderma lucidum inhibits proliferation of human breast cancer cells by down-regulation of estrogen receptor and NF-kappaB signaling.:Int J Oncol. 2006 Sep;29(3):695-703.Jiang J, Slivova V, Sliva D.Cancer Research Laboratory, Methodist Research Institute, Indianapolis, IN 46202, USA.

Ganoderma lucidum, an oriental medical mushroom, has been used in Asia for the prevention and treatment of a variety of diseases, including cancer. We have previously demonstrated that G. lucidum inhibits growth and induces cell cycle arrest at G0/G1 phase through the inhibition of Akt/NF-kappaB signaling in estrogen-independent human breast cancer cells. However, the molecular mechanism(s) responsible for the inhibitory effects of G. lucidum on the proliferation of estrogen-dependent (MCF-7) and estrogen-independent (MDA-MB-231) breast cancer cells remain to be elucidated. Here, we show that G. lucidum inhibited the proliferation of breast cancer MCF-7 and MDA-MB-231 cells by the modulation of the estrogen receptor (ER) and NF-kappaB signaling. Thus, G. lucidum down-regulated the expression of ERalpha in MCF-7 cells but did not effect the expression of ERbeta in MCF-7 and MDA-MB-231 cells. In addition, G. lucidum inhibited estrogen-dependent as well as constitutive transactivation activity of ER through estrogen response element (ERE) in a reporter gene assay. G. lucidum decreased TNF-alpha-induced (MCF-7) as well as constitutive (MDA-MB-231) activity of NF-kappaB. The inhibition of ER and NF-kappaB pathways resulted in the down-regulation of expression of c-myc, finally suppressing proliferation of estrogen-dependent as well as estrogen-independent cancer cells. Collectively, these results suggest that G. lucidum inhibits proliferation of human breast cancer cells and contain biologically active compounds with specificity against estrogen receptor and NF-kappaB signaling, and implicate G. lucidum as a suitable herb for chemoprevention and chemotherapy of breast cancer.

Pre-administration of Ganoderma lucidum spore reduces incidence of neural tube defects induced by retinoic acid in pregnant mice.:Zhong Xi Yi Jie He Xue Bao. 2006 Jul;4(4):368-73.Zhang W, Zeng YS, Xiong Y, Chen SJ, Zhong ZQ.Division of Neurosciences, Department of Histology and Embryology, Zhongshan Medical College, Sun Yat-sen University, Guangzhou, Guangdong Province 510080, China.

OBJECTIVE: To explore whether pre-administration of Ganoderma lucidum spore (GASP) can reduce incidence of neural tube defects (NTDs) induced by all-trans retinoic acid (ATRA) in pregnant mice. METHODS: Twenty pregnant mice were randomly divided into four groups: normal control group, solvent-treated group, ATRA-induced group, and GASP-treated plus ATRA-induced group. GASP solution, which was prepared with solvent (sodium carboxymethyl cellulose), was fed to the pregnant mice in the GASP-treated plus ATRA-induced group twice a day from embryo (E) 0 d to E10.5 d. The same dose of solvent was given to the pregnant mice in the solvent-treated group. At E7.75 d, ATRA (50 mg/kg) was given to the pregnant mice in both ATRA-induced group and GASP-treated plus ATRA-induced group for single time. Embryos were sampled from pregnant mice at E10.5 d. Then the incidence rate of NTDs in mouse embryo was calculated and the crown-rump length of mouse embryo was measured. The positive rate of nestin expression and the distribution of cell cycle of embryonic neural tube neuroepithelial cells were detected by histochemical staining technique and flow cytometry respectively. Reverse transcription-polymerase chain reaction method was used to detect the gene expressions of cyclin-dependent protein kinase 2 (Cdk2) and Cdk4 mRNAs. RESULTS: The incidence rates of NTDs in mouse embryos in the ATRA-induced group and the GASP-treated plus ATRA-induced group were 79.41% and 21.67% respectively, while the crown-rump length of mouse embryos in

these two groups were (3.62+/-1.27) mm and (5.84+/-0.92) mm respectively. The positive rate of nestin expression in embryonic neural tube neuroepithelial cells of mouse embryo at E10.5 d in the ATRA-induced group was 32.44%, while that in the GASP-treated plus ATRA-induced group was 77.65%. The cell cycle of embryonic neural tube neuroepithelial cells was obviously arrested at G(0)/G(1) phase in the ATRA-induced group as compared with that in the GASP-treated plus ATRA-induced group. The Cdk4 mRNA was transcripted at a high level in embryonic neural tube in the GASP-treated plus ATRA-induced group, but the Cdk2 mRNA was not detected in this group. CONCLUSION: Pre-administration of GASP can reduce the incidence of NTDs induced by ATRA in pregnant mice.

Reishi polysaccharides induce immunoglobulin production through the TLR4/TLR2-mediated induction of transcription factor Blimp-1.:J Biol Chem. 2006 Aug 25;281(34):24111-23. Epub 2006 Jun 23.Lin KI, Kao YY, Kuo HK, Yang WB, Chou A, Lin HH, Yu AL, Wong CH.Genomics Research Center, Academia Sinica, Taipei 115, Taiwan. kuoilin@gate.sinca.edu.tw

The polysaccharides of Ganoderma lucidum (Reishi) possess immunomodulation activities; however, their mode of molecular action in regulating each cellular subset in the immune system is still not clear. Here, we investigate the function of the main polysaccharide fraction of Reishi (Reishi-F3) in B lymphocyte activation/differentiation. We find that Reishi-F3 causes mouse splenic B cell activation and differentiation to IgM-secreting plasma cells, and the process depends on Reishi-F3-mediated induction of Blimp-1, a master regulator capable of triggering the changes of a cascade of gene expression during plasmacytic differentiation. In human peripheral B lymphocytes, although Reishi-F3 fails to induce their activation, it is able to enhance antibody secretion, which is associated with Blimp-1 mRNA induction. The function of Reishi-F3 depends on the Toll-like receptors TLR4/TLR2 as neutralizing antibodies against TLR4/TLR2 block Reishi-F3-mediated induction of Blimp-1 mRNA and Ig secretion. We have shown that interaction of Reishi-F3 with TLR4/TLR2 followed by signaling through p38 MAPK is involved in the induction of Blimp-1 mRNA, whereas signaling through ERK, p38 MAPK, JNK, and IKK complex is involved in Reishi-F3-mediated Ig secretion. Furthermore, the differential mechanism of Reishi-F3 in mouse and human B cell activation is probably due to the presence of Blimp-1 regulatory site in human CD86 promoter. These results establish the signaling and molecular mechanisms of Reishi-F3 on promoting antibody secretion.

Anti-hepatitis B activities of ganoderic acid from Ganoderma lucidum.:Biotechnol Lett. 2006 Jun;28(11):837-41. Epub 2006 May 31.Li YQ, Wang SF.College of Life Science, South China Normal University, Guangzhou 510631, PR China. liyq9168@hotmail.com

Ganoderic acid, from Ganoderma lucidum, at 8 microg/ml inhibited replication of hepatitis B virus (HBV) in HepG2215 cells over 8 days. Production of HBV surface antigen and HBV e antigen were 20 and 44% of controls without ganoderic acid. Male KM mice were significantly protected from liver injury, induced with carbon tetrachloride, by treatment with ganoderic acid at 10 mg and 30 mg/kg x d (by intravenous injection) 7 days. Ganoderic acid at the same dosage also significantly protected the mice from liver injury induced by M. bovis BCG plus lipopolysaccharide (from Escherichia coli 0127:B8).

Optimization of nutrient medium for submerged cultivation of Ganoderma lucidum (Curt.: Fr.) P. Karst:Mikrobiologiia. 2006 Mar-Apr;75(2):186-92.Avtonomova AV, Krasnopol'skaia LM, Maksimov VN.

The dependence of the amount of the grown vegetative mycelium of Ganoderma lucidum on the composition of the nutrient medium has been studied under conditions of submerged cultivation. The medium was optimized using full factorial and steepest ascent experimental designs. The addition of two carbon sources to the medium considerably improved the submerged growth of the fungus. An optimized medium provided for a high yield (20-20.95 g/l) of the morphologically homogeneous mycelium and shortened the cultivation period to 3-4 days.

Antimutagenic activity of methanolic extract of Ganoderma lucidum and its effect on

hepatic damage caused by benzo[a]pyrene.:J Ethnopharmacol. 2006 Sep 19;107(2):297-303. Epub 2006 Apr 6.Lakshmi B, Ajith TA, Jose N, Janardhanan KK.Department of Microbiology, Amala Cancer Research Centre, Amala Nagar, Thrissur 680555, Kerala, India.

The antimutagenic activity of the methanolic extract of the fruiting bodies of Ganoderma lucidum (Fr.) P. Krast. occurring in South India was investigated. The activity was assayed by Ames Salmonella mutagenicity test using histidine mutants of Salmonella typhimurium tester strains, TA98, TA100 and TA102. The methanolic extract of the mushroom significantly inhibited (P<0.001) the in vitro sodium azide (NaN(3)), N-methyl-N'-nitro-N-nitrosoguanidine (MNNG) and 4-nitro-o-phenylenediamine (NPD), and benzo[a]pyrene (B[a]P) induced his(+) revertants in a dose dependent manner. In vivo antimutagenic activity of extract was also assayed by determining the mutagenicity of the urine of rats administrated with B[a]P as a mutagen. The prior administration of extract markedly inhibited mutagenicity induced by B[a]P. The results indicated that the methanolic extract of Ganoderma lucidum occurring in South India possessed significant antimutagenic activity. The effect of B[a]P on hepatic enzymes, such as serum glutamate oxaloacetate transaminase (GOT), glutamate pyruvate transaminase (GPT) and alkaline phosphtase (ALP), were also evaluated. The extract prevented the increase of SGOT, SGPT, and ALP activities consequent to B[a]P challenge, and enhanced the levels of reduced glutathione (GSH) and activities of glutathione peroxidase (GPx), glutathione-S-transferase (GST), superoxide dismutase (SOD), and catalase (CAT). The extract also profoundly inhibited lipid peroxidation induced by B[a]P. The results revealed that Ganoderma lucidum extract restored antioxidant defense and prevented hepatic damage consequent to the challenge by B[a]P.

Primary study on proteomics about Ganoderma lucidium spores promoting survival and axon regeneration of injured spinal motor neurons in rats:Zhong Xi Yi Jie He Xue Bao. 2006 May;4(3):298-302.Zhang W, Zeng YS, Wang Y, Liu W, Cheng JJ, Chen SJ.Division of Neuroscience, Department of Histology and Embryology, Zhongshan Medical College, Sun Yat-sen University, Guangzhou, Guangdong Province 510080, China.

OBJECTIVE: To detect some proteins associated with the effect of ganoderma lucidium spores (GASP) on promoting the survival and axon regeneration of injured spinal motor neurons in rats. METHODS: The rats were divided into normal control group, untreated group and GASP-treated group, and the rats in the last two groups received ventral root avulsion. GASP preparation was fed to the rats in the GASP-treated group for 14 days. The gray matter tissues of the lumbar spinal were sampled from rats in each group after 14 days following ventral root avulsion, and the extracted proteins from these tissues were detected by using 2-dimensional electrophoresis. Matrix assisted laser desorption/ionization time-of-flight mass spectroscopy (MALDI-TOF MS) was utilized to identify the differentially expressed proteins among these three groups. RESULTS: There were six kinds of proteins differentially expressed among the three groups, which were collapsin response mediator protein 2 (CRMP-2), F-actin capping protein beta subunit (FCP-beta), isocitrate dehydrogenase [NAD] subunit beta (IDH-beta), ATPase, glutamate oxaloacetate transaminase-1 (GOT1) and M2 pyruvate kinase (M2-PK). The expression levels of CRMP-2, IDH-beta, ATPase and GOT1 were higher in the GASP-treated group than those in the untreated group, while the expression levels of FCP-beta and M2-PK were lower than those in the untreated group. CONCLUSION: GASP maybe promotes the survival and axon regeneration of injured spinal motor neurons in rats by virtue of up- or down-regulating the expression levels of the proteins mentioned above.

Polysaccharide purified from Ganoderma lucidum induces gene expression changes in human dendritic cells and promotes T helper 1 immune response in BALB/c mice.:Mol Pharmacol. 2006 Aug;70(2):637-44. Epub 2006 May 2.Lin YL, Lee SS, Hou SM, Chiang BL.Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan, Republic of China.

Ganoderma lucidum is a medicinal mushroom in China and other Asian countries. The polysaccharide from G. lucidum (PS-G) is a branched (1-->6)-beta-d-glucan moiety. In this study, we examined the effects of PS-G on human monocyte-derived dendritic cells (DCs) with microarray analysis by Human Genome U133 Plus 2.0 GeneChip. In comparing mean signal values between PS-G-treated DCs with untreated DCs, 3477 (17%) probe sets were up-regulated, and 4418 (19%) probe sets were down-regulated after PS-G treatment. These results demonstrate that genes associated with phagocytosis (CD36, CD206, and CD209) are

decreased and genes associated with proinflammatory chemokines (CCL20, CCL5, and CCL19), cytokines [interleukin (IL)-27, IL-23A, IL-12A, and IL-12B], and costimulatory molecules (CD40, CD54, CD80, and CD86) are increased. To confirm the microarray data, we further investigated the effect of PS-G on antigen-specific antibody and cytokine production in BALB/c mice. Immunization with ovalbumin (OVA)/PS-G showed that the anti-OVA IgG2a levels were significantly increased compared with OVA alone in BALB/c mice. Together, our data demonstrate that PS-G could effectively promote the activation and maturation of immature DCs, preferring a T helper 1 response. Furthermore, the results also demonstrate that the data from microarray analysis could be correlated with the in vivo effect of the immune-enhancing compound.

A laccase from the medicinal mushroom Ganoderma lucidum.:Appl Microbiol Biotechnol. 2006 Sep;72(3):508-13. Epub 2006 Apr 25.Wang HX, Ng TB.State Key Laboratory for Agrobiotechnology and Department of Microbiology, China Agricultural University, Beijing 100094, China.

A protein demonstrating laccase activity and potent inhibitory activity towards human immunodeficiency virus (HIV)-1 reverse transcriptase (IC50 1.2 microM) was isolated from fresh fruiting bodies of the medicinal mushroom Ganoderma lucidum. The laccase had a novel N-terminal sequence and a molecular mass of 75 kDa, which is higher than the range (55-56 kDa) reported for most other mushroom laccases. It was isolated by sequential chromatography on DEAE-cellulose and Affi-gel blue gel and adsorption on Con A-Sepharose. Unlike some of the previously isolated laccases, it was adsorbed only on Con A-Sepharose. The enzyme required a pH of 3-5 and a temperature of 70 degrees C to exhibit maximal activity. Minimal activity was detected at pH 6 and 7. Activity was undetectable at pH 8 and 9 and after exposure to 100 degrees C for 10 min.

Ganoderma lucidum extract inhibits proliferation of SW 480 human colorectal cancer cells.:Exp Oncol. 2006 Mar;28(1):25-9.Xie JT, Wang CZ, Wicks S, Yin JJ, Kong J, Li J, Li YC, Yuan CS.Tang Center for Herbal Medicine Research, the Pritzker School of Medicine, University of Chicago, USA.

AIM: Ganoderma lucidum is a commonly used Chinese herb and an important ingredient in traditional Chinese medicine herbal formulations for immune dysfunction related illnesses. The effects of this medicinal mushroom on human colorectal cancer cells have not yet been evaluated. In this study, we investigated the effects of Ganoderma lucidum extract using SW 480 human colorectal cancer cell line. MATERIALS AND METHODS: Two different fractions of Ganoderma lucidum extract, i.e., a fraction containing mainly polysaccharides (GLE-1), and a triterpenoid fraction without polysaccharides (GLE-2) were analyzed. Their antiproliferative activity was evaluated by cell proliferation assay and 3H-thymidine incorporation assay. Scavenging effects of DPPH radical were assessed using ESR-spectroscopy. RESULTS: Our data showed that both GLE-1 and GLE-2 significantly inhibited the proliferation of SW 480 cells. The inhibitory effect of GLE-2 was much stronger than that of GLE-1. GLE-1 inhibited DNA synthesis in the cells and reduced the formation of DPPH radicals. CONCLUSION: Ganoderma lucidum extract inhibits proliferation of human colorectal cancer cells and possesses antioxidant properties.

Enhanced induction of mitochondrial damage and apoptosis in human leukemia HL-60 cells by the Ganoderma lucidum and Duchesnea chrysantha extracts.:Cancer Lett. 2007 Feb 8;246(1-2):210-7. Epub 2006 Mar 29.Kim KC, Kim JS, Son JK, Kim IG.Environmental Radiation Research Division, Department of Radiation Biology, Korea Atomic Energy Research Institute, Yusong, Daejeon, South Korea.

Combined treatment with the medicinal mushroom Ganoderma lucidum and the herb Duchesnea chrysantha extracts (GDE) causes a synergistic induction of mitochondrial damage and apoptosis in HL-60 cells. GDE treatment is selectively toxic to HL-60 leukemia cells whereas no cytotoxic effect is observed in normal peripheral blood mononuclear cells. GDE-induced apoptosis is associated with Bcl-2 down-regulation, Bax translocation, mitochondrial cytochrome c release and caspase-3 activation, suggesting that apoptosis by this combination occurs through the mitochondria-dependent pathway. The present findings suggest that this combination merits

further investigation as a potential therapeutic agent for the treatment of cancer.

Identification of medicinal mushroom species based on nuclear large subunit rDNA sequences.:J Microbiol. 2006 Feb;44(1):29-34.Lee JS, Lim MO, Cho KY, Cho JH, Chang SY, Nam DH.Institute of Biotechnology, College of Pharmacy, Yeungnam University, Gyongsan 712-749, Republic of Korea.

The purpose of this study was to develop molecular identification method for medical mushrooms and their preparations based on the nucleotide sequences of nuclear large subunit (LSU) rDNA. Four specimens were collected of each of the three representative medicinal mushrooms used in Korea: Ganoderma lucidum, Coriolus versicolor, and Fomes fomentarius. Fungal material used in these experiments included two different mycelial cultures and two different fruiting bodies from wild or cultivated mushrooms. The genomic DNA of mushrooms were extracted and 3 nuclear LSU rDNA fragments were amplified: set 1 for the 1.1-kb DNA fragment in the upstream region, set 2 for the 1.2-kb fragment in the middle, and set 3 for the 1.3-kb fragment downstream. The amplified gene products of nuclear large subunit rDNA from 3 different mushrooms were cloned into E. coli vector and subjected to nucleotide sequence determination. The sequence thus determined revealed that the gene sequences of the same medicinal mushroom species were more than 99.48% homologous, and the consensus sequences of 3 different medicinal mushrooms were more than 97.80% homologous. Restriction analysis revealed no useful restriction sites for 6-bp recognition enzymes for distinguishing the 3 sequences from one another, but some distinctive restriction patterns were recognized by the 4-bp recognition enzymes AccII and HhaI. This analysis was also confirmed by PCR-RFLP experiments on medicinal mushrooms.

Anti-hepatitis activities in the broth of Ganoderma lucidum supplemented with a Chinese herbal medicine.:Am J Chin Med. 2006;34(2):341-9.Li Y, Yang Y, Fang L, Zhang Z, Jin J, Zhang K.College of Life Science, South China Normal University, Guangzhou 510631, China. liyq9168@hotmail.com

The anti-hepatitis B virus activity and hepatoprotective activity of a liquid fermentation broth of Ganoderma lucidum were investigated. The cultured broth was supplemented with aqueous extract of Radix Sophorae flavescentis, a kind of Chinese herbal medicine. Our results indicated that the cultured broth had effects of anti-hepatitis B virus activity in vitro and protected mice from liver damage in vivo. Our results also indicated that the co-fermentation broth of Ganoderma lucidum in the presence of aqueous extract of Radix Sophorae flavescentis has better medicinal effects than simply mixing these two ingredients together, suggesting a potential novel way to prepare Chinese herbal mixtures.

In vitro and in vivo protective effects of proteoglycan isolated from mycelia of Ganoderma lucidum on carbon tetrachloride-induced liver injury.:World J Gastroenterol. 2006 Mar 7;12(9):1379-85.Yang XJ, Liu J, Ye LB, Yang F, Ye L, Gao JR, Wu ZH.College of Life Sciences, Wuhan University, Wuhan 430072, Hubei Province, China.

AIM: To investigate the possible mechanism of the protective effects of a bioactive fraction,Ganoderma lucidum proteoglycan (GLPG) isolated from Ganoderma lucidum mycelia, against carbon tetrachloride-induced liver injury. METHODS: A liver injury model was induced by carbon tetrachloride. Cytotoxicity was measured by MTT assay.The activities of alanine aminotransferase (ALT) and aspartate aminotransferase (AST) were determined with an automatic multifunction-biochemical analyzer and the levels of superoxide dismutase (SOD)and TNF-alpha were determined following the instructions of SOD kit and TNF radioimmunoassay kit. Liver sections were stained with hematoxylin and eosin (H and E) for histological evaluation and examined under light microscope. RESULTS: We found that GLPG can alleviate the L-02 liver cells injury induced by carbon tetrachloride (CCl_4) through the measurements of ALT and AST activities and the administration of GLPG to L-02 cells did not display any toxicity. Furthermore, histological analysis of mice liver injury induced by CCl_4 with or without GLPG pretreatment indicated that GLPG can significantly suppress the toxicity induced by CCl_4 in mice liver. We also found that GLPG reduced TNF-alpha level induced by CCl_4 in the plasma of mice, whereas increased SOD activity in the rat serum. CONCLUSION: GLPG has hepatic protective activity against CCl_4-induced injury both in vitro and in vivo. The possible anti-hepatotoxic mechanisms may be related to the suppression of TNF-alpha level and the free radical scavenging activity.

Quantitative determination of six major triterpenoids in Ganoderma lucidum and related species by high performance liquid chromatography.:J Pharm Biomed Anal. 2006 Jun 7;41(3):838-44. Epub 2006 Mar 10.Wang XM, Yang M, Guan SH, Liu RX, Xia JM, Bi KS, Guo DA.Shanghai Research Center for Modernization of Traditional Chinese Medicine, Shanghai Institute of Materia Medica, Shanghai Institute of Biological Sciences, Guo Shoujing Road 199, Zhangjiang, Shanghai 201203, PR China.

A reversed-phase liquid chromatographic method was developed for the quantitative determination of six triterpenoids, namely ganoderic acids C2, B, AM1, K, H and D in Ganoderma lucidum and its related species. Samples were extracted with chloroform in ultrasonic bath. The optimal conditions of separation and detection were achieved on an Agilent Zorbax SB-C18 column (250 mmx4.6 mm, 5 microm), with a linear gradient of acetonitrile and 0.03% aqueous phosphoric acid (v/v), at a flow rate of 1.0 ml/min, detected at 252 nm. All calibration curves showed good linearity (r2>0.999) within test ranges. The relative deviation of this method was less than 2% for intra- and inter-day assays, and the percentage recovery of the method was 93-103%, with relative standard deviation (R.S.D.) less than 5%. The current assay method was applied to quantitative determination of constituents of triterpenoids in 36 different samples of G. lucidum and its related species. The results indicated that the developed method could be readily utilized as a quality control method for G. lucidum and related species.

Ameliorative effect of Ganoderma lucidum on carbon tetrachloride-induced liver fibrosis in rats.:World J Gastroenterol. 2006 Jan 14;12(2):265-70.Lin WC, Lin WL.Department of Pharmacology, China Medical University, 91 Hsueh Shih Road, Taichung 404, Taiwan, China. wclin@mail.cmu.edu.tw

AIM: To investigate the effects of Reishi mushroom, Ganoderma lucidum extract (GLE), on liver fibrosis induced by carbon tetrachloride (CCl4) in rats. METHODS: Rat hepatic fibrosis was induced by CCl4. Forty Wistar rats were divided randomly into 4 groups: control, CCl4, and two GLE groups. Except for rats in control group, all rats were administered orally with CCl4 (20%, 0.2 mL/100 g body weight) twice a week for 8 weeks. Rats in GLE groups were treated daily with GLE (1,600 or 600 mg/kg) via gastrogavage throughout the whole experimental period. Liver function parameters, such as ALT, AST, albumin, and albumin/globulin (A/G) ratio, spleen weight and hepatic amounts of protein, malondiladehyde (MDA) and hydroxyproline (HP) were determined. Histochemical staining of Sirius red was performed. Expression of transforming growth factor beta1 (TGF-beta1), methionine adenosyltransferase (MAT1) 1A and MAT2A mRNA were detected by using RT-PCR. RESULTS: CCl4 caused liver fibrosis, featuring increase in plasma transaminases, hepatic MDA and HP contents, and spleen weight; and decrease in plasma albumin, A/G ratio and hepatic protein level. Compared with CCl4 group, GLE (600, 1,600 mg/kg) treatment significantly increased plasma albumin level and A/G ratio ($P < 0.05$) and reduced the hepatic HP content ($P < 0.01$). GLE (1,600 mg/kg) treatment markedly decreased the activities of transaminases ($P < 0.05$), spleen weight ($P < 0.05$) and hepatic MDA content ($P < 0.05$); but increased hepatic protein level ($P < 0.05$). Liver histology in the GLE (1,600 mg/kg)-treated rats was also improved ($P < 0.01$). RT-PCR analysis showed that GLE treatment decreased the expression of TGF-beta1 ($P < 0.05$-0.001) and changed the expression of MAT1A ($P < 0.05$-0.01) and MAT2A ($P < 0.05$-0.001). CONCLUSION: Oral administration of GLE significantly reduces CCl4-induced hepatic fibrosis in rats, probably by exerting a protective effect against hepatocellular necrosis by its free-radical scavenging ability.

5alpha-reductase inhibitory effect of triterpenoids isolated from Ganoderma lucidum.:Biol Pharm Bull. 2006 Feb;29(2):392-5.

5alpha-Reductase inhibitory activity-guided fractionation of the EtOH extract of the fruiting body of Ganoderma lucidum (LEYSS.:FR.) KARST. (Ganodermataceae), which is called Reishi, or Mannentake in Japan and Lingzhi in China, led to the isolation of two active compounds which were ganoderic acid DM and 5alpha-lanosta-7,9(11),24-triene-15alpha,26-dihydroxy-3-one with an IC(50) of 10.6 microM and 41.9 microM respectively. A carboxyl group of side chain of ganoderic acid DM is essential to elicit the inhibitory activity because of much less activity of its methyl ester.

Ganoderma extract prevents albumin-induced oxidative damage and chemokines synthesis in cultured human proximal tubular epithelial cells.:Nephrol Dial Transplant. 2006 May;21(5):1188-97. Epub 2006 Jan 24.Lai KN, Chan LY, Tang SC, Leung JC.Department of Medicine, University of Hong Kong, Queen Mary Hospital, 102 Pokfulam Road, Hong Kong. knlai@hkucc.hku.hk

BACKGROUND: Ganoderma lucidum (Ganoderma or lingzhi) is widely used as an alternative medicine remedy to promote health and longevity. Recent studies have indicated that components extracted from Ganoderma have a wide range of pharmacological actions including suppressing inflammation and scavenging free radicals. We recently reported that tubular secretion of interleukin-8 (IL-8) induced by albumin is important in the pathogenesis of tubulointerstitial injury in the proteinuric state. In this study, we explored the protective effect of Ganoderma extract (LZ) on albumin-induced kidney epithelial injury. METHODS: Growth arrested human proximal tubular epithelial cells (PTECs) were incubated with 0.625 to 10 mg/ml human serum albumin (HSA) for up to 72 h. HSA induced DNA damage and apoptosis in PTEC in a dose- and time-dependent manner. Co-incubation of PTEC with 4-64 microg/ml LZ significantly reduced the oxidative damage and cytotoxic effect of HSA in a dose-dependent manner ($P<0.001$). Increased release of IL-8 and soluble intercellular adhesion molecules-1 (sICAM-1) in PTEC induced by HSA was ameliorated by co-incubation with Ganoderma (16 microg/ml). To explore the components of LZ that exhibited most protective effect in HSA-induced PTEC damages, LZ was further separated into two sub-fractions, LZF1 (MW <30 kDa) and LZF2 (MW <3 kDa), by molecular sieving using millipore membrane. PTEC were incubated with 5 mg/ml HSA in the presence of different doses of LZF1, LZF2 or unfractionated LZ. RESULTS: There was no difference in the degree of protection from HSA-induced cytotoxicity or oxidative DNA damage between different fractions of LZ. However, low molecular weight LZ (<3 kDa) was most effective in reducing sICAM-1 released from HSA-activated PTEC whereas the high molecular weight LZ (unfractionated LZ) was more effective in diminishing IL-8 production. CONCLUSIONS: Our results suggest that Ganoderma significantly reduces oxidative damages and apoptosis in PTEC induced by HSA. The differential reduction of IL-8 or sICAM-1 released from HSA-activated PTEC by different components of the LZ implicates that components of Ganoderma with different molecular weights could play different roles and operate different mechanisms in preventing HSA-induced PTEC damage.

Ganoderma lucidum causes apoptosis in leukemia, lymphoma and multiple myeloma cells.:Leuk Res. 2006 Jul;30(7):841-8. Epub 2006 Jan 19.M¨¹ller CI, Kumagai T, O'Kelly J, Seeram NP, Heber D, Koeffler HP.Cedars-Sinai Medical Center, David Geffen School of Medicine at UCLA, Los Angeles, CA, United States. MullerCI@cshs.org

Over many centuries, herbal remedies have treated a variety of ailments. This empiric observational approach has produced a number of leads for formulated medicines. Ganoderma lucidum extract was screened for its anti-proliferative activity using a panel of 26 human cancer cell lines. The six most sensitive hematologic cell lines were: HL-60 (ED50 26 microg/ml), U937 (63 microg/ml), K562 (50 microg/ml), Blin-1 (38 microg/ml), Nalm-6 (30 microg/ml) and RPMI8226 (40 microg/ml). Cell cycle analyses revealed a G2/M arrest, most prominently in HL-60 cells. Four hematopoietic cell lines (HL-60, Blin-1, U937, RPMI8226) were examined for apoptosis, which ranged between 21 and 92%. After exposure to G. lucidum extract, HL-60 cells became multinucleated with an increased DNA content. These results indicate that G. lucidum extract has a profound activity against leukemia, lymphoma and multiple myeloma cells and may be a novel adjunctive therapy for the treatment of hematologic malignancies.

Analysis of genetic diversity in Ganoderma population with a novel molecular marker SRAP.:Appl Microbiol Biotechnol. 2006 Sep;72(3):537-43. Epub 2006 Jan 13.Sun SJ, Gao W, Lin SQ, Zhu J, Xie BG, Lin ZB.College of Life Science, Fujian Agriculture and Forestry University, Fuzhou 350002, People's Republic of China.

Genetic marker technology designed to detect naturally occurring polymorphisms at the DNA level had become an invaluable and revolutionizing tool for both applied and basic studies of fungi. To eliminate the confusion on the taxonomy of Ganoderma strains, in this study, a collection of 31 accessions representative of morphotypes and some unclassified types was used for analyzing molecular diversity using a novel molecular marker sequence-related amplified polymorphism (SRAP). This collection included commercial cultivars and wild varieties that

represented the great diversification of types from different countries and regions. The experimental results showed that 50 out of 95 combinations of primers turned out to be polymorphic, and 85 polymorphism bands were obtained using six combinations. Based on the appearances of markers, the genetic similarity coefficients were calculated, and genetic variations were observed (0 approximately 1) among the 31 different Ganoderma strains. The group of Ganoderma lucidum showed significant differences from the group of Ganoderma sinense. Moreover, G. lucidum in China was also different from G. lucidum in Yugoslavia. At the same time, cluster analysis successfully categorized these 31 Ganoderma strains into five groups. These results revealed the genetic diversity of Ganoderma strains and their correlation with geographic environments. It also suggested SRAP marker could be used in the taxonomic analysis of fungi. To our knowledge, this is the first application of SRAP marker on the systematics of Ganoderma strains within basidiomycetes.

Ganoderma lucidum mycelium and spore extracts as natural adjuvants for immunotherapy.:J Altern Complement Med. 2005 Dec;11(6):1047-57.Chan WK, Lam DT, Law HK, Wong WT, Koo MW, Lau AS, Lau YL, Chan GC.Department of Paediatrics and Adolescent Medicine, Hong Kong Jockey Club Clinical Research Centre, Faculty of Medicine, The University of Hong Kong, Hong Kong, SAR, China.

OBJECTIVES: Ganoderma lucidum (GL) is one of the most commonly used Chinese herbs in the oriental community, with more than 30% of pediatric cancer patients taking GL. The immunomodulating and anticancer effects exerted by GL extracts have been demonstrated by in vitro and in vivo studies. There was, however, no comparison between the immunomodulating effects of GL mycelium extract (GL-M) and spore extracts on human immune cells. Dendritic cells (DCs) are professional antigen-presenting cells and their role in DC-based tumor vaccine has been well defined. The possibility of GL as natural adjuvant for human DCs remains unknown. DESIGN: This study explored the differential effect of GL-M and GL spore extract (GL-S) on proliferation and Th1/Th2 cytokine mRNA expression of human peripheral blood mononuclear cells (PBMCs) and monocytes. Their effects on the phenotypic and functional maturation of human monocyte-derived DCs were also investigated. RESULTS: GL-M induced the proliferation of PBMCs and monocytes, whereas GL-S showed a mild suppressive effect. Both extracts could stimulate Th1 and Th2 cytokine mRNA expression, but GL-M was a relatively stronger Th1 stimulator. Different from GL-S, GL-M enhanced maturation of DCs in terms of upregulation of CD40, CD80, and CD86, and also reduced fluorescein isothiocyanate-dextran endocytosis. Interestingly, GLM- treated DCs only modestly enhanced lymphocyte proliferation in allogenic mixed lymphocyte culture with mild enhancement in Th development. CONCLUSION: These findings provide evidences that GL-M has immunomodulating effects on human immune cells and therefore can be used as a natural adjuvant for cancer immunotherapy with DCs.

Comparison of the immunomodulatory effects of spore polysaccharides and broken spore polysaccharides isolated from Ganoderma lucidum on murine splenic lymphocytes and peritoneal macrophages in vitro.:Beijing Da Xue Xue Bao. 2005 Dec 18;37(6):569-74.Wang PY, Wang SZ, Lin SQ, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center, Beijing 100083, China.

OBJECTIVE: To compare the immunomodulatory effects of spore polysaccharides (GI-SP) and broken spore polysaccharides (GI-BSP) isolated from Ganoderma lucidum(Leyss et Fr.) Karst. on murine splenic lymphocytes and peritoneal macrophages in vitro. METHODS: Mixed lymphocyte culture reaction (MLR), lymphocyte proliferation in the presence or absence of mitogen, and the cytotoxic activity of splenic natural killer (NK) cells were detected with MTT assay in vitro. The percentage of phagocytosis of neutral red (NR) by mouse peritoneal macrophages was detected by colorimetric assay. Splenic T-lymphocyte subpopulations were measured with flow cytometry(FCM). IL-2, IFN-gamma and TNF-alpha in the culture supernatants were detected by ELISA and biological assay. Nitric oxide (NO) production was examined by Griess reaction. RESULTS: At the concentration range of 0.2-12.8 mg/L, GI-SP and GI-BSP were shown to increase lymphocyte proliferation in the presence or absence of mitogen, enhance NK cytotoxic activity, augment the production of TNF-alpha and NO in GI-SP- or GI-BSP-activated macrophages, as well the percentage of phagocytosis of NR by macrophages in vitro. Both GI-SP and GI-BSP could promote MLR, however, at the dose of 12.8 mg/L, GI-BSP showed higher activity than GI-SP in the proliferation of lymphocytes. These two kinds of polysaccharide could significantly increase the secretion of IL-2 and IFN-gamma in doublejway MLR at the

concentrations of 0.2-12.8 mg/L, but Gl-BSP had stronger effects than Gl-SP at the same concentrations. Both Gl-SP and Gl-BSP could increase the ratio of T-lymphocyte subpopulations in double-way MLR. At the concentrations of 0.2-12.8 mg/L or 3.2-12.8 mg/L, Gl-BSP demonstrated more significant activity in increasing the percentage of the CD4(+) or CD8(+) subset than Gl-SP. At the concentrations of 0.2-0.8 mg/L, the ratio of the CD4(+) and CD8(+) subset in the Gl-BSP treated group was higher than that of the Gl-SP treated group. CONCLUSION: Gl-SP and Gl-BSP have similar immunomodulatory effects in vitro, as though the immunomodulatory effects of Gl-BSP are stronger than that of Gl-SP.

Secondary metabolites from Ganoderma lucidum and Spongiporus leucomallellus.:Phytochemistry. 2006 Jan;67(2):202-11. Epub 2005 Dec 13.Campos Ziegenbein F, Hanssen HP, K?nig WA.Institut f¨¹r Organische Chemie, Universit?t Hamburg, Martin-Luther-King-Platz-6, D-20146 Hamburg, Germany. FerCampos@aol.com

The hydrodistillates and solvent extracts of the fruit bodies of Ganoderma lucidum (Fr.) P. Karst. and Spongiporus leucomallellus (Murril) A. David were investigated. The constituents in both oils comprised hydrocarbons, monoterpenes, sesquiterpenes, and fatty acids. Major volatiles of G. lucidum were trans-anethol, R-(-)-linalool, S-(+)-carvone and alpha-bisabolol, while the essential oil of S. leucomallellus contained relatively large amounts of R-(-)-1-octene-3-ol, R-(-)-linalool, 1-hepten-3-one and (Z)-nerolidol. From the n-hexane extract of G. lucidum, the steroid ester ergosta-7,22-diene-3beta-yl pentadecanoate could be identified. From S. leucomallellus two constituents showing structures of 3,4-seco-lanostane type triterpene acids were identified as (+)-23-oxo-3,4-seco-lanosta-4(28),7(8),9(11),24(31)-tetraene-3,26-dicarboxylic acid and (+)-20-hydroxy-23-oxo-3,4-seco-lanosta-4(28),7(8),9(11),24(31)-tetraene3,26-dicarboxylic acid, respectively. Cytotoxicity and antimicrobial activity of selected compounds were investigated using standard tests.

Anticancer effects of Ganoderma lucidum: a review of scientific evidence.:Nutr Cancer. 2005;53(1):11-7.Yuen JW, Gohel MD.Department of Health Technology and Informatics, The Hong Kong Polytechnic University, Kowloon, SAR, China.

"Lingzhi" (Ganoderma lucidum), a popular medicinal mushroom, has been used in China for longevity and health promotion since ancient times. Investigations into the anticancer activity of lingzhi have been performed in both in vitro and in vivo studies, supporting its application for cancer treatment and prevention. The proposed anticancer activity of lingzhi has prompted its usage by cancer patients. It remains debatable as to whether lingzhi is a food supplement for health maintenance or actually a therapeutic "drug" for medical proposes. Thus far there has been no report of human trials using lingzhi as a direct anticancer agent, despite some evidence showing the usage of lingzhi as a potential supplement to cancer patients. Cellular immune responses and mitogenic reactivity of cancer patients have been enhanced by lingzhi, as reported in two randomized and one nonrandomized trials, and the quality of life of 65% of lung cancer patients improved in one study. The direct cytotoxic and anti-angiogenesis mechanisms of lingzhi have been established by in vitro studies; however, clinical studies should not be neglected to define the applicable dosage in vivo. At present, lingzhi is a health food supplement to support cancer patients, yet the evidence supporting the potential of direct in vivo anticancer effects should not be underestimated. Lingzhi or its products can be classified as an anticancer agent when current and more direct scientific evidence becomes available.

Ganoderma lucidum inhibits inducible nitric oxide synthase expression in macrophages.:Mol Cell Biochem. 2005 Jul;275(1-2):165-71.Woo CW, Man RY, Siow YL, Choy PC, Wan EW, Lau CS, O K.Department of Physiology, University of Manitoba, Winnipeg, Manitoba, Canada.

Nitric oxide (NO) is a principal mediator in many physiological and pathological processes. Overproduction of NO via the inducible nitric oxide synthase (iNOS) has cytotoxic effect through the formation of peroxynitrite with superoxide anion. The iNOS is mainly expressed in macrophages and is able to produce large amount of NO. The expression of iNOS is mainly regulated at the transcriptional level. The iNOS-mediated NO production plays a role in the development of atherosclerosis. Ganoderma lucidum (G. lucidum, Linzhi or Reishi) is a traditional herbal medicine which is commonly used as health supplement. Several studies have demonstrated its effectiveness against cancer, immunological disorders and cardiovascular

diseases. The objective of the present study was to investigate the effect of G. lucidum on iNOS-mediated NO production in macrophages. Human monocytic cell (THP-1) derived macrophages were incubated with lipopolysaccharide (LPS) for 24 h. Such treatment significantly stimulated NO production (253% versus the control). Such a stimulatory effect was resulted from increased iNOS mRNA expression (270% versus the control) and iNOS activity (169.5% versus the control) in macrophages. The superoxide anion level was also elevated (150% versus the control) in LPS-treated macrophages. Treatment of macrophages with G. lucidum extract (100 microg/ml) completely abolished LPS-induced iNOS mRNA expression and NO production. Such an inhibitory effect of G. lucidum was mediated via its antioxidant action against LPS-induced superoxide anion generation in macrophages. These results suggest that G. lucidum may exert a therapeutic effect against atherosclerosis via ameliorating iNOS-mediated NO overproduction in macrophages.

Effects of ganoderma lucidum polysaccharides on serum lipids and lipoperoxidation in experimental hyperlipidemic rats.:Zhongguo Zhong Yao Za Zhi. 2005 Sep;30(17):1358-60.Chen WQ, Luo SH, Ll HZ, Yang H.School of Basicial Medicine, Guangdong College of Pharmacy, Guangzhou 510224, China.

OBJECTIVE: To investigate the effect of ganoderma lucidum polysaccharides on blood lipid and lipoperoxidation from the experimental hyperlipidemic rats. METHOD: 50 rats were randomly divided into normal group, hyperlipidemia control group, experimental group 1, 2 and 3 in which the rats were treated with ganoderma lucidum polysaccharides at dosages of 200 mg x kg(-1) and 400 mg x kg(-1) and 800 mg x kg(-1) respectively. Apart from the rats in control group, all the rats in other groups were fed with high fat forage for 30 days. The blood was collected from the tails of rats for measuring the serum TC, TG, HDL-C, LDL-C, GSH-Px, SOD and LPO. RESULT: Ganoderma lucidum polysaccharides could significantly decrease the serum contents of TC, TG, LDL-c in the experimental hyperlipidemic rats ($P < 0.01$), and markedly increase the level of serum HDL-C ($P < 0.05$), Mean Level of blood LPO in the experimental groups treated by ganoderma lacidum polysaccharides at different dosages were much lower than that in hyper lipidema group, and the GSH-Px and SOD activities of blood in the group of ganoderma were much higher than those in hyperlipidema group. CONCLUSION: Ganoderma can regulate lipid metabolism, enhance the antioxidation and reduce the lipid peroxidation in the rats with hyperlipidemia.

Soothing effect of Ganoderma lucidum antlered form on cyclophosphamide-induced adverse reaction.:Gan To Kagaku Ryoho. 2005 Oct;32(11):1586-8.

The immunological functions of Ganoderma lucidum antlered form (AF) (Rokkaku-Reishi in Japanese), a variant type of Ganoderma lucidum, were investigated in C57BL/6 mice treated with cyclophosphamide (CY). Ganoderma lucidum AF alleviated CY-induced decrease in body weight and abnormal increase in blood neutrophil level, when the mice were fed a diet containing 2.5% Ganoderma lucidum AF starting one week before CY treatment (150 mg/kg, ip). The recovery of CD8+ and NK1.1+ cells in the spleen was accelerated in Ganoderma lucidum AF group compared to the control group. Ganoderma lucidum AF also both alleviated CY-induced splenic lymphopenia and suppressed the abnormal increase in splenocytes 7 days after CY treatment. These results suggest that ingestion of Ganoderma lucidum AF is beneficial for improvement of quality of life reduced by anti-cancer chemotherapeutic drugs such as CY.

Effects of extracts of Chinese medicines on Ganoderma lucidum in submerged culture.:Wei Sheng Wu Xue Bao. 2003 Aug;43(4):519-22.Yang H, Wu T, Zhang K.Key Laboratory of Industrial Biotechnology of Ministry of Education, Southern Yangtze University, Wuxi 214036, China. yanghl99@163.com

Effects of water and ethanol extracts of 10 Chinese medicines, such as Astragalus membranaceus, Coix lachryma-jobi, etc., on biomass and exopolysaccharide of Ganoderma lucidum were studied by submerged culture. The results showed: water extracts of all medicines can improve the culture of G. lucidum except of A. membranaceus, ethanol extracts of C. lachryma-jobi, Dioscorea opposita, Codonopsis pilosula, and Achyranthes bidentata(< 187.5g Medicine/L substrate) can also increase the biomass of G. lucidum, but the ethanol extracts of Angelica sinensis, Dendrobium nobile check the growth of G. lucidum. The production of

exopolysa-ccharide can be improved by all the Chinese medicines and their dosage used in this experiment, Although A. sinensis, D. Nobile check the growth of G. lucidum, they could stimulate the secretion of exopolysaccharide in lower dosage. It is concluded that some Chinese medicines, such as C. lachryma-jobi, D. opposita, C. pilosula, etc. can be processed by the fermentation of G. lucidum, and bio-active compound can be produced by adding appropriate Chinese medicine in the substrate to culture G. lucidum.

Ganoderma lucidum polysaccharides peptide inhibits the growth of vascular endothelial cell and the induction of VEGF in human lung cancer cell.:Life Sci. 2006 Feb 23;78(13):1457-63. Epub 2005 Nov 2.Cao QZ, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center, 38 Xueyuan Road, Beijing, 100083, China.

Ganoderma lucidum Polysaccharide Peptide (Gl-PP) has shown some effects as anti-tumors in mice and potential anti-angiogenesis. In this study, we elucidated the possible mechanism of Gl-PP action on anti-angiogenesis of tumor. Our research indicated that the proliferation of HUVECs was inhibited by Gl-PP in a dose-dependent fashion, but not because of cytotoxicity. Flow cytometric studies revealed that Gl-PP treatment of HUVECs could induce cell apoptosis directly. Moreover, addition of Gl-PP also led to a reduction of Bcl-2 anti-apoptotic protein expression and an increase of Bax pro-apoptotic protein expression of HUVECs. Therefore, inducing cell apoptosis by Gl-PP might be the mechanism of inhibiting HUVEC proliferation. Human lung carcinoma cells PG when exposed to high dose of Gl-PP in hypoxia for 18 h resulted in a decrease in the secreted VEGF. Taken together, these findings support the hypothesis that the key attribute of the anti-angiogenic potential of Gl-PP is that it may directly inhibit vascular endothelial cell proliferation or indirectly decrease growth factor expression of tumor cells.

Effects of ganoderma lucidum extract on chemotherapy-induced nausea and vomiting in a rat model.:Am J Chin Med. 2005;33(5):807-15.Wang CZ, Basila D, Aung HH, Mehendale SR, Chang WT, McEntee E, Guan X, Yuan CS.Tang Center for Herbal Medicine Research, Department of Anesthesia and Critical Care, University of Chicago, Chicago, IL 60637, USA.

Chemotherapy is highly cytotoxic, causing a number of severe adverse effects such as nausea and vomiting. Herbal medicines, which can often be used on a daily basis for prolonged treatment, may be clinically beneficial. Ganoderma lucidum or Lingzhi mushroom has been recognized as a remedy in treating a number of medical conditions, including balancing immunity and decreasing drug-induced side effects. It has been shown that rats react to emetic stimuli, like the chemotherapy agent cisplatin, by increased consumption of kaolin, known as pica; and this rat model has been utilized to evaluate novel anti-emetic compounds. In this study, we evaluated the effects of a G. lucidum extract (SunRecome, the most commonly used Lingzhi mushroom extract in China) in attenuating cisplatin-induced nausea and vomiting in the rat pica model. We observed that intraperitoneal cisplatin injection caused a significant increase in kaolin intake at 24, 48, 72 and 96 hours, reflecting cisplatin's nausea and vomiting action. This cisplatin-induced kaolin intake dose-dependently decreased after 1, 3 and 10 mg/kg G. lucidum extract injection ($p < 0.01$). In addition, there was a significant reduction of food intake after cisplatin. The cisplatin-induced food intake reduction improved significantly after G. lucidum extract administrations in a dose-related manner ($p < 0.01$), suggesting a supportive effect of the extract on general body condition. Future controlled clinical trials are needed to evaluate the safety and effectiveness of this herbal medication.

In vitro inhibitory efects on HBsAg and HBeAg secretion of 3 new components produced by Ganoderma lucidum in the medium contained Radix sophorae flavescentis extract.:Wei Sheng Wu Xue Bao. 2005 Aug;45(4):643-6.Li YQ, Zhang KC.College of Life Science, South China Normal University, Guangzhou 510631, China. liyq2004@126.com

In order to enhance the medical effects of Ganoderma lucidum submergedly cultured broth, the aqueous extract of Radix sophorae flavescentis, a traditional Chinese medicine, was added into the cultivation medium of G. lucidum. The organic acids were extracted with ethanol, chloroform, 5% $NaHCO_3$ and chloroform in turn from the cultured broth of Ganoderma lucidum which cultivation medium contained Radix sophorae flavescentis extract. Six new components were separated from the organic acids with preparative HPLC. Their inhibitory effects on HBsAg and HBeAg secretion of HBV DNA transferred HepG2 cell (2.2.15 cell) were investigated. The results

indicate that 3 components of the six have significant inhibitory effects on the antigen secretion.

Effect of Ganoderma lucidum on the quality and functionality of Korean traditional rice wine, yakju.:J Biosci Bioeng. 2004;97(1):24-8.Kim JH, Lee DH, Lee SH, Choi SY, Lee JS.Department of Genetic Engineering, Paichai University, Daejeon 302-735, Korea.

The goal of this study was to develop a high value Korean traditional rice wine possessing the pharmaceutical functionality of Ganoderma lucidum. The effects of the fruiting body of G. lucidum on the alcohol fermentation of Korean traditional rice wine, yakju, were investigated. Optimal fermentation conditions for the preparation of G. lucidum-yakju consisted of the koji added at 15% and a fermentation period of 15 d at 25 degrees C. The effects of the amount of G. lucidum added on the acceptability and functionality of G. lucidum-yakju were investigated. G. lucidum GL-1 yakju brewed by adding 0.1% G. lucidum into the mash showed the best acceptability and its angiotensin I-converting enzyme (ACE) inhibitory activity and SOD-like activity were 63% and 42%, respectively, both of which are higher than those of yakju. The high ACE inhibitory activity of G. lucidum GL-1 yakju was found to result from ganoderic acid K in G. lucidum on the basis of physical and spectral data. However, the fibrinolytic activity and antioxidant activity of G. lucidum GL-1 yakju were very low, while tyrosinase inhibitory activity was not determined. From these results, G. lucidum GL-1 yakju may become a new functional Korean traditional rice wine with antihypertensive properties.

Effect of mycelial culture broth of Ganoderma lucidum on the growth characteristics of human cell lines.: J Biosci Bioeng. 2001;92(6):550-5.Chung WT, Lee SH, Kim JD, Park YS, Hwang B, Lee SY, Lee HY.Division of Food and Biotechnology, Kangwon National University, Chunchon 200-701, Korea

Two types of purified samples, water-soluble (sample A; M. W, 1.2 x 10(6) dalton) and water-insoluble (sample C; M. W., 1.0 x 10(6) dalton) samples, were obtained through consecutive separation processes from the culture broth of Ganoderma lucidia mycelium. It was found that both samples from the culture broth were very effective in inhibiting the growth of several human cancer cell lines, having a 93-85% growth inhibition on Hep3B, AGS and A549 with the least cytotoxicity on the normal human lung cell line, WRL68 of less than 25% the highest supplementation concentration of 1.0 mg/l. In general, the sample C showed greater inhibition of cancer cell growth than the sample A. The same trend was also observed in antimutagenicity using the Chinese hamster ovary cell line (CHO test) or Salmonella typhimurium (Ames test). The CHO test showed that sample C had higher antimutagenicity on mutagens 4NQO or MMNG than sample A (approximately 40% vs approximately 25%). The percentage of antimutagenicity from the Ames test was lower than that from the CHO test, possibly due to the difference in the sensitivity of mutagens. The water-insoluble sample greatly enhanced the growth of the human T cell line (H9) up to 1 x 10(5) with sample supplementation at 1.0 mg/l concentration from 4.3 x 10(4) without sample supplementation as well as improved the secretion level of both IL-6 and TNF-alpha up to 100 pg/ml from approximately 40 pg/ml without sample supplementation. The kinetics of response to the immune cell growth was illustrated by the response time obtained when the sample concentration was increased. The water-insoluble sample can be used for effectively treating cancer in that it accelerated apoptosis of human carcinoma cells up to 70% compared to less than 50% for the control. The sample also increased the differentiation ratio of HL-60 cells up to 58% after four days of cultivation, compared to 18% in the case of no sample supplementation. These results can be used in implying that the insoluble part of G. lucidium mycelium culture broth must be related to controlling signal transduction, resulting in the regulation of cancer cell growth.

Cellular and molecular mechanisms of immuno-modulation by Ganoderma lucidum.:J Pharmacol Sci. 2005 Oct;99(2):144-53.Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center. linzb@public3.bta.net.cn

Ganoderma lucidum (Leyss. ex Fr.) Karst. (Lingzhi or Reishi) has been used for a long time in China to prevent and treat various human diseases. G. lucidum polysaccharides extracted from G. lucidum are one of efficacious ingredient groups of G. lucidum. A number of reports have demonstrated that G. lucidum polysaccharides modulate immune function both in vivo and in vitro. The immuno-modulating effects of G. lucidum polysaccharides were extensive, including promoting the function of antigen-presenting cells, mononuclear phygocyte system, humoral

immunity, and cellular immunity. Cellular and molecular mechanisms, possible receptors involved, and triggered signaling cascades have also been studied in vitro. However, whole animal experiments are still needed to further establish the mechanism of the immuno-modulating effects by G. lucidum. Evidence-based clinical trials are also needed.

Bistage control of pH for improving exopolysaccharide production from mycelia of Ganoderma lucidum in an air-lift fermentor.:J Biosci Bioeng. 1999;88(6):646-50.Lee KM, Lee SY, Lee HY.Division of Environmental and Biological Engineering, Kangwon National University, Chunchon 200-701, Korea.

It was found that pH control definitely affects mycelial cell growth and exopolysaccharide (EPS) production of the mycelial cultivation of Ganoderma lucidum. Compared to the case of uncontrolled pH cultivation, a culture system whose pH was kept constant at 3 and 6 exhibited improved mycelial cell growth and EPS production, respectively. The bistage pH control technique, that is, shifting the pH from 3 to 6 at the initial phase of the exponential growth, is introduced to improve cell growth and EPS production. This technique can greatly increase EPS production to 20.1 g/l from 4.1 g/l in the case of uncontrolled pH cultivation, without adverse effects on cell growth as in the case of constant maintenance of a high pH. It was also proved that bistage pH control retained the desirable morphologies of the mycelia during cultivation and resulted in low viscosity and yield stress of the culture broth. It will be useful for the application of the culture process to mycelial growth in a large-scale fermentor.

Effect of an herbal formula containing Ganoderma lucidum on reduction of herpes zoster pain: a pilot clinical trial.:Am J Chin Med. 2005;33(4):517-23

Administration of hot water extracts of a herbal formula containing Ganoderma lucidum, WTMCGEPP (Wisteria floribunda 0.38, Trapa natans 0.38, Miristica agrans 0.38, Coix lachryma-jobi 0.75, cultivated Ganoderma lucidum 0.75, Elfuinga applanata 0.38, tissue cultured Panax ginseng 0.3, and Punica granatum 0.38: numerals designate dry weight gram/dose), decreased herpes zoster pain for five Japanese patients suffering from shingles. Pain relief started within a few days of intake and was almost complete within 10 days. Two acute herpes zoster with manifestations including trigeminal nerve ophthalmia (both 74 years old), lower body zoster (70 years old), herpes zoster oticus (17 years old), and leg herpes (28 years old), responded quickly to treatment and no patient developed post-herpetic neuralgia (PHN) after more than one year of follow-up.

Ganoderma lucidum mycelia enhance innate immunity by activating NF-kappaB.:J Ethnopharmacol. 2006 Jan 16;103(2):217-22. Epub 2005 Sep 15.

Ganoderma lucidum is a popular medicinal mushroom in China and Japan for its immunomodulatory and antitumor effects. The goal of this research is to investigate the effect of dried mycelia of Ganoderma lucidum produced by submerged cultivation on the enhancement of innate immune response. We found that Ganoderma lucidum mycelia (0.2-1.6 mg/ml) stimulated TNF-alpha and IL-6 production after 8h treatment in human whole blood. IFN-gamma release from human whole blood was also enhanced after 3 day-culture with Ganoderma lucidum mycelia (0.2-1.0mg/ml). However, Ganoderma lucidum mycelia did not potentiate nitric oxide production in RAW264.7 cells. To better understand the possible immuno-enhancement mechanisms involved, we focused on nuclear factor (NF)-kappaB activation. Electrophoretic mobility shift assay revealed that the Ganoderma lucidum mycelia (1.6 mg/ml) activated kappaB DNA binding activity in RAW264.7 cells. These results provide supporting evidences for the immunomodulatory effect of Ganoderma lucidum mycelia.

Solid-state fermentation of cornmeal with the basidiomycete Ganoderma lucidum for degrading starch and upgrading nutritional value.:J Appl Microbiol. 2005;99(4):910-5.Han JR, An CH, Yuan JM.School of Life Science and Technology, Shanxi University, Taiyuan, China. hjr@sxu.edu.cn

AIMS: The objective of this research was to study the ability of the basidiomycete Ganoderma

lucidum to degrade starch and upgrade nutritional value of cornmeal during solid-state fermentation (SSF). METHODS AND RESULTS: On the basal medium that consisted of cornmeal and salt solution, alpha-amylase activity of G. lucidum reached its maximum value of 267 U g(-1) of culture on day 20 after inoculation. Prolongation of fermentation time from 10 to 25 days increased significantly the degradation rate of starch and ergosterol yield (a kind of physiologically active substances of G. lucidum, also as an indicator of mycelial biomass) ($P < 0.01$). Supplementation of glucose, sucrose or maltose to the basal medium also caused a significant increase in either the degradation rate of starch or the ergosterol yield as compared with control ($P < 0.01$). Among five kinds of nitrogen sources supplemented, yeast extract, casamino acid and peptone were more effective than (NH4)2SO4 and NH4NO3, and yeast extract gave the highest degradation rate of starch and ergosterol yield, followed by peptone. Through orthogonal experiments, the theoretical optimum culture medium for SSF of this fungus was the following: 100 g cornmeal, ground to 30-mesh powder, moistened with 67 ml of nutrient salt solution supplemented with 3 g yeast extract and 7.5 g glucose per litre. CONCLUSIONS: Under the optimum culture condition, the degradation rate of starch reached its maximum values of 70.4%; the starch content of the fermented product decreased from 64.5 to 25.3%, while the reducing sugar content increased from 4.2 to 20.6%. SSF also produced a significant increase ($P < 0.01$) from 11.0 to 16.5% in protein content. SIGNIFICANCE AND IMPACT OF THE STUDY: After SSF by G. lucidum, the digesting and absorbing ratio of cornmeal was strikingly increased and some active substances originated from G. lucidum remained in the fermented product. This implied that cornmeal could be processed into many kinds of special functional foods by SSF of G. lucidum.

Purification and characteristic of proteinase inhibitor GLPIA2 from Ganoderma lucidum by submerged fermentation.:Se Pu. 2005 May;23(3):267-9.Tian Y, Zhang K.The Key Laboratory of Industrial Biotechnology, Ministry of Education, Southern Yangtze University, Wuxi 214036, China. yapingtian@hotmail.com

A proteinase inhibitor GLPIA2 was purified to homogeneity from Ganoderma lucidum by submerged fermentation. The purification was carried out by ethanol fractional precipitation (30%-80%), gel-filtration on Superdex 200 column (30 cm x 1.1 cm i.d.) and anion exchange on Source 30Q column (10 cm x 1.6 cm i.d.). The gel chromatographic conditions were as follows: 50 mmol/L sodium phosphate as mobile phase with a flow rate of 1 mL/min with the effluent collection of 1 mL/tube and detection at 280 nm. The anion exchange chromatographic conditions were as follows: 50 mmol/L Tris-HCl (pH 8.8) containing different amounts of NaCl as mobile phase with a flow rate of 2 mL/min with the effluent collection of 5 mL/tube and detection at both 215 nm and 280 nm. Two active fractions named GLPIA1 and GLPIA2 corresponding to proteinase A inhibitory activities were pooled and lyophilized. GLPIA2 only has the absorption at 215 nm. The relative molecular mass of the inhibitor was 15,000 as estimated by sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE). The amino acid composition of GLPIA2 was analyzed by high performance liquid chromatography. The chromatographic conditions were as follows: C18 column (125 mm x 4.0 mm i.d.) with column temperature of 40 degrees C; a mixture of 20 mmol/L sodium acetate-methanol-acetonitrile as mobile phase with a flow rate of 1 mL/min and detection at 338 nm. The results indicate that GLPIA2 is rich in acidic amino acid (Glu) and low in aromatic amino acids (Phe and Tyr). The interaction of some proteinases with GLPIA2 was investigated. The inhibitors are more potent against pepsin and yeast proteinase A than other proteinases.

Effects of water-soluble Ganoderma lucidum polysaccharides on the immune functions of patients with advanced lung cancer.:J Med Food. 2005 Summer;8(2):159-68.Gao Y, Tang W, Dai X, Gao H, Chen G, Ye J, Chan E, Koh HL, Li X, Zhou S.Institute of Food, Nutrition and Human Health, Massey University, New Zealand.

Preclinical studies have established that the polysaccharide fractions of Ganoderma lucidum have potential antitumor activity. Recent clinical studies have demonstrated that G. lucidum polysaccharides enhance host immune functions [e.g., enhanced natural killer (NK) cell activity] in patients with advanced solid tumors, although an objective response was not observed. This open-label study aimed to evaluate the effects of water-soluble G. lucidum polysaccharides (Ganopoly, Encore International Corp., Auckland, New Zealand) on immune functions in patients with advanced lung cancer. Thirty-six patients were enrolled and treated with 5.4 g/day Ganopoly for 12 weeks. In the 30 cancer patients who completed the trial, treatment with Ganopoly did not significantly alter the mean mitogenic reactivity to phytohemagglutinin, mean counts of CD3,

CD4, CD8, and CD56, mean plasma concentrations of interleukin (IL)-2, IL-6, and interferon (IFN)-gamma, or NK activity in the patients, but the results were significantly variable. However, some cancer patients demonstrated markedly modulated immune functions. The changes in IL-1 were correlated with those for IL-6, IFN-gamma, CD3, CD8, and NK activity ($P < .05$), and IL-2 changes were correlated with those for IL-6, CD8, and NK activity. The results suggest that subgroups of cancer patients might be responsive to Ganopoly in combination with chemotherapy/radiotherapy. Further studies are needed to explore the efficacy and safety of Ganopoly used alone or in combination with chemotherapy/radiotherapy in lung cancer patients.

Effects of Ganoderma lucidum polysaccharides on proliferation and cytotoxicity of cytokine-induced killer cells.:Acta Pharmacol Sin. 2005 Sep;26(9):1130-7.Zhu XL, Lin ZB.Department of Pharmacology, School of Basic Medical Science, Peking University Health Science Center, Beijing 100083, China.

AIM: To study the effects (and the mechanisms thereof) of Ganoderma lucidum polysaccharides (GI-PS) on the proliferation and the anti-tumor activity of cytokine-induced killer (CIK) cells, and to make use of CIK cells as a means to investigate the interactions between GI-PS and cytokines. METHODS: CIK cells were prepared by using the standard protocol as a positive control. Experimental groups also underwent the standard protocol, except that GI-PS (400 mg/L or 100 mg/L) was added and the dose of anti-CD3 and interleukin-2 they received was reduced by 50% and 75%, respectively. For negative controls, GI-PS in the experimental protocol was replaced with soluble starch or methylcellulose (400 mg/L or 100 mg/L). CIK cell proliferation, cytotoxicity, and phenotype were determined by using the Trypan blue exclusion method, MTT assay, and flow cytometry. RESULTS: By synergizing cytokines, GI-PS (400 mg/L or 100 mg/L) could decrease the amount of cytokine in lymphokine activated killer (LAK) cells and CIK cells culture, but had no significant effect on the proliferation, cytotoxicity, or phenotype of LAK cells, or CIK cells induced by cytokines at higher doses alone, in which CIK cells expanded about 80-fold and the main effectors, CD3+NK1.1+ cells, expanded by more than 15%. The cytotoxicity of CIK cells in experimental groups was 79.3%+/-4.7%, 76.9%+/-6.8% versus the positive control 80.7%+/-6.8% against P815 ($P>0.05$) and 88.9%+/-5.5%, 84.7%+/-7.9% versus the positive control 89.8%+/-4.5% against YAC-1 ($P>0.05$). The activity of GI-PS could mostly be blocked by anti-CR3. CONCLUSION: GI-PS was shown to be a promising biological response modifier and immune potentiator. The effect of GI-PS on CIK cells is possibly mediated primarily through complement receptor type 3.

Ganoderic acid produced from submerged culture of Ganoderma lucidum induces cell cycle arrest and cytotoxicity in human hepatoma cell line BEL7402.:Biotechnol Lett. 2005 Jun;27(12):835-8.Yang HL.School of Life & Environmental Science, Wenzhou University, Wenzhou, People's Republic of China. yanghl999@yahoo.com

Ganoderic acid (GA), produced by submerged culture of Ganoderma lucidum, at 500 microg/ml, caused nearly a 70% inhibition of the growth of human hepatoma cell line BEL7402 but not of a normal human liver cell line L02. Flow cytometry analyses showed that GA blocked the BEL7402 cell cycle at the transition from G(1)to S phase.

Ganodermin, an antifungal protein from fruiting bodies of the medicinal mushroom Ganoderma lucidum.:Peptides. 2006 Jan;27(1):27-30. Epub 2005 Jul 21.Wang H, Ng TB.Department of Microbiology, College of Biological Science, China Agricultural University, Beijing, China.

A 15-kDa antifungal protein, designated ganodermin, was isolated from the medical mushroom Ganoderma lucidum. The isolation procedure utilized chromatography on DEAE-cellulose, Affi-gel blue gel, CM-Sepharose and Superdex 75. Ganodermin was unadsorbed on DEAE-cellulose and adsorbed on Affi-gel blue gel and CM-Sepharose. Ganodermin inhibited the mycelial growth of Botrytis cinerea, Fusarium oxysporum and Physalospora piricola with an IC50 value of 15.2 microM, 12.4 microM and 18.1 microM, respectively. It was devoid of hemagglutinating, deoxyribonuclease, ribonuclease and protease inhibitory activities.

A prospective, randomized, double-blind, placebo-controlled study of the platelet and global hemostatic effects of Ganoderma lucidum (Ling-Zhi) in healthy volunteers.:Anesth Analg. 2005 Aug;101(2):423-6, table of contents.Kwok Y, Ng KF, Li CC, Lam CC, Man RY.Department of Anaesthesiology, Queen Mary Hospital, Hong Kong SAR, China.

Ganoderma lucidum is a Chinese herbal medicine popular with cancer patients. Previous in vitro studies suggested that Ganoderma lucidum might impair hemostasis. In this prospective, randomized double-blind study, healthy volunteers received orally Ganoderma lucidum capsules 1.5 g (n = 20) or placebo (n = 20) daily for 4 wk. We monitored subjects before drug administration and at 4 and 8 wk thereafter by routine coagulation screen, fibrinogen concentration, von Willebrand ristocetin cofactor activity, platelet function analyzer PFA-100, and thrombelastography. There were no significant between-group differences and all measurements remained within the normal range. Ganoderma lucidum ingestion over 4 wk was not associated with impairment of hemostasis. IMPLICATIONS: Ingestion of Ganoderma lucidum does not cause impairment of hemostatic function in healthy volunteers, despite earlier in vitro reports that it may cause platelet inhibition and may have other antithrombotic and fibrinolytic activity. The use of Ganoderma lucidum preoperatively is unlikely to increase the risk of surgical bleeding in otherwise healthy patients.

Anti-androgenic activities of Ganoderma lucidum.:J Ethnopharmacol. 2005 Oct 31;102(1):107-12.

The inhibitory effects of methanol extracts of 19 edible and medicinal mushrooms on 5alpha-reductase activity were examined. The extract of Ganoderma lucidum Fr. Krast (Ganodermataceae) showed the strongest 5alpha-reductase inhibitory activity. The treatment of the fruit body of Ganoderma lucidum or the extract prepared from it significantly inhibited the testosterone-induced growth of the ventral prostate in castrated rats. These results showed that Ganoderma lucidum might be a useful ingredient for the treatment of benign prostatic hyperplasia (BPH).

Chemistry of polysaccharide Lzps-1 from Ganoderma lucidum spore and anti-tumor activity of its total polysaccharides.:Yao Xue Xue Bao. 2005 Apr;40(4):347-50.Jiang Y, Wang H, L¨¹ L, Tian GY.Shanghai Institute of Organic Chemistry, Shanghai 200032, China.

AIM: To study the structure and anti-tumor activity of polysaccharide from Ganoderma lucidum spore treated with microwave. METHODS: DEAE-cellulose and Sephadex G-50 column chromatography were used to isolate and purify the polysaccharide whose structure was characterized by using chemical and spectral methods. RESULTS AND CONCLUSION: One polysaccharide, named Lzps-1 was obtained from the water extract, with its molecular weight estimated by HPGPC to be 8000. Its structure was investigated to be glucan. The total polysaccharides, Lzps processed antitumor activity against sarcoma 180 and Lewis lung cancer in mice and enhanced the NK cell activity. Lzps-1 is obtained for the first time from Ganoderma spore Lzps has anti-tumor activity.

A quantum chemical and statistical study of ganoderic acids with cytotoxicity against tumor cell.:Eur J Med Chem. 2005 Oct;40(10):972-6. Epub 2005 Jul 11.Yang HL, Chen GH, Li YQ.School of Life and Environmental Sciences, Wenzhou University, Middle Xueyuan Road, Wenzhou 325027, China. yangh1999@yahoo.com

A set of molecular properties (variables) of 24 ganoderic acids with cytotoxicities against Meth-A tumor cells was calculated by the molecular orbital semi-empirical method AM1 and ChemPropStd. Pattern recognition techniques, principal component analysis (PCA) and hierarchical cluster analysis (HCA) were employed to reduce dimensionality and investigate which subset of variables could be more effective for classifying the ganoderic acids according to their degree of cytotoxicities against tumor cells. The PCA and HCA studies showed that EHOMO (highest occupied molecular orbital energy), Mulliken electronegativity (chi), electronic energy (Eel), log P (octanol/water partition coefficient), and Connolly molecular area (MA) are the most important variables for the classification between the ganoderic acids with higher and lower

cytotoxicities against tumor cells.

Effect of 26-oxygenosterols from Ganoderma lucidum and their activity as cholesterol synthesis inhibitors.:Appl Environ Microbiol. 2005 Jul;71(7):3653-8.Hajjaj H, Mac¨¦ C, Roberts M, Niederberger P, Fay LB.Nestl¨¦ Research Centre, Nestec Ltd., Vers-chez-les-Blanc, P.O. Box 44, 1000 Lausanne 26, Switzerland.

Ganoderma lucidum is a medicinal fungus belonging to the Polyporaceae family which has long been known in Japan as Reishi and has been used extensively in traditional Chinese medicine. We report the isolation and identification of the 26-oxygenosterols ganoderol A, ganoderol B, ganoderal A, and ganoderic acid Y and their biological effects on cholesterol synthesis in a human hepatic cell line in vitro. We also investigated the site of inhibition in the cholesterol synthesis pathway. We found that these oxygenated sterols from G. lucidum inhibited cholesterol biosynthesis via conversion of acetate or mevalonate as a precursor of cholesterol. By incorporation of 24,25-dihydro-[24,25-3H2]lanosterol and [3-3H]lathosterol in the presence of ganoderol A, we determined that the point of inhibition of cholesterol synthesis is between lanosterol and lathosterol. These results demonstrate that the lanosterol 14alpha-demethylase, which converts 24,25-dihydrolanosterol to cholesterol, can be inhibited by the 26-oxygenosterols from G. lucidum. These 26-oxygenosterols could lead to novel therapeutic agents that lower blood cholesterol.

Effect of the oil from ganoderma lucidum spores on pathological changes in the substantia nigra and behaviors of MPTP-treated mice.:Di Yi Jun Yi Da Xue Xue Bao. 2005 Jun;25(6):667-71.Zhu WW, Liu ZL, Xu HW, Chu WZ, Ye QY, Xie AM, Chen L, Li JR.Department of Neurology, First Affiliated Hospital, SUN Yat-sen University, Guangzhou 510080, China. zhuweiwen11@126.com

OBJECTIVE: To investigate the oil from the spores of ganoderma lucidum, a rare Chinese herb, on the behaviors and pathological changes in the substantia nigra pars compacta (SNpc) in mouse models of Parkinson's disease (PD) induced by MPTP. METHODS: C57BL mice were divided into 3 groups, and the ganoderma spores oil + MPTP group were treated with ganoderma spores oil for 8 days, together with subcutaneous injection of MPTP (30 mg/kg) starting on the third day for 6 days; MPTP group were pretreated with normal saline before subcutaneous MPTP injection, and the normal control group received pretreatment with normal saline before subcutaneous normal saline injection. The behavioral changes of the mice in different groups were observed by pole test, dopamine and its metabolic products in the striatum determined by HPLC, tyrosine hydroxylase (TH) positive cells detected by immunofluorescence method, and expression of TH protein by Western blotting. RESULTS: The mice in the ganoderma spores oil + MPTP group presented significantly less involuntary movement of the limbs in the pole test than the mice in MPTP group. The levels of dopamine and DOPAC in the striatum of ganoderma spores oil-treated mice were increased as compared with those in MPTP group. The number of surviving TH-positive neurons in SNpc of mice in ganoderma spores oil + MPTP group was significantly greater than that in MPTP group, with also significantly increased TH protein expression. CONCLUSION: Ganoderma spores oil has neuroprotective effect for preventing doparminergic neuron from impairment by MPTP.

Ganoderic acid Sz, a new lanostanoid from the mushroom Ganoderma lucidum.:Nat Prod Res. 2005 Jul;19(5):461-5.Li C, Yin J, Guo F, Zhang D, Sun HH.tPharmanex Shanghai R&D, 116 Lane 572, Bi Po Road, Shanghai, 201203 China.

A new lanostanoid, ganoderic acid SZ (1), isolated from a lipophilic extract of the fruiting body of Ganoderma lucidum, is a geometric Z-isomer of the known ganoderic acid S (2). The structure of ganoderic SZ (1) was deduced mainly by 1D and 2D NMR studies. During the course of this study, 12 known lanostanoids have also been isolated and characterized.

Antitumor activity and underlying mechanisms of ganopoly, the refined polysaccharides extracted from Ganoderma lucidum, in mice.:Immunol Invest. 2005;34(2):171-98.Gao Y, Gao H, Chan E, Tang W, Xu A, Yang H, Huang M, Lan J, Li X, Duan W, Xu C, Zhou

S.Institute of Food, Nutrition and Human Health, Massey University, Auckland, New Zealand.

Ganopoly is an aqueous polysaccharide fraction extracted from G. lucidum by patented biochemical technique and has been marketed as an over-the-counter product for chronic diseases including cancer and hepatopathy in many Asian countries. This study was undertaken to explore the anti-tumour effect and the underlying mechanisms of Ganopoly in mice and human tumor cell lines. The maximum tolerated dose (MTD) of Ganopoly in mice was estimated to be 100 mg/kg from a pilot study. Treatment of mice with oral Ganopoly for 10 days significantly reduced the tumour weight of sarcoma-180 in a dose-dependent manner, with inhibition rates of 32.3, 48.2 and 84.9% and growth delays of 1.5, 3.5, and 13.1 days at 20, 50, and 100 mg/kg, respectively. Incubation of Ganopoly at 0.05-1.0 mg/ml for 48 hours showed little or negligible cytotoxicity against human tumor CaSki, SiHa, Hep3B, HepG2, HCT116 HT29, and MCF7 cells in vitro. In contrast, 10 mg/ml of Ganopoly caused significant cytotoxicity in all tumour cells tested except MCF7, with marked apoptotic effect observed in CaSki, HepG2, and HCT116 cells, as indicated by nuclear staining and DNA fragmentation. In addition, Ganopoly enhanced concanavalin A-stimulated proliferation of murine splenocytes by 35.3% at 10 mg/ml, and stimulated the production of nitric oxide in thioglycollate-primed murine peritoneal macrophages in a concentration-dependent manner over 0.05-10 mg/ml. Addition of Ganopoly at 1 mg/ ml to murine peritoneal macrophages also potentiated lipopolysaccharide-induced nitric oxide production by 64.2%. Treatment of healthy mice or mice bearing sarsoma-180 with oral Ganopoly over 20-100 mg/kg for 7 day significantly increased the expression of both TNF-alpha and IFN-gamma (at both mRNA and protein levels) in splenocytes in a dose-dependent manner. Moreover, treatment of Ganopoly over 20-100 mg/kg significantly increased cytotoxic T lymphocyte cytotoxicity and NK activity in mice. The overall findings indicated that Ganopoly had antitumor activity with a broad spectrum of immuno-modulating activities and may represent a novel promising immunotherapeutic agent in cancer treatment.

Formulation and in vitro/in vivo evaluation of combining DNA repair and immune enhancing nutritional supplements.:Phytomedicine. 2005 Apr;12(4):255-63.Pero RW, Amiri A, Sheng Y, Welther M, Rich M.Department of Cell and Molecular Biology, Section for Tumor Immunology, University of Lund, Lund, Sweden. rwpero@attglobal.net

Combining nutritional supplements to achieve synergistic benefit is a common practice in the nutraceutical industry. However, establishing added health benefit from a combination of natural ingredients is often assumed, untested and without regard to the principle of metabolic competition between the active components. Here, we report on the combination of a cat's claw water extract (C-Med-100, carboxy alkyl esters = active ingredients) + medicinal mushroom extracts (Cordyceps sinensis, Grifola blazei, Grifolafrondosa, Trametes versicolor and Ganoderma lucidum, polysaccharides = active ingredients) + nicotinamide + zinc into a formulation designed to optimize different modes of immunostimulatory action, and yet that would avoid metabolic antioxidant competition yielding less than expected efficacious effects. Isobole curve analyses of these two active classes of ingredients determined by growth inhibition of HL-60 human leukemic cells in vitro confirmed they were indeed synergistic when in combination, and not metabolically competitive. Furthermore, an in vivo study showed significant health benefit for 14 subjects treated for 4 weeks with the unique C-Med-100/mushroom extract formulation in that they had reduced pain, reduced fatigue, weight loss and a reduced presence of DNA damage in peripheral blood assessed by (8-OH) guanine DNA adducts and elevation in serum protein thiols. Because this broad-based panel of clinical parameters indicating clinical efficacy has never been demonstrated before for either of the active ingredients evaluated alone in humans, these data were taken as strong evidence that the combination of C-Med-100 + mushroom extracts + nicotinamide + zinc gave additive or synergistic effects to health benefit, and thus supported no efficacious limits from metabolic competition regarding this particular formulation.

Polysaccharide purified from Ganoderma lucidum induced activation and maturation of human monocyte-derived dendritic cells by the NF-kappaB and p38 mitogen-activated protein kinase pathways.:J Leukoc Biol. 2005 Aug;78(2):533-43. Epub 2005 May 13.Lin YL, Liang YC, Lee SS, Chiang BL.Graduate Institute of Clinical Medicine, College of Medicine, National Taiwan University, Taipei, Taiwan, ROC.

Ganoderma lucidum, a fungus native to China, has been widely used to promote health and longevity in the Chinese. The polysaccharide component with a branched (1-->6)-beta-D-glucan

moiety of G. lucidum (PS-G) has been reported to exert anti-tumor activity and activation of natural killer cells. In this study, we investigated the effects of PS-G on human monocyte-derived dendritic cells (DC). Treatment of DC with PS-G resulted in the enhanced cell-surface expression of CD80, CD86, CD83, CD40, CD54, and human leukocyte antigen (HLA)-DR, as well as the enhanced production of interleukin (IL)-12p70, p40, and IL-10 and also IL-12p35, p40, and IL-10 mRNA expression, and the capacity for endocytosis was suppressed in DC. In addition, treatment of DC with PS-G resulted in enhanced T cell-stimulatory capacity and increased T cell secretion of interferon-gamma and IL-10. Neutralization with antibodies against Toll-like receptor (TLR)-4 inhibited the PS-G-induced production of IL-12 p40 and IL-10, suggesting a vital role for TLR-4 in signaling DC upon incubation with PS-G. Further study showed that PS-G was able to augment inhibitor of kappaB (IkappaB) kinase and nuclear factor (NF)-kappaB activity and also IkappaB alpha and p38 mitogen-activated protein kinase (MAPK) phosphorylation. Further, inhibition of NF-kappaB by helenalin and p38 MAPK by SB98059 prevented the effects of PS-G in the expression of CD80, CD86, CD83, CD40, CD54, and HLA-DR and production of IL-12p70, p40, and IL-10 in various degrees. Taken together, our data demonstrate that PS-G can effectively promote the activation and maturation of immature DC, suggesting that PS-G may possess a potential in regulating immune responses.

Polysaccharides of Ganoderma lucidum: factors affecting their production.:Prikl Biokhim Mikrobiol. 2005 Mar-Apr;41(2):194-9.Baabitskaia VG, Shcherba VV, Puchkova TA, Smirnov DA.

The conditions of polysaccharide production by the fungus Ganoderma lucidum were optimized. The maximal yield of endopolysaccharides and exopolysaccharides was observed at 25-30 degrees C, initial pH of culture medium 4.0-6.0, and at a C : N ratio of approximately 18 : 1 and 25 : 1, respectively. The greatest yield of mycelium was reached at a more intensive aeration, and the maximal yield of polysaccharides was observed at a less intensive aeration. The optimal ratio between fungus growth and polysaccharide production was observed at 100 rpm and an aeration of 1.0-1.5 1/1 medium min.

A randomized, double-blind and placebo-controlled study of a Ganoderma lucidum polysaccharide extract in neurasthenia.:J Med Food. 2005 Spring;8(1):53-8.Tang W, Gao Y, Chen G, Gao H, Dai X, Ye J, Chan E, Huang M, Zhou S.New Zealand Institute of Natural Medicine Research, Auckland, New Zealand

Ganoderma lucidum has been widely used to treat various diseases, including cancer, diabetes, and neurasthenia in many Asian countries. This randomized, double-blind, placebo-controlled parallel study aimed to investigate the efficacy and safety of a polysaccharide extract of G. lucidum (Ganopoly) in Chinese patients with neurasthenia. One hundred thirty-two patients with neurasthenia according to the diagnosis criteria of the 10th International Classification of Diseases were included in this study. Written consents were obtained from the patients, and the study was conducted in accordance with Good Clinical Practice guidelines. Patients were randomized to receive Ganopoly or placebo orally at 1,800 mg three times a day for 8 weeks. Efficacy assessments comprised the Clinical Global Impression (CGI) improvement of severity scale and the Visual Analogues Scales for the sense of fatigue and well-being. In 123 assessable patients in two treatment groups at the end of the study, Ganopoly treatment for 8 weeks resulted in significantly lower scores after 8 weeks in the CGI severity score and sense of fatigue, with a respective reduction of 15.5% and 28.3% from baseline, whereas the reductions in the placebo group were 4.9% and 20.1%, respectively. The score at day 56 in the sense of well-being increased from baseline to 38.7% in the Ganopoly group compared with 29.7% in the placebo group. The distribution of the five possible outcomes from very much improved to minimally worse was significantly different (X (2) = 10.55; df = 4; P = .0322) after treatment with Ganopoly or placebo. There was a percentage of 51.6% (32 of 62) in the Ganopoly group rated as more than minimally improved compared with 24.6% (15 of 61) in the placebo group (X (2) = 9.51; df = 1; P = .002). Ganopoly was well tolerated in the study patients. These findings indicated that Ganopoly was significantly superior to placebo with respect to the clinical improvement of symptoms in neurasthenia.

New anticancer agents: in vitro and in vivo evaluation of the antitumor and antimetastatic actions of various compounds isolated from medicinal plants.:In Vivo. 2005 Jan-Feb;19(1):37-60.

In this review, in the search for the development of new anticancer drugs, the effects of compounds isolated from various medicinal plants on tumor growth and metastasis, using mice bearing a highly metastatic drug-resistant mouse tumor, were studied. The antitumor and antimetastatic actions of stilbene derivatives isolated from Polygonum and Cassia species were examined. Among the stilbene derivatives, resveratrol and cassiagrol A (stilbene dimer) displayed antitumor and antimetastatic actions through the inhibition of tumor-induced neovascularization in in vitro and in vivo models. It was found that two chalcone derivatives from Angelica keiskei roots also inhibited tumor growth and metastasis in tumor-bearing mice through the inhibition of tumor-induced neovascularization and/or the inhibition of immune suppression caused by tumors. Recently, basidiomycete fungi have been used for the treatment of cancer. Then, the low molecular weight substances were isolated from Agaricus blazei and Ganoderma lucidum as antitumor and antimetastatic substances. It is suggested that these substances of basidiomycete also inhibited tumor growth and metastasis to the lung through the inhibition of tumor-induced neovascularization and/or the inhibition of immune suppression caused by tumors.

Ganoderma lucidum suppresses angiogenesis through the inhibition of secretion of VEGF and TGF-beta1 from prostate cancer cells.:Biochem Biophys Res Commun. 2005 Apr 29;330(1):46-52.Stanley G, Harvey K, Slivova V, Jiang J, Sliva D.Cancer Research Laboratory, Methodist Research Institute, 1800 N Capitol Ave, E504, Indianapolis, IN 46202, USA.

Ganoderma lucidum (G. lucidum) is a popular medicinal mushroom that has been used as a home remedy for the general promotion of health and longevity in East Asia. The dried powder of G. lucidum, which was recommended as a cancer chemotherapy agent in traditional Chinese medicine, is currently popularly used worldwide in the form of dietary supplements. We have previously demonstrated that G. lucidum induces apoptosis, inhibits cell proliferation, and suppresses cell migration of highly invasive human prostate cancer cells PC-3. However, the molecular mechanism(s) responsible for the inhibitory effects of G. lucidum on the prostate cancer cells has not been fully elucidated. In the present study, we examined the effect of G. lucidum on angiogenesis related to prostate cancer. We found that G. lucidum inhibits the early event in angiogenesis, capillary morphogenesis of the human aortic endothelial cells. These effects are caused by the inhibition of constitutively active AP-1 in prostate cancer cells, resulting in the down-regulation of secretion of VEGF and TGF-beta1 from PC-3 cells. Thus, G. lucidum modulates the phosphorylation of Erk1/2 and Akt kinases in PC-3 cells, which in turn inhibits the activity of AP-1. In summary, our results suggest that G. lucidum inhibits prostate cancer-dependent angiogenesis by modulating MAPK and Akt signaling and could have potential therapeutic use for the treatment of prostate cancer.

Antioxidant activity of Ganoderma lucidum in acute ethanol-induced heart toxicity.:Phytother Res. 2004 Dec;18(12):1024-6.Wong KL, Chao HH, Chan P, Chang LP, Liu CF.Department of Anesthesiology, Mackay Memorial Hospital, Taipei, Taiwan.

The hot water extract of the mushroom Ganoderma lucidum was shown to have antioxidative effect against heart toxicity. Investigations into the mechanisms of action, level of lipid peroxidation level in vivo, and superoxide scavenging activity were also conducted. The mice were divided into six groups with ten animals in each group. Ganoderma lucidum, at doses of 10, 25 and 50 mg/kg (p.o.) was administered. Superoxide anions were assayed by UV spectrophotometer using the cytochrome C reduction method. The results of this study showed that Ganoderma lucidum exhibited a dose-dependent antioxidative effect on lipid peroxidation and superoxide scavenging activity in mouse heart homogenate. Additionally, this result indicated that heart damage induced by ethanol shows a higher malonic dialdehyde level compared with heart homogenate treated with Ganoderma lucidum. It is concluded that the antioxidative activity may therefore contribute to the cardioprotective effect of Ganoderma lucidum, and may therefore protect the heart from superoxide induced damage.

Possible mechanism underlying the antiherpetic activity of a proteoglycan isolated from the mycelia of Ganoderma lucidum in vitro.:J Biochem Mol Biol. 2005 Jan 31;38(1):34-40.Li Z, Liu J, Zhao Y.School of Stomatology, Wuhan University, Wuhan 430079, Hubei, China. Lizubing@sina.com

GLPG (Ganoderma lucidum proteoglycan) was a bioactive fraction obtained by the liquid

fermentation of the mycelia of Ganoderma lucidum, EtOH precipitation, and DEAE-cellulose column chromatography.GLPG was a proteoglycan with a carbohydrate: protein ratio of 10.4: 1. Its antiviral activities against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) were investigated using a cytopathic inhibition assay. GLPG inhibited cell death in a dose-dependent manner in HSV-infected cells. In addition, it had no cytotoxic effect even at 2 mg/ml. In order to study the mode of action of the antiviral activity of GLPG, cells were treated with GLPG before, during, and after infection, and viral titer in the supernatant of cell culture 48 h post-infection was determined using a TCID((50)) assay. The antiviral effects of GLPG were more remarkable before viral treatment than after treatment. Although the precise mechanism has yet to be defined, our work suggests that GLPG inhibits viral replication by interfering with the early events of viral adsorption and entry into target cells. Thus, this proteoglycan appears to be a candidate anti-HSV agent.

Protective effects of a water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia and Agaricus blazei murill against X-irradiation in B6C3F1 mice: Increased small intestinal crypt survival and prolongation of average time to animal death.:Int J Mol Med. 2005 Mar;15(3):401-6.

Radioprotective effects of a water-soluble extracts from cultured medium of Ganoderma lucidum (Rei-shi) mycelia (designed as MAK) and Agaricus blazei (Agaricus) against the shortening of survival time or the injury of crypt by X-irradiation were investigated in male B6C3F1 mice. MAK and Agaricus at three different doses were mixed into basal diet into biscuits at 5, 2.5 and 1.25% and administered from 1 week before irradiation. MAK (5% group) significantly prolonged animal survival as compared with basal diet group (control group) after 7 Gy of X-ray irradiation at a dose rate of 2 Gy min(-1). At doses of 8, 10 and 12 Gy X-irradiation at a dose rate of 4 Gy min(-1) MAK (5% group) significantly increased crypt survival as compared to other groups. These results suggest that MAK can act as a radioprotective agent.

Influence of Ganoderma lucidum on blood biochemistry and immunocompetence in horses.:Am J Chin Med. 2004;32(6):931-40.Lai SW, Lin JH, Lai SS, Wu YL.Department of Veterinary Medicine, National Taiwan University, Taipei 106, Taiwan.

The characteristic ingredients of Ganoderma lucidum, such as polysaccharides, triterpenoids, nucleic acids and small proteins, have been found and proved to have many special pharmacological properties. Mice and rats have been extensively used to investigate the effects of G. lucidum. Experiments with horses as an animal model for investigating the effects of G. lucidum have never been reported. The purpose of this investigation was to understand the influence of G. lucidum feeding on blood biochemistry and immunocompetence in horses. Complete blood count (CBC) and blood biochemistry were surveyed routinely. Cellular-mediated immunity was monitored by flow cytometry to survey the percentage changes of CD5+, CD4+, CD8+ T-lymphocytes and B-lymphocytes in the peripheral blood lymphocytes (PBLs). The effect of G. lucidum on humoral immunity was experimented by fast plate agglutination test to survey the change and manifestation of the titer of specific anti-egg albumin antibodies in the serum after egg albumin injection. The findings on CBC and blood biochemistry indicated that G. lucidum was quite safe to horses. Experimental result on cell-mediated immunity showed that G. lucidum could increase the percentage of CD5+, CD4+ and CD8+ T-lymphocytes in PBLs ($p < 0.001$). Experimental result on humoral immunity showed that G. lucidum could help the horses to produce a significantly higher quantity of specific antibodies in a shorter time ($p < 0.001$).

Ganoderma lucidum polysaccharide fractions accelerate healing of acetic acid-induced ulcers in rats.:J Med Food. 2004 Winter;7(4):417-21.Gao Y, Tang W, Gao H, Chan E, Lan J, Zhou S.Institute of Food, Nutrition and Human Health, Massey University, Auckland, New Zealand.

The polysaccharide (PS) fractions from several medicinal herbs have been reported to have anti-ulcer effects against experimental ulcers in the rat. The water-soluble PS fractions from Ganoderma lucidum (Reishi mushroom) have been shown to inhibit indomethacin-induced gastric mucosal lesions in rats. This study aimed to investigate the effect of the PS fraction from G. lucidum on the healing of gastric ulcers induced by acetic acid in the rat and to elucidate the underlying mechanisms involved. The abdomen of rats was incised, and the stomach was

treated with 10 M acetic acid (100 microL) for 1 minute, and then treated with G. lucidum PS (0.1, 0.5, or 1.0 g/kg) intragastrically, once a day for 14 consecutive days. The results indicated that the oral administration of G. lucidum PS at 0.5 and 1.0 g/kg for 2 weeks caused a significant acceleration of ulcer healing by 40.1% and 55.9%, respectively. In the mechanistic studies, additional rats were treated with 10 M acetic acid to induce acute ulcers, and then treated with G. lucidum PS (1.0 g/kg) for 3, 7, 10, or 14 days. Exposure of the rat stomach to acetic acid led to decreased mucus and increased prostaglandin levels. Treatment with G. lucidum PS at 1.0 g/kg significantly ($P < .05$) suppressed or restored the decreased gastric mucus levels and increased gastric prostaglandin concentrations compared with the control group. These results indicates that G. lucidum PS is an active component with healing efficacy on acetic acid-induced ulcers in the rat, which may represent a useful herbal preparation for the prevention and treatment of peptic ulcers.

Comparative study on triterpenes in different Ganoderma species.:Zhong Yao Cai. 2004 Aug;27(8):575-6.Xing Z, Yu Q, Zhang J, Pan Y.Edible Fungi Institute, Shanghai Academy of Agricultural Sciences, Shanghai.

The triterpene profiles of different Ganoderma products was analysed by HPLC. The results showed that the seven-day fermented mycelia had little triterpene and different growth stages fruiting bodies almost had changeless triterpene. Compared with the fruiting body, the triterpene level of spore was lower. Among different Ganoderma species, Ganoderma atrum had little triterpenes too.

Ganoderma lucidum suppresses endothelial cell cytotoxicity and proteinuria in persistent proteinuric focal segmental glomerulosclerosis (FSGS) nephrosis.:Clin Hemorheol Microcirc. 2004;31(4):267-72.Futrakul N, Panichakul T, Butthep P, Futrakul P, Jetanalin P, Patumraj S, Siriviriyakul P.Department of Physiology, King Chulalongkorn Memorial Hospital, Bangkok, Thailand. fmednft@md2.md.chula.ac.th

A persistent proteinuria is commonly observed in nephrotic patient with focal segmental glomerulosclerosis (FSGS) under treatment with prednisolone+/-cyclophosphamide or with vasodilators (ACEI+AII receptor antagonist, calcium channel blocker and antiplatelet agent). Fourteen such patients with persistent proteinuria were subject to be treated with Ganoderma lucidum. Initial study revealed an enhanced endothelial cell cytotoxicity induced by patient's serum, and an altered immunocirculatory balance with predominant proinflammatory cytokine TNF alpha activity in the presence of defective anti-inflammatory cytokine interleukin-10. Treatment with Ganoderma lucidum suppressed endothelial cell cytotoxicity, restored immunocirculatory balance and successfully suppressed proteinuria in all of these 14 patients.

Cellular and physiological effects of Ganoderma lucidum (Reishi).:Mini Rev Med Chem. 2004 Oct;4(8):873-9.Sliva D.Methodist Research Institute, Clarian Health Partners, Inc., Indianapolis, IN 46202, USA. dsliva@clarian.org

In Asia, a variety of dietary products have been used for centuries as popular remedies to prevent or treat different diseases. A large number of herbs and extracts from medicinal mushrooms are used for the treatment of diseases. Mushrooms such as Ganoderma lucidum (Reishi), Lentinus edodes (Shiitake), Grifola frondosa (Maitake), Hericium erinaceum (Yamabushitake), and Inonotus obliquus (Chaga) have been collected and consumed in China, Korea, and Japan for centuries. Until recently, these mushrooms were largely unknown in the West and were considered 'fungi' without any nutritional value. However, most mushrooms are rich in vitamins, fiber, and amino acids and low in fat, cholesterol, and calories. These mushrooms contain a large variety of biologically active polysaccharides with immunostimulatory properties, which contribute to their anticancer effects. Furthermore, other bioactive substances, including triterpenes, proteins, lipids, cerebrosides, and phenols, have been identified and characterized in medicinal mushrooms. This review summarizes the biological effects of Ganoderma lucidum upon specific signaling molecules and pathways, which are responsible for its therapeutic effects.

Extract of Reishi polysaccharides induces cytokine expression via TLR4-modulated protein kinase signaling pathways.:J Immunol. 2004 Nov 15;173(10):5989-99.Hsu HY, Hua KF, Lin CC, Lin CH, Hsu J, Wong CH.Faculty of Medical Technology, Institute of Biotechnology in Medicine, National Yang-Ming University, 155 Li-Nong Street, Shih-Pai, Taipei, Taiwan. hyhsu@ym.edu.tw

We have demonstrated that an extract of Ganoderma lucidum (Reishi or Ling-Zhi) polysaccharides (EORP) exerts immunomodulating activities by stimulating the expression of inflammatory cytokines from mouse spleen cells. Interestingly, via responding to LPS in genetic variation of murine macrophage HeNC2 and GG2EE cell lines, and using TLR4 Ab blockage in human blood-derived monocytic macrophages, we have found that the TLR4, but not complement receptor type 3, is a putative receptor of EORP, mediating the consequent immunomodulating events associated with IL-1 gene expression. Based on our studies of reactive oxygen species production, polymyxin B inhibition, and protein tyrosine kinase (PTK) activity, we ruled out the possibility of LPS contamination in EORP. We have found that EORP differentially modulates the protein kinase (PK)-mediated signal transduction pathways associated with inflammatory cytokine IL-1. In human macrophages and murine macrophage J774A.1 cells, EORP was found to up-regulate IL-1 secretion and pro-IL-1 (precursor of IL-1) as well as IL-1-converting enzyme expression. Specifically, EORP rapidly stimulates PTK-mediated phosphorylation, followed by induction of PKs and activation of MAPKs: ERK, JNK, and p38. Using PK inhibitors in the kinase activity assays, Western blot analyses and IL-1 ELISA, we have extensively examined and dissected the role of individual PK in the regulation of pro-IL-1/IL-1. Our findings establish that EORP-mediated signaling pathways are involved in the pro-IL-1/IL-1 regulation: PTK/protein kinase C/MEK1/ERK and PTK/Rac1/p21-activated kinase/p38.

Anti-tumor and immunoregulatory activities of Ganoderma lucidum and its possible mechanisms.:Acta Pharmacol Sin. 2004 Nov;25(11):1387-95.Lin ZB, Zhang HN.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China. linzb@public3.bta.net.cn

Ganoderma lucidum (G lucidum) is a medicinal fungus with a variety of biological activities. It has long been used as a folk remedy for promotion of health and longevity in China and other oriental countries. The most attractive character of this kind of medicinal fungus is its immunomodulatory and anti-tumor activities. Large numbers of studies have shown that G lucidum modulate many components of the immune system such as the antigen-presenting cells, NK cells, T and B lymphocytes. The water extract and the polysaccharides fraction of G lucidum exhibited significant anti-tumor effect in several tumor-bearing animals mainly through its immunoenhancing activity. Recent studies also showed that the alcohol extract or the triterpene fraction of G lucidum possessed anti-tumor effect, which seemed to be related to the cytotoxic activity against tumor cells directly. Preliminary study indicated that antiangiogenic effect may be involved antitumor activity of G lucidum.

Possible mode of action of antiherpetic activities of a proteoglycan isolated from the mycelia of Ganoderma lucidum in vitro.: J Ethnopharmacol. 2004 Dec;95(2-3):265-72.Liu J, Yang F, Ye LB, Yang XJ, Timani KA, Zheng Y, Wang YH.Key laboratory of Virology, Ministry of Education, College of Life science, Wuhan University, Wuhan 430072, Hubei, China.

A bioactive fraction (GLPG) was extracted and purified from the mycelia of Ganoderma lucidum by EtOH precipitation and DEAE-cellulose column chromatography. GLPG was a proteoglycan and had a carbohydrate:protein ratio of 10.4:1. Its antiviral activities against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) were investigated by the cytopathic effect (CPE) inhibition assay in cell culture. This kind of polysaccharide inhibited the development of the cytopathic effect in dose-dependent manner in HSV-infected cells, moreover did not show any cytotoxic effects on cells even when a concentration was as high as 2000 microg/ml. In order to study the possible mode of action of the antiviral activity of GLPG, cells were treated with GLPG before, during and after infection, and the viral titers in the supernatant of cell culture 48 h post-infection were tested by TCID(50) assay. The antiviral effects in pre-treated and treated during virus infection with GLPG were more remarkable than the treatment of post-infection. Although the precise mechanism has yet to be defined, our work suggested that GLPG inhibits viral replication by interfering with the early events of viral adsorption and entry into target cells. Thus, this proteoglycan seems to be a potential candidate for anti-HSV agents.

Ganoderma lucidum extracts inhibit growth and induce actin polymerization in bladder cancer cells in vitro.:Cancer Lett. 2004 Dec 8;216(1):9-20.Lu QY, Jin YS, Zhang Q, Zhang Z, Heber D, Go VL, Li FP, Rao JY.Center for Human Nutrition, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA 90095, USA.

This study was conducted to investigate chemopreventive effects of Ganoderma lucidum using a unique in vitro human urothelial cell (HUC) model consisted of HUC-PC cells and MTC-11 cells. Ethanol and water extracts of fruiting bodies and spores of the G. lucidum were used to examine growth inhibition, actin polymerization status, and impact of actin remodeling on cell migration and adhesion. Results showed that ethanol extracts had a stronger growth inhibition effect than water extracts. Cell cycle analysis showed that the growth inhibition effect was associated with G2/M arrest. At non-cytotoxic concentrations (40-80 microg/ml), these extracts induced actin polymerization, which in turn inhibited carcinogen 4-aminobiphenyl induced migration in both cell lines. The increased actin polymerization was associated with increased stress fibers and focal adhesion complex formation, however, expression of matrix metalloproteinase-2 and focal adhesion kinase (total and phospholated) were unchanged, which suggests that other mechanisms may be involved.

Ganoderma lucidum suppresses growth of breast cancer cells through the inhibition of Akt/NF-kappaB signaling.:Nutr Cancer. 2004;49(2):209-16.Jiang J, Slivova V, Harvey K, Valachovicova T, Sliva D.Cancer Research Laboratory, Methodist Research Institute, Indianapolis, IN 46202, USA.

Ganoderma lucidum (Reishi, Lingzhi) is a popular Asian mushroom that has been used for more than 2 millennia for the general promotion of health and was therefore called the "Mushroom of Immortality." Ganoderma lucidum was also used in traditional Chinese medicine to prevent or treat a variety of diseases, including cancer. We previously demonstrated that Ganoderma lucidum suppresses the invasive behavior of breast cancer cells by inhibiting the transcription factor NF-kappaB. However, the molecular mechanisms responsible for the inhibitory effects of Ganoderma lucidum on the growth of highly invasive and metastatic breast cancer cells has not been fully elucidated. Here, we show that Ganoderma lucidum inhibits proliferation of breast cancer MDA-MB-231 cells by downregulating Akt/NF-kappaB signaling. Ganoderma lucidum suppresses phosphorylation of Akt on Ser473 and downregulates the expression of Akt, which results in the inhibition of NF-kappaB activity in MDA-MB-231 cells. The biological effect of Ganoderma lucidum was demonstrated by cell cycle arrest at G0/G1, which was the result of the downregulation of expression of NF-kappaB-regulated cyclin D1, followed by the inhibition of cdk4. Our results suggest that Ganoderma lucidum inhibits the growth of MDA-MB-231 breast cancer cells by modulating Akt/NF-kappaB signaling and could have potential therapeutic use for the treatment of breast cancer.

Effects of Ganoderma lucidum on apoptotic and anti-inflammatory function in HT-29 human colonic carcinoma cells.:Phytother Res. 2004 Sep;18(9):768-70.Hong KJ, Dunn DM, Shen CL, Pence BC.Department of Pathology, Texas Tech University Health Sciences Center, Lubbock 79430, USA.

Ling Zhi extract (LZE) is a herbal mushroom preparation which been used world wide for the prevention and treatment of various cancers. The current study was designed to evaluate these claims in human colon cancer cells in terms of cancer preventive mechanisms. Results have demonstrated induction of apoptosis, anti-inflammatory action and differential cytokine expression during induced inflammation in the human colonic carcinoma cell line, HT-29. LZE caused no cytotoxicity in HT-29 cells at doses less than 10,000 microg/ml. Increasing concentrations of LZE reduced prostaglandin E2 production, but increased nitric oxide production. LZE treatment induced apoptosis by increasing the activity of caspase-3. RT-PCR showed that LZE at a concentration of 5000 microg/ml decreased the expression of cyclooxygenase-2 mRNA. Among 42 cytokines tested by protein array in this study, supplementation of LZE at doses of 500 and 5000 microg/ml to HT-29 cells reduced the expression of interleukin-8, macrophage inflammatory protein 1-delta, vascular epithelial growth factor, and platelet-derived growth factor. These results suggest that LZE has pro-apoptotic and anti-inflammatory functions, as well as inhibitory effects on cytokine expression during early

inflammation in colonic carcinoma cells, which may be of significance in the use of Chinese herbal alternative medicines for cancer prevention.

Novel antioxidant peptides from fermented mushroom Ganoderma lucidum.:J Agric Food Chem. 2004 Oct 20;52(21):6646-52.Sun J, He H, Xie BJ.College of Food Science and Technology, Huazhong Agricultural University, Wuhan, Hubei 430070, People's Republic of China.

Oxidative stress has been linked with the pathogenesis of many human diseases including cancer, aging, and atherosclerosis. The present study investigates the antioxidant activities of peptides isolated from the medicinal mushroom, Ganoderma lucidum. G. lucidum has been shown to possess potent antioxidant activity with little or no side effects. Polysaccharide, polysaccharide-peptide complex, and phenolic components of G. lucidum have been proposed to be responsible for this antioxidant effect. However, research has shown that the G. lucidum peptide (GLP) is the major antioxidant component of G. lucidum. The objective of this study was to evaluate the antioxidant activity of this peptide using different oxidation systems. GLP showed potent antioxidant activities in both lightproof soybean oil and lard systems, assessed by lipid peroxidant value. Compared to butylated hydroxytoluene, GLP showed a higher antioxidant activity in the soybean oil system. Soybean lipoxygenase activity was blocked by GLP in a dose-dependent manner with an IC50 value of 27.1 microg/mL. GLP showed scavenging activity toward hydroxyl radicals produced in a deoxyribose system with an IC50 value of 25 microg/mL, and GLP effectively quenched superoxide radical anion produced by pyrogallol autoxidation in a dose-dependent manner. Malondialdehyde level has been used as the oxidation index in many biological systems. GLP showed substantial antioxidant activity in the rat liver tissue homogenates and mitochondrial membrane peroxidation systems. The auto-hemolysis of rat red blood cells was also blocked by GLP in a dose-dependent manner. On the basis of these results, it is concluded that GLP is the major constituent responsible for the antioxidant activity of G. lucidum. GLP could play an important role in the inhibition of lipid peroxidation in biological systems through its antioxidant, metal chelating, and free radical scavenging activities.

Polysaccharides of Ganoderma lucidum alter cell immunophenotypic expression and enhance CD56+ NK-cell cytotoxicity in cord blood.:Bioorg Med Chem. 2004 Nov 1;12(21):5603-9.Chien CM, Cheng JL, Chang WT, Tien MH, Tsao CM, Chang YH, Chang HY, Hsieh JF, Wong CH, Chen ST.Institute of Biological Chemistry and the Genomics Research Center, Academia Sinica, Nankang, Taipei 115, Taiwan.

In our previous study, a fucose-containing glycoprotein fraction (F3), isolated from the water-soluble extracts of Ganoderma lucidum, was shown to stimulate mice spleen cell proliferation and cytokine expression. We now further investigate the effect of F3 on the immunophenotypic expression in mononuclear cells (MNCs). When human umbilical cord blood (hUCB) MNCs were treated with F3 (10-100 microg/mL) for 7days, the population of CD14+CD26+ monocyte/macrophage, CD83+CD1a+ dendritic cells, and CD16+CD56+ NK-cells were 2.9, 2.3, and 1.5 times higher than those of the untreated controls ($p<0.05$). B-cell population has no significant change. T cell growth was, however, slightly inhibited and CD3 marker expression decreased approximately 20% in the presence of higher concentrations of F3 (100 microg/mL). We also found that F3 is not harmful to human cells in vitro, and after F3 treatment, NK-cell-mediated cytotoxicity was significantly enhanced by 31.7% ($p<0.01$) at effector/target cell ratio (E/T) 20:1, but was not altered at E/T 5:1.

Studies on the immuno-modulating and anti-tumor activities of Ganoderma lucidum (Reishi) polysaccharides.:Bioorg Med Chem. 2004 Nov 1;12(21):5595-601.Chen HS, Tsai YF, Lin S, Lin CC, Khoo KH, Lin CH, Wong CH.The Genomic Research Center, Academia Sinica, No. 128 Academia Road, Section 2, Nan-Kang, Taipei 11529, Taiwan.

We describe here the isolation of Reishi polysaccharides for the study of their effect on cytokine expression in mouse splenocytes. A fraction (F3) has been shown to activate the expression of IL-1, IL-6, IL-12, IFN-gamma, TNF-alpha, GM-CSF, G-CSF, and M-CSF, and from this three subfractions have been prepared where F3G1 activates IL-1, IL-12, TNF-alpha, and G-CSF, F3G2 activates all the cytokines as F3 does, and F3G3 activates only IL-1 and TNF-alpha. Together with previous studies, the mode of action on macrophages has been proposed where F3 binds to TLR4 receptor and activates extracellular signal-regulated kinase (ERK), c-Jun N-

terminal kinase (JNK) and p38 to induce IL-1 expression.

Links between morphology and physiology of Ganoderma lucidum in submerged culture for the production of exopolysaccharide.: J Biotechnol. 2004 Oct 19;114(1-2):153-64.Wagner R, Mitchell DA, Sassaki GL, de Almeida Amazonas MA.Departamento de Bioqu¨ªmica e Biologia Molecular, Universidade Federal do Paran¨¢, Caixa Postal 19046, Centro Polit¨¦cnico, Curitiba 81530-990, Paran¨¢, Brazil.

Ganoderma lucidum was grown in submerged culture in shake flasks on a medium containing peptone, yeast extract and glucose. In pre-cultures, inoculated from an agar-grown culture, morphological and metabolic events were linked: the pellets originally produced protuberances when glucose was present in the medium, although glucose was not consumed. The protuberances were then liberated into the medium as second-generation pellets, at which time glucose consumption began and the rate of exopolysaccharide (EPS) production increased. The synchrony between events was repeated in cultures fed with either glucose or peptone and yeast extract. In main cultures, inoculated from a 16-day-old pre-culture, the biomass concentration increased linearly, while glucose consumption and EPS production were initially slow but then accelerated. Protuberances were produced and liberated similarly to the pre-culture, but there was less synchrony amongst the pellets. When glucose was added to such a culture on day 10, an EPS concentration of 5.7 g L(-1) was achieved on day 13, this being the highest reliable EPS concentration yet reported for submerged culture of G. lucidum. We conclude that a greater understanding of the morphological and physiological events during the culture of G. lucidum will allow the proposal of culture strategies to improve EPS production.

Isolation and characterization of alpha-glucosidase inhibitor from the fungus Ganoderma lucidum.:J Microbiol. 2004 Sep;42(3):223-7.Kim SD, Nho HJ.Department of Biological Engineering, Seokyeong University, Seoul 136-704, Korea. sdkim@skuniv.ac.kr

An alpha-glucosidase inhibitor, SKG-3, was isolated from the fruiting bodies of Ganoderma lucidum and its physico-chemical properties were characterized. It was a highly specific and effective reversible inhibitor of alpha-glucosidase. It showed very potent inhibitory activity against alpha-glucosidase with an IC50 value of 4.6 micro g/ml, but no activity for any other glycosidases tested. Enzyme activity could be recovered upon dialysis, thus providing evidence for the reversibility of the inhibition. A Lineweaver-Burk plot indicated that the SKG-3 inhibition of alpha-glucosidase was competitive.

Immune receptors for polysaccharides from Ganoderma lucidum.:Biochem Biophys Res Commun. 2004 Oct 8;323(1):133-41.Shao BM, Dai H, Xu W, Lin ZB, Gao XM.Department of Immunology, Peking University Health Science Center, School of Basic Medical Sciences, Beijing, China.

This study was designed to identify and characterize the immune receptors for polysaccharides from Ganoderma lucidum, a Chinese medicinal fungus that exhibits anti-tumor activities via enhancing host immunity. We herein demonstrate that G. lucidum polysaccharides (GLPS) activated BALB/c mouse B cells and macrophages, but not T cells, in vitro. However, GLPS was unable to activate splenic B cells from C3H/HeJ mice that have a mutated TLR4 molecule (incapable of signal transduction) in proliferation assays. Rat anti-mouse TLR4 monoclonal antibody (Ab) inhibited the proliferation of BALB/c mouse B cells under GLPS stimulation. Combination of Abs against mouse TLR4 and immunoglobulin (Ig) achieved almost complete inhibition of GLPS-induced B cell proliferation, implying that both membrane Ig and TLR4 are required for GLPS-mediated B cell activation. In addition, GLPS significantly inhibited the binding of mouse peritoneal macrophages with polysaccharides from Astragalus membranaceus, which is known to bind directly with TLR4 on macrophage surface. Moreover, GLPS induced IL-1beta production by peritoneal macrophages from BALB/c, but not C3H/HeJ, mice, suggesting that TLR4 is also involved in GLPS-mediated macrophage activation. We Further identified a unique 31 kDa serum protein and two intracellular proteins (ribosomal protein S7 and a transcriptional coactivator) capable of binding with GLPS in co-precipitation experiments. Our results may have important implications for our understanding on the molecular mechanisms of immunopotentiating polysaccharides from traditional Chinese medicine.

A preliminary report on solid-state fermentation of Ganoderma lucidum with Radix Astragali containing medium.:Zhong Xi Yi Jie He Xue Bao. 2004 May;2(3):216-8.Institute of Medicinal Fungi & Bio-Technology of Traditional Chinese Medicine, College of Pharmacy, Nanjing University of Traditional Chinese Medicine, Nanjing, Jiangsu Province 210029, China.

OBJECTIVE: To test the practicability of the solid-state fermentation for medicinal fungi by fermenting Ganoderma lucidum with Radix Astragali containing medium. METHODS: Ganoderma lucidum was fermented in ordinary medium, drug-containing medium (containing Radix Astragali) and selenium-rich drug-containing medium respectively. The polysaccharide contents of fermentation products from the three kinds of culture media were tested at different time, and the changes were compared. RESULTS: The polysaccharide contents of fermentation products from the three kinds of culture media were 4.65%, 3.76% and 4.50% respectively and their relative standard deviation were 1.61%, 1.99% and 1.86% respectively. By observing the changes of the contents of polysaccharide, protein and total saponin in fermentation products from the drug-containing medium at different time, it was found that the 28th fermentation day was the time when secondary metabolism was most active, and it should be the fermented terminal point. CONCLUSION: The fermentative combination of Ganoderma lucidum and Radix Astragali is practicable.

Ganoderma lucidum spore extract inhibits endothelial and breast cancer cells in vitro.:Oncol Rep. 2004 Sep;12(3):659-62.Lu QY, Sartippour MR, Brooks MN, Zhang Q, Hardy M, Go VL, Li FP, Heber D.Department of Medicine, Center for Human Nutrition, University of California-Los Angeles, Los Angeles, CA 90095, USA.

This study was conducted to investigate the anti-proliferative activities of medicinal mushroom Ganoderma lucidum (Rei-shi or Mannentake). We have identified an alcohol extract from the spore of Ganoderma lucidum that inhibits the in vitro proliferation of human umbilical vein endothelial cells and MDA-MB231 human breast cancer cells. Further fractionation of the alcohol extract revealed that the ethyl acetate fraction inhibited both cell lines in a dose-dependent manner from 2 to 40 micro g/ml. Our results suggest that the alcohol extract from the spore of Ganoderma lucidum may possess potential anti-tumor and anti-angiogenic activities.

Enhancement of mycelial growth and polysaccharide production in Ganoderma lucidum (the Chinese medicinal fungus, 'Lingzhi') by the addition of ethanol.:Biotechnol Lett. 2004 May;26(10):841-4.Yang HL, Wu TX, Zhang KC.Key Laboratory of Industrial Biotechnology, Ministry of Education, Southern Yangtze University, Wuxi, PR China.

Methanol, ethanol, 1-propanol and 2-propanol, at 1.5% (v/v), enhanced the growth and polysaccharide production of Ganoderma lucidum. Ethanol was the most effective at 1.5% (v/v) for increasing the biomass production, however, the maximal polysaccharide concentration was produced with 2% (v/v) ethanol in the medium. There was no new polysaccharide component produced by the addition of ethanol.

Xylanase production by Ganoderma lucidum on liquid and solid state fermentation.:Indian J Exp Biol. 2003 Jun;41(6):620-6.Malarvizhi K, Murugesan K, Kalaichelvan PT.Centre for Advanced Studies in Botany, University of Madras, Guindy Campus, Chennai 600 025, India.

Ganoderma lucidum, a white rot fungus, was exploited for its potentials to produce xylanase employing shake and solid-state culture conditions. Different culture conditions such as pH, temperature, carbon and nitrogen requirements for its growth and production of xylanase were optimized. The culture media pH 6.0-7.0 and temperatures 30 degrees-35 degrees C significantly promoted the growth as well as xylanase secretion into the media. Xylan and peptone were found to be the suitable carbon and nitrogen sources. Among the different agrowastes used, wheat bran was found to be the best substrate for the test fungus for the production of xylanase than sugarcane bagasse and rice bran in solid-state fermentation.

Polysaccharide extract isolated from ganoderma lucidum protects rat cerebral cortical neurons from hypoxia/reoxygenation injury.:J Pharmacol Sci. 2004 Jun;95(2):294-8.Zhao HB, Lin SQ, Liu JH, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center, Beijing, China.

The effect of polysaccharide extract isolated from Ganoderma lucidum (GI-PS) on rat cortical neuronal cultures exposed to hypoxia/reoxygenation (H/R) was studied in vitro. GI-PS (1, 10, 100 microg/ml) increased neuron viability following H/R as measured by the inhibition of MTT reduction. GI-PS also significantly reduced malondialdehyde content and reactive oxygen species production and increased the manganese superoxide dismutase (Mn-SOD) activity; furthermore, the translocation of nuclear factor-kappa B induced by H/R was blocked. These findings suggest that GI-PS might be useful in treating H/R-induced oxidative stress and Mn-SOD might play a critical role in the neuroprotective effect of GI-PS against H/R injury.

Medicinal mushroom extracts inhibit ras-induced cell transformation and the inhibitory effect requires the presence of normal cells.:Carcinogenesis. 2004 Jul;25(7):1177-83.Hsiao WL, Li YQ, Lee TL, Li N, You MM, Chang ST.Biomedical Science, School of Chinese Medicine, Hong Kong Baptist University, Hong Kong, China. bowhsiao@hkbu.edu.hk

Previously, we developed a simple Rat 6 (R6) cell system by which the inhibitory effects of non-cytotoxic chemicals can be assessed by focus formation assay upon transfection of ras oncogene to the host cells. Using this system, two well studied medicinal mushrooms Ganoderma lucidum and Tricholoma lobayense with anticancer potential were examined for their possible advert effects on cell transformation induced by ras oncogene. Results indicated that both species of mushrooms yielded strong inhibitory effects on ras-induced cell transformation. Further study on T.lobayense indicated that the DEAE-column-bound, polysaccharides (PS)-peptide enriched, but not the unbound fraction, showed strong inhibition in a dosage-dependent manner. Subsequent time course study revealed that the continued presence of the extract in the transfected cultures was required for a maximum inhibitory effect. At the same time, we also observed that significant levels of inhibition occurred even when the application of the extract was delayed until day 12 after transfection. Using a stable transformed cell line, R6/GFP-Ras expressing green fluorescent protein-ras fusion protein in a co-culture assay with normal R6 cells, we demonstrated that R6/GFP-Ras cells grew into green fluorescent foci with striking transforming morphology in the absence of extracts. However, in the presence of extracts, R6/GFP-Ras cells, in most cases, remained as small colonies compiled with only a few green fluorescent cells. Moreover, the inhibitory effect requires the presence of R6 cells. In our study, mushroom extracts have no effect on the growth of individually cultured normal and transformed R6 cells. It is noteworthy that the extracts do not affect the level, or the subcellular localization of the Ras protein. Collectively, the data strongly suggest that the inhibitory effect of the mushroom extracts is not due to a direct killing of the transformed cells, rather, it may be mediated through the surrounding normal R6. While the general understanding of the antitumor effect of PS and PSPC is mediated through the cytokines released by activated macrophages and T-lymphocytes, our data may provide a novel alternative mechanism that the mushroom PS peptides may exert anticancer effect by targeting the ras-mediated signaling pathway.

Activation of mouse macrophages by the alkali-extracted polysaccharide from spore of Ganoderma lucidum.:Xi Bao Yu Fen Zi Mian Yi Xue Za Zhi. 2004 Mar;20(2):142-4.Tang QJ, Zhang JS, Pan YJ, Reutter W, Fan H.Institute of Molecularbiology and Biochemistry, Free University Berlin, Berlin, Germany. tangqingjiu2003@yahoo.com.cn

AIM: To investigate the activation of mouse macrophages by the alkali-extracted polysaccharides from the spore of Ganoderma lucidum (LZSBS). METHODS: The mouse macrophages cultured in-vitro were stimulated by LZSBS. IL-1beta and TNF-alpha in the culture supernatants were detected by ELISA. NO production was detected by Griess assay. The percentage of phagocytosis of latex beads by mouse macrophages was counted under microscope. RESULTS: The mouse macrophages stimulated by LZSBS increased in volume and darkened in appearance under phase-contrast microscope. LZSBS-activated mouse macrophages secreted IL-1beta and TNF-alpha produced a large amount of NO. The percentage of phagocytosis of latex beads by mouse macrophages was also significantly increased in the presence of LZSBS. CONCLUSION: LZSBS can activate markedly the mouse macrophages.

Quantitative determination of bitter principles in specimens of Ganoderma lucidum using high-performance liquid chromatography and its application to the evaluation of ganoderma products.:Chem Pharm Bull. 2004 Jun;52(6):688-95.

For quantitative determination of 19 triterpene constituents, including six ganoderma alcohols (1-6) and 13 ganoderma acids (7-19), in the products of Ganoderma lucidum, an analytical system was developed using high-performance liquid chromatography with an ODS column. The mobile phase was a linear gradient of 1% AcOH/H(2)O-CH(3)CN and 2% AcOH/H(2)O-CH(3)CN, and the elution profile was monitored at 243 and 250 nm for ganoderma alcohols and acids, respectively. The relative standard deviations of this method were less than 2.35% and 2.18% (n=5) for intraday and interday assays, and the recoveries were 90.9-100.8% and 93.4-103.9% for constituents of alcohol and acid groups, respectively. This system was applied to a quantitative determination of the constituents in 10 different products of G. lucidum: six usual umbrella forms of the fruiting bodies, three antlered forms of the fruiting bodies and spores, and eight specimens from the same G. lucidum strain, which was parasitized on logs from different plants or different fungus beds. The analytical results indicated that the quantity and composition of these triterpenes differed appreciably among various specimens, but the relative ratio of the alcohols and acids was not significantly different when the same strain of G. lucidum was used.

Selenium distribution in a Se-enriched mushroom species of the genus Ganoderma.:J Agric Food Chem. 2004 Jun 16;52(12):3954-9.Zhao L, Zhao G, Zhao Z, Chen P, Tong J, Hu X. DAPR Laboratory, College of Food Science and Nutritional Engineering, China Agricultural University, Beijing 100083, People's Republic of China.

Data reported here show that Ganoderma lucidum could biotransform inorganic selenite in the substrate into organic forms by intergrating Se into proteins (56-61%) and polysaccharides (11-18%) and other components. Furthermore, water- and alkaline-soluble protein components were mainly responsible for the storage of organic Se, and Se-Met accounts for only a minor (8.2-18.3%) amount of the selenocompounds present in proteins. The molecular mass of most proteins or protein subunits containing Se was no more than 16 kDa. A low concentration of Se (<100 microg/g) in the substrate facilitated the synthesis of total protein and amino acids in G. lucidum, but a high concentration of Se (>150 microg/g) played a reverse role. Additionally, Se concentration in the culture had no significant effect on the distribution of the amino acids and proteins.

Effect of medicinal plant extracts on forced swimming capacity in mice.:J Ethnopharmacol. 2004 Jul;93(1):75-81.Jung K, Kim IH, Han D.Food Processing Technology, Korea Food Research Institute, San 46-1, Baekhyun-dong, Bundang-ku, Songnam-si, Kyonggi-do, 463-746, Republic of Korea.

The tonic effect of Cordyceps militaris (CM), Paecilomyces japonia (PJ), Phellinus linteus (PL), Ganoderma lucidum (GL), Grifola frondosa (GF), and Panax ginseng (PG) was examined based on the forced swimming capacity and the change of biochemical parameters in ICR mice. The treatment groups were orally administered medicinal plant extracts (500 mg/kg per day), while the control group received distilled water for 4 weeks. The swimming times to exhaustion were longer in the CM, PJ, and GF groups than in the control group ($P < 0.05$). Plasma TG levels were lower in the treatment groups than in the control group. Plasma glucose levels were not significantly different between the control group and each treatment group except the PG group. Plasma lactate and ammonia levels of the PJ and GF groups were lower than those of the control group ($P < 0.05$). There were no significant differences in the content of liver and gastrocnemius muscle glycogen between the control group and each treatment group. In conclusion, PJ and GF extracts enhanced the forced swimming capacity of mice by increasing fat utilization and by delaying the accumulation of plasma lactate and ammonia.

Immunomodulatory and antimicrobial effects of some traditional chinese medicinal herbs: a review.:Curr Med Chem. 2004 Jun;11(11):1423-30.Tan BK, Vanitha J.Department of Pharmacology, Faculty of Medicine, National University of Singapore, 18 Medical Drive,

Singapore 117597. phctankh@nus.edu.sg

The current practice of ingesting phytochemicals to support the immune system or to fight infections is based on centuries-old tradition. We review reports on seven Chinese herbs, (Aloe vera Mill. (Aloaceae), Angelica species (Umbelliferae), Astragalus membranaceus Bunge. (Leguminosae), Ganoderma lucidum (Fr.) Karst. (Ganodermataceae), Panax ginseng C.A Mey. (Araliaceae), Scutellaria species (Lamiaceae) and Zingiber officinale Rosc. (Zingiberaceae) with emphasis to their immunomodulatory and antimicrobial activities. While some of these herbaceous plants have a direct inhibitory effect on microbial organisms, we observe that each plant has at least one compound that selectively modulates cells of the immune system. The successful derivation of pure bioactive compounds from Ganoderma lucidum, ginseng and Zingiber officinale supports the traditional practice of using these plants to stimulate the immune system. As many modern drugs are often patterned after phytochemicals, studying the influence of each compound on immune cells as well as microbes can provide useful insights to the development of potentially useful new pharmacological agents.

Antitumor and anti-angiogenic activity of Ganoderma lucidum polysaccharides peptide.:Acta Pharmacol Sin. 2004 Jun;25(6):833-8.Cao QZ, Lin ZB.Department of Pharmacology, Health Science Center, Peking University, Beijing 100083, China.

AIM: To investigate the antitumor and anti-angiogenic activity of Ganoderma lucidum polysaccharides peptide (GLPP). METHODS: Antitumor effect of GLPP was observed in tumor-bearing mice in vivo. At the same time, the effects of GLPP on proliferation of tumor cells and human umbilical cord vascular endothelial cell (HUVEC) were detected by MTT assay in vitro. Subsequently, spleen lymphocytes proliferation of nude mice was stimulated by LPS or ConA. To investigate the anti-angiogenic effect of GLPP, GLPP 80 microg per disc and GLPP-treated serum 10 microL per disc were added to the chick chorioallantoic membrane (CAM) respectively in vivo. RESULTS: GLPP 50, 100, and 200 mg/kg inhibited growth of Sarcoma 180 in BALB/c mice markedly by 35.2 %, 45.2 %, and 61.9 %, respectively. GLPP which was directly added to the cultured medium did not inhibit PG cell proliferation in vitro; but GLPP-treated serum 50, 100, 200 mg/kg potently inhibited PG cell proliferation by 22.5 %, 26.8 %, and 30.3 %, respectively; and reduced the xenograft (human lung carcinoma cell PG) in BALB/c nude mice greatly in vivo by 55.5 %, 46.0 %, and 46.8 %, respectively. Lymphocytes proliferation of nude mice could be stimulated by LPS 5 mg/L but not by ConA 2.5 mg/L, indicating that GLPP could not promote the T lymphocyte proliferation and neutral red phagocytosis of peritoneal macrophages of nude mice. The CAM assay showed that GLPP and GLPP-treated serum had anti-angiogenic effect. GLPP (1, 10, and 100 mg/L) inhibited HUVEC proliferation in vitro with the inhibitory rate of 9.4 %, 15.6 %, and 40.4 %, respectively. CONCLUSION: GLPP has antitumor and anti-angiogenic activity. The anti-angiogenesis of GLPP may be a new mechanism underlying its anti-tumor effects.

Study on preparation process and analytical methods of ESAC from Ganoderma lucidum.:Zhongguo Zhong Yao Za Zhi. 2003 Apr;28(4):332-4.Huang SM, Yang XL, Wang BW, Zhu HS, Xu JL.School of Life Sciences and Technology, Beijing Institute of Technology, Beijing 100081, China.

OBJECTIVE: To develop the procedure for separating the ethanol-soluble and acidic components (ESAC) from Ganoderma lucidum, and to establish a method for quantifying ESAC in G. lucidum. METHOD: The ethanol extract of G. lucidum was extracted with a saturated NaHCO3 solution, acidified and re-extracted by chloroform to obtain ESAC. The quantitative analysis of ESAC was based on the characteristic color reaction between ESAC and H2SO4. RESULT: The optimal conditions for separating ESAC on a 10 g scale are as follows: ratio of material and ethanol (mL), 1:15; immersing time, 24 h; volume of saturated NaHCO3 and chloroform, 1300 mL; extract 3 times. The condition for measuring ESAC is as follows: sample weight, 1 g; solution volume, 1.5 mL; immuersing time, 0.5 h; detecting reagent, 50% H2SO4 in ethanol; heating time in 100 degrees C water bathe, 3 min; measuring wavelength, 490 nm. CONCLUSION: The procedure for ESAC preparation is simple and well-designed, and the established method for ESAC can be used for the qualitative analysis of the G. lucidum related products.

Immuno-potentiating effects of the antler-shaped fruiting body of Ganoderma lucidum

(Rokkaku-Reishi).:Biosci Biotechnol Biochem. 2004 Apr;68(4):881-7.

The immuno-potentiating effects of the antler-shaped fruiting body of Ganoderma lucidum (Rokkaku-Reishi, RR), which has been used as a traditional supplement for human health, were investigated in mice. BALB/c mice were administered orally with RR for 3 days at a dose of 50 mg/kg or 500 mg/kg, and interferon-gamma (IFN-gamma) production by splenocytes in response to lipopolysaccharide (LPS) was examined on day 4. The oral administration of 500 mg/kg of RR resulted in a significant increase ($p<0.05$) in IFN-gamma production. Stimulation of splenic adherent cells from these mice with LPS also resulted in a significant increase ($p<0.05$) in interleukin-12 (IL-12) production compared with that from the control mice, suggesting that splenic macrophages were activated by RR administration. Furthermore, 500 mg/kg of RR administered for 14 days resulted in a significant increase ($p<0.05$) in IFN-gamma production by splenocytes in response to both LPS and concanavalin A (Con A). These results suggest that not only splenic macrophages but also T cells were activated by the long-term treatment with RR in vivo. On the other hand, the production of interleukin-4 (IL-4), which is known as an allergic disease-related cytokine, was not affected by the long-term treatment with RR. Our results suggest that the oral administration of RR resulted in Th1-associated immuno-potentiating activities in vivo.

Ganoderma lucidum inhibits proliferation and induces apoptosis in human prostate cancer cells PC-3.:Int J Oncol. 2004 May;24(5):1093-9.Jiang J, Slivova V, Valachovicova T, Harvey K, Sliva D.Cancer Research Laboratory, Methodist Research Institute, E504, Indianapolis, IN 46202, USA.

Ganoderma lucidum (Reishi), an oriental medical mushroom, has been widely used in Asian countries for centuries to prevent or treat different diseases, including cancer. However, the mechanism(s) responsible for the effects of Ganoderma lucidum on cancer cells remain to be elucidated. We have previously demonstrated that Ganoderma lucidum down-regulated the expression of NF-kappaB-regulated urokinase plasminogen activator (uPA) and uPA receptor (uPAR), which resulted in suppression of cell migration of highly invasive human breast and prostate cancer cells. In this study, we investigated the effects of Ganoderma lucidum on cell proliferation, cell cycle, and apoptosis in human prostate cancer cells PC-3. Our data demonstrate that Ganoderma lucidum inhibits cell proliferation in a dose- and time-dependent manner by the down-regulation of expression of cyclin B and Cdc2 and by the up-regulation of p21 expression. The inhibition of cell growth was also demonstrated by cell cycle arrest at G2/M phase. Furthermore, Ganoderma lucidum induced apoptosis of PC-3 cells with a slight decrease in the expression of NF-kappaB-regulated Bcl-2 and Bcl-xl. However, the expression of proapoptotic Bax protein was markedly up-regulated, resulting in the enhancement of the ratio of Bax/Bcl-2 and Bax/Bcl-xl. Thus, Ganoderma lucidum exerts its effect on cancer cells by multiple mechanisms and may have potential therapeutic use for the prevention and treatment of cancer.

Genetic transformation and mutant isolation in Ganoderma lucidum by restriction enzyme-mediated integration.:FEMS Microbiol Lett. 2004 Apr 15;233(2):201-4.Kim S, Song J, Choi HT.Microbial Physiology Laboratory, Division of Life Sciences, Kangwon National University, Chunchon 200-701, South Korea.

A white-rot basidiomycete Ganoderma lucidum has long been used as a medicinal mushroom in Asia, and it has an array of enzymes important for wood degrading activity. There have been many reports about the ingredients which show health aiding effects. In order to analyze gene functions and introduce foreign genes into this fungus, genetic transformation is required. We have successfully transformed G. lucidum to geneticin resistance using pJS205-1 which has the antibiotic resistance genes against geneticin and phosphinothricin. Many different mutants have been generated during the transformation by restriction enzyme mediated integration, and the transformation yield was 4-17 transformants (microg plasmid DNA)(-1). The plasmid was integrated stably into the recipient chromosome, which was confirmed by PCR with the plasmid-specific primers.

Cholesterol-lowering properties of Ganoderma lucidum in vitro, ex vivo, and in hamsters and minipigs.:Lipids Health Dis. 2004 Feb 18;3:2.Berger A, Rein D, Kratky E, Monnard I, Hajjaj H, Meirim I, Piguet-Welsch C, Hauser J, Mace K, Niederberger P.Nestl¨¦ Research Center, Lausanne 26, 1000, Switzerland. aberger@paragen.com

INTRODUCTION: There has been renewed interest in mushroom medicinal properties. We studied cholesterol lowering properties of Ganoderma lucidum (Gl), a renowned medicinal species. RESULTS: Organic fractions containing oxygenated lanosterol derivatives inhibited cholesterol synthesis in T9A4 hepatocytes. In hamsters, 5% Gl did not effect LDL; but decreased total cholesterol (TC) 9.8%, and HDL 11.2%. Gl (2.5 and 5%) had effects on several fecal neutral sterols and bile acids. Both Gl doses reduced hepatic microsomal ex-vivo HMG-CoA reductase activity. In minipigs, 2.5 Gl decreased TC, LDL- and HDL cholesterol 20, 27, and 18%, respectively ($P < 0.05$); increased fecal cholestanol and coprostanol; and decreased cholate. CONCLUSIONS: Overall, Gl has potential to reduce LDL cholesterol in vivo through various mechanisms. Next steps are to: fully characterize bioactive components in lipid soluble/insoluble fractions; evaluate bioactivity of isolated fractions; and examine human cholesterol lowering properties. Innovative new cholesterol-lowering foods and medicines containing Gl are envisioned.

Hypoglycemic effect of Ganoderma lucidum polysaccharides.:Acta Pharmacol Sin. 2004 Feb;25(2):191-5.Zhang HN, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University, Beijing 100083, China.

AIM: To investigate the hypoglycemic effect of Ganoderma lucidum polysaccharides (Gl-PS) in the normal fasted mice and its possible mechanism. METHODS: Normal fasted mice were given a single dose of Gl-PS 25, 50, and 100 mg/kg by i.p. and the serum glucose was measured at 0, 3, and 6 h after administration. Gl-PS 100 mg/kg were also given by i.p. and the serum glucose and insulin levels were measured at 0 min, 30 min, 1 h, 3 h, 6 h, and 12 h. Pancreatic islets were isolated and incubated with glucose 5.6 mmol/L and different concentration of Gl-PS, the insulin content of islets and insulin release were examined. The islets fluorescent intensity of [Ca2+]i was also studied with a confocal microscope. Verapamil and egtazic acid were used to testify whether the insulin-releasing effect of Gl-PS was mediated by its ability to raise the Ca2+ influx. RESULTS: Gl-PS dose-dependently lowered the serum glucose levels at 3 h and 6 h after administration. Gl-PS 100 mg/kg raised the circulating insulin levels at 1 h after administration. In vitro, Gl-PS had no effect on islets insulin content, but it stimulated the insulin release after incubation with glucose 5.6 mmol/L. Confocal microscope showed that Gl-PS 100 mg/L had the capacity to raise the [Ca2+]i. The insulin-releasing effect of Gl-PS was inhibited by verapamil/egtazic acid. CONCLUSION: Gl-PS possesses the hypoglycemic effect on normal mice; one mechanism is through its insulin-releasing activity due to a facilitation of Ca2+ inflow to the pancreatic beta cells.

Ganoderma lucidum ("Lingzhi"), a Chinese medicinal mushroom: biomarker responses in a controlled human supplementation study.:Br J Nutr. 2004 Feb;91(2):263-9.Wachtel-Galor S, Tomlinson B, Benzie IF.Ageing & Health Group, School of Nursing, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR, China.

Lingzhi (Ganoderma lucidum) is a woody mushroom highly regarded in traditional medicine and is widely consumed in the belief that it promotes health and longevity, lowers the risk of cancer and heart disease and boosts the immune system. However, objective scientific validation of the putative health benefits of Lingzhi in human subjects is lacking, and issues of possible toxicity must be addressed. The present double-blinded, placebo-controlled, cross-over intervention study investigated the effects of 4 weeks Lingzhi supplementation on a range of biomarkers for antioxidant status, CHD risk, DNA damage, immune status, and inflammation, as well as markers of liver and renal toxicity. It was performed as a follow-up to a study that showed that antioxidant power in plasma increased after Lingzhi ingestion, and that 10 d supplementation was associated with a trend towards an improved CHD biomarker profile. In the present study, fasting blood and urine from healthy, consenting adults (n 18; aged 22-52 years) was collected before and after 4 weeks supplementation with a commercially available encapsulated Lingzhi preparation (1.44 g Lingzhi/d; equivalent to 13.2 g fresh mushroom/d) or placebo. No significant change in any of the variables was found, although a slight trend toward lower lipids was again seen, and antioxidant capacity in urine increased. The results showed no evidence of liver, renal or DNA toxicity with Lingzhi intake, and this is reassuring. The present study of the effects in healthy, well-nourished subjects provides useful, new scientific data that will support controlled intervention trials using at-risk subjects in order to assess the therapeutic effect of Lingzhi in the promotion of healthy ageing.

A distinctive ribonuclease from fresh fruiting bodies of the medicinal mushroom Ganoderma lucidum.:Biochem Biophys Res Commun. 2004 Feb 6;314(2):519-22.Wang HX, Ng TB, Chiu SW.Department of Microbiology, College of Biological Science, China Agricultural University, Beijing, China.

A ribonuclease with an N-terminal sequence distinct from other mushroom ribonucleases was isolated from fresh fruiting bodies of the medicinal mushroom Ganoderma lucidum. The ribonuclease was adsorbed on DEAE-cellulose and Q-Sepharose, and unadsorbed on CM-Sepharose. It possessed a molecular mass of 42 kDa as judged by gel filtration by fast protein liquid chromatography on Superdex 75 and sodium dodecyl sulfate-polyacrylamide gel electrophoresis. Its molecular mass was similar to that of straw mushroom ribonuclease but much higher compared with those of other mushroom ribonucleases. The ribonuclease was unique among mushroom ribonucleases in that it exhibited the highest potency toward poly(U), followed by poly(A). Its activity toward poly(G) and poly(C) was about one-half of that toward poly(A) and one-quarter of that toward poly(U). A pH of 4.0 and a temperature of 60 degrees C were required for optimal activity of the enzyme. The optimum pH was low compared with those reported for other mushroom ribonucleases.

Treatment of glomerular endothelial dysfunction in steroid-resistant nephrosis with Ganoderma lucidum, vitamins C, E and vasodilators.:Clin Hemorheol Microcirc. 2003;29(3-4):205-10.Futrakul N, Boonyen M, Patumraj S, Siriviriyakul P, Tosukhowong P, Futrakul P.Departments of Physiology and Pediatrics, King Chulalongkorn Memorial Hospital, Bangkok 10330, Thailand. fmedpft@md2.md.chula.ac.th

Glomerular endothelial dysfunction is believed to be responsible for the proteinuria and nephronal damage, namely tubulointerstitial fibrosis and glomerulosclerosis, observed in severe nephrosis such as focal segmental glomerulosclerosis. A dysfunctioning glomerular endothelium is likely to be induced by oxidative stress and oxidized LDL as well as altered immunocirculatory balance with a defective anti-inflammatory pathway. A defective release of vasodilator inconjunction with enhanced production of angiotensin II induces hemodynamic maladjustment by preferential constriction at the efferent arteriole. Such a hemodynamic maladjustment exerts two significant hemodynamic impacts. Close to the efferent constriction, it induces intraglomerular hypertension and glomerulosclerosis. Far from the efferent constriction, it reduces peritubular capillary flow, which eventually leads to tubulointerstitial fibrosis. Treatment with a vasodilator improves the hemodynamic maladjustment but does not completely suppress proteinuria. A successful suppression of proteinuria is accomplished by using Ganoderma lucidum and vitamins C and E. The beneficial effect of Ganoderma lucidum appears to be multifactorial, including the modulation of immunocirculatory balance, antilipid, vasodilator, antiplatelet and improved hemorheology. Together with vitamins C and E, this helps to neutralize oxidative stress and suppress the toxic effect to the glomerular endothelial function.

Effectiveness of Dp2 nasal therapy for Dp2- induced airway inflammation in mice: using oral Ganoderma lucidum as an immunomodulator.:J Microbiol Immunol Infect. 2003 Dec;36(4):236-42.Liu YH, Tsai CF, Kao MC, Lai YL, Tsai JJ.Section of Allergy and Immunology, Cathay General Hospital, Taipei, Taiwan, ROC.

Nasal immunotherapy with allergen has been reported to be effective for airway allergic disease. A group of 50 male Balb/c mice were immunized intraperitoneally with recombinant Dermatophagoides pteronyssinus group 2 (rDp2), then oral feeding with Ganoderma lucidum (known as "Ling Zhi," LZ OT) and intranasal therapy with native Dp2 (Dp2 NT) were given, the mice then received intratracheal challenge with rDp2 at 28 days and 35 days after immunization. Airway hypersensitivity to methacholine was measured 30 min (early phase) and 24 h (late phase) after the second challenge. The cytokine producing CD4 cells in PBL and interferon-gamma (IFN-gamma) concentrations in bronchoalveolar lavage fluid and sera were measured on 37 days after immunization. Both Dp2 NT and LZ OT downregulated total inflammatory cell infiltration in the airway. Dp2 NT reduced IL-5+/CD4+ cells and increased IFN-gamma+/CD4+ cells. When LZ OT was added to Dp2 NT, the reduction of IL-5+/CD4+ cells was diminished and the increment of IFN-gamma+/CD4+ cells was increased. LZ OT alone increased both IL-5+/CD4+ cells and IFN-gamma+/CD4+ cells. When LZ OT was added to Dp2 NT, IgG2a was further increased to a significant level. LZ OT alone significantly suppressed IgG1 and increased

IgG2a production. When lung function was measured after therapy, early phase airway hypersensitivity to methacholine significantly suppressed by Dp2 NT, while late phase hypersensitivity was suppressed but not to a significant level. When LZ OT was added to Dp2 NT, the suppression of late phase airway hypersensitivity to methacholine reached a significant level. In this mouse model of Dp2-induced airway hypersensitivity, Dp2 NT downregulated airway inflammatory cell infiltration and decreased immediate airway hypersensitivity to methacholine. When LZ OT was coadministered, the airway lymphocytes and circulatory IFN-gamma+/CD4+ were both increased and late phase airway hypersensitivity was decreased. These results suggest that Dp2 NT might have a therapeutic effect on Dp2-induced airway hypersensitivity and LZ OT might also have an effect on Dp2 NT immunotherapy.

Ganoderma lucidum (Reishi) in cancer treatment.:Integr Cancer Ther. 2003 Dec;2(4):358-64.Sliva D.Cancer Research Laboratory, Methodist Research Institute, Indianapolis, IN 46202, USA. d-silva@clarian.org

The popular edible mushroom Ganoderma lucidum (Reishi) has been widely used for the general promotion of health and longevity in Asian countries. The dried powder of Ganoderma lucidum was popular as a cancer chemotherapy agent in ancient China. The authors recently demonstrated that Ganoderma lucidum inhibits constitutively active transcription factors nuclear factor kappa B (NF-kappaB) and AP-1, which resulted in the inhibition of expression of urokinase-type plasminogen activator (uPA) and its receptor uPAR. Ganoderma lucidum also suppressed cell adhesion and cell migration of highly invasive breast and prostate cancer cells, suggesting its potency to reduce tumor invasiveness. Thus, Ganoderma lucidum clearly demonstrates anticancer activity in experiments with cancer cells and has possible therapeutic potential as a dietary supplement for an alternative therapy for breast and prostate cancer. However, because of the availability of Ganoderma lucidum from different sources, it is advisable to test its biologic activity.

Anti-angiogenic and inhibitory activity on inducible nitric oxide production of the mushroom Ganoderma lucidum.:J Ethnopharmacol. 2004 Jan;90(1):17-20.Song YS, Kim SH, Sa JH, Jin C, Lim CJ, Park EH.Bioanalysis and Biotransformation Research Center, Korea Institute of Science and Technology, PO Box 131, Seoul 130-650, South Korea.

Fresh fruit bodies of Ganoderma lucidum were extracted with 70% ethanol at room temperature. The extract (GL) showed significant anti-angiogenic activity, which was detected using a chick embryo chorioallantoic membrane assay. GL significantly inhibited LPS-induced NO production in RAW 264.7 macrophages. These results support the anti-tumor effect of Ganoderma lucidum.

Lucidenic acids P and Q, methyl lucidenate P, and other triterpenoids from the fungus Ganoderma lucidum and their inhibitory effects on Epstein-Barr virus activation..:J Nat Prod. 2003 Dec;66(12):1582-5.

A new triterpene acid, lucidenic acid P (1a), and two new triterpene acid methyl esters, methyl lucidenates P (1b) and Q (2b), were isolated and characterized from the fruiting body of the fungus Ganoderma lucidum. Their structures were elucidated on the basis of spectroscopic methods. In addition, eight known triterpene acids, lucidenic acids A (3a), C (4a), D(2) (5a), E(2) (6a), and F (7a) and ganoderic acids E (9a), F (10a), and T-Q (11a), and six known triterpene acid methyl esters, methyl lucidenates A (3b), D(2) (5b), E(2) (6b), F (7b), and L (8b) and methyl ganoderate F (10b), were isolated and identified from the fungus. All of the triterpenoids, with the exception of 7a, were evaluated with respect to their inhibitory effects on the induction of Epstein-Barr virus early antigen (EBV-EA) by 12-O-tetradecanoylphorbol-13-acetate (TPA) in Raji cells, which is known to be a primary screening test for antitumor promoters. All of the compounds tested showed potent inhibitory effects on EBV-EA induction (96-100% inhibition at 1 x 10(3) mol ratio/TPA).

Scale-up of a liquid static culture process for hyperproduction of ganoderic acid by the medicinal mushroom Ganoderma lucidum.:Biotechnol Prog. 2003 Nov-Dec;19(6):1842-6.Tang YJ, Zhong JJ.State Key Laboratory of Bioreactor Engineering, East China University of Science

and Technology, 130 Meilong Road, Shanghai 200237, China.

Scale-up of a liquid static culture process was studied for hyperproduction of ganoderic acid (GA) by a famous Chinese traditional medicinal mushroom, Ganoderma lucidum. Initial volumetric oxygen transfer coefficient (K(L)a) and area of liquid surface per liquid volume (A(s)) were identified as key factors affecting cell growth and GA accumulation in liquid static cultures of G. lucidum, on the basis of which a multilayer static bioreactor was designed. At a low initial K(L)a level of 2.1 h(-1), a thick layer of white mycelia was formed on the liquid surface, and an optimal production of total GA (i.e., GA production in the liquid and on the liquid surface) was obtained. Both the formation of white mycelia and production of GA on the liquid surface were enhanced with an increase of A(s) within the range as investigated (0.24-1.53 cm(2)/mL). At an A(s) value of 0.90 cm(2)/mL, the total GA production reached maximum. A successful scale-up from a 20-mL static T-flask to a 7.5-L three-layer static bioreactor was achieved based on initial K(L)a. The maximum biomass (20.8 +/- 0.1 g DW/L), GA content (4.96 +/- 0.13 mg/100 mg DW), and total GA production (976 +/- 35 mg/L) were attained in static bioreactors. Not only GA content but also its production obtained in this work were the highest ever reported.

Ganoderma lucidum ('Lingzhi'); acute and short-term biomarker response to supplementation..:Int J Food Sci Nutr. 2004 Feb;55(1):75-83.Wachtel-Galor S, Szeto YT, Tomlinson B, Benzie IF.Ageing & Health Group, School of Nursing, The Hong Kong Polytechnic University, Kowloon, Hong Kong SAR.

Ganoderma lucidum (Lingzhi) is a popular Chinese herb with an impressive array of reputed health benefits, including antioxidant properties. However, these require scientific validation. The aim of this study was to investigate in vitro antioxidant capacity of Lingzhi, absorption and systemic distribution of Lingzhi antioxidants, and effects of short-term (10 days) supplementation on biomarkers of antioxidant status, coronary heart disease (CHD) risk and DNA damage. In this double-blinded, placebo-controlled, cross-over intervention study, blood and urine samples were collected from 10 healthy volunteers at 0 (fasting) and 45, 90, 135 and 180 min post-ingestion of a single dose (1.1g) of Lingzhi. Repeat fasting samples were collected after 10 days' supplementation with 0.72 g/d Lingzhi. The acute response (up to 3 hours) was also investigated with a larger dose (3.3 g) of Lingzhi (n=7). Results showed that the total antioxidant capacity (as the FRAP value) of an aqueous suspension of Lingzhi was 360 micromol/g. Ingestion of Lingzhi caused a significant post-ingestion increase (mean+/-SEM 23+/-3 micromol/L; P<0.05) in plasma antioxidant capacity, with peak response at 90 min. Average increase of 29+/-11% (P<0.05) in urine antioxidant capacity was seen within 3 hours of ingestion. After 10 days' supplementation with 0.72 g per day of Lingzhi, fasting plasma lipid standardised alpha-tocopherol concentration and urine antioxidant capacity increased (P<0.05). Fasting plasma ascorbic acid and total alpha-tocopherol concentrations and erythrocyte SOD and GPx activities increased slightly but non-significantly with supplementation. Plasma lipids and uric acid tended to decrease, but changes were not statistically significant. No discernable differences were seen in other variables measured. Results indicate that Lingzhi intake causes an acute increase in plasma antioxidant capacity. No deleterious effects on measured variables were seen. The pattern of biomarker response after supplementation indicated possible benefit in terms of antioxidant status and CHD risk, but further study is needed to elucidate the nature and longer-term effects of the absorbable antioxidants from Lingzhi.

Fingerprint profiling of acid hydrolyzates of polysaccharides extracted from the fruiting bodies and spores of Lingzhi by high-performance thin-layer chromatography.:J Chromatogr A. 2003 Nov 7;1018(1):85-95.Di X, Chan KK, Leung HW, Huie CW.Department of Chemistry, Hong Kong Baptist University, 224 Waterloo Road, Kowloon Tong, Hong Kong, China.

Modern extraction and planar chromatographic instrumentation were employed for the fingerprint profiling of carbohydrates from an important and popular medicinal mushroom commonly known as Lingzhi. For the first time, the feasibility of employing the high-performance thin-layer chromatography (HPTLC) peak profiles (fingerprints) of carbohydrates for the screening of various Lingzhi species/products was demonstrated. An analytical procedure was developed such that upon acid hydrolysis of the polysaccharides extracted from various Lingzhi samples, fingerprint profiles that reveal the relative amounts of the degradation products, such as mono- and oligosaccharides, can be obtained using HPTLC plates (Si 50000) for separation and 4-

aminobenzoic acid as the post-chromatographic derivatization reagent for detection. Also, using automated multiple development (AMD), the acid hydrolyzates from Lingzhi, consisting of simple and more complex sugars, can be separated simultaneously with high degree of automation. An important finding was that unique fingerprint patterns were observed in the monosaccharide profiles between two highly valued Lingzhi species, Ganoderma applanatum and Ganoderma lucidum, under total or partial acid hydrolysis conditions. Additionally, the HPTLC fingerprint profiles of carbohydrates were obtained from the extracts of the spores and fruiting bodies of Lingzhi and compared.

In vitro analysis of the properties of Beiqishen tea.:Nutrition. 2003 Oct;19(10):869-75.Bl¨¢zovics A, Szentmih¨¢lyi K, Lugasi A, Bal¨¢zs A, Hagym¨¢si K, B¨¢nyai E, Then M, Rapavi E, H¨¦thelyi E.II Department of Medicine, Semmelweis University, Budapest, Hungary. blaz@bel2.sote.hu

OBJECTIVE: Chinese Beiqishen tea was studied in an in vitro test system. METHODS: Phytochemical screening, trace element analysis, and the analysis of antioxidant properties were carried out. Characteristic constituents were determined by chromatographic (capillary gas chromatography and GCQ Ion Trap mass spectrometry) and spectrometric (ultraviolet and UV-VIS) methods. Element concentrations were determined by inductively coupled plasma optical emission spectrometry. Antioxidant capacity was studied by spectrophotometric and luminometric techniques using a Berthold Lumat 9501 luminometer. Hydrogen-donating activity, reducing power, and total scavenger capacity were measured. RESULTS: Total polyphenol content was 20.77 +/- 0.52 g/100 g of drug; total flavonoid content was 0.485 +/- 0.036 g/100 g of drug; and tannin content was 9.063 +/- 0.782 g/100 g of drug. Caffeine content was 1.08 mg/100 g of drug. Essential oils were identified by gas chromatography: (+)-limonene (21%), p-cymene (1.7%), estragol (3.2%), beta-ocimene (1.4%), and thymol (2.6%). Metallic ion analysis showed significantly high concentrations of Al, As, Ba, Cr, Cu, Fe, Mn, Ni, and Ti in the drug. Antioxidant and scavenger properties were identified as a function of concentration. CONCLUSIONS: The tea infusion contained some non-desirable trace elements and caffeine in addition to polyphenols and tannins in high concentrations. Therefore, the consumption of this tea may involve risks.

Biologic activity of spores and dried powder from Ganoderma lucidum for the inhibition of highly invasive human breast and prostate cancer cells.:J Altern Complement Med. 2003 Aug;9(4):491-7.Sliva D, Sedlak M, Slivova V, Valachovicova T, Lloyd FP, Ho NW.Cancer Research Laboratory, Methodist Research Institute, Clarian Health Partners Inc., Indianapolis, IN 46202, USA. dsliva@clarian.org

OBJECTIVE: Ganoderma lucidum has been used in East Asia as a home remedy to prevent or cure cancer. Furthermore, Ganoderma lucidum is one of the herbs in the herbal mixture PC-SPES that has become an alternative herbal therapy for prostate cancer. Because the dried powder of ganoderma is commercially available as a dietary supplement itself, the purpose of this study was to evaluate the biologic activity of samples of Ganoderma lucidum from different sources. METHODS: Samples of Ganoderma lucidum were characterized morphologically and evaluated for their ability to inhibit cell migration of highly invasive breast cancer MDA-MB-231 cells and prostate cancer PC-3 cells. Because the inhibition of cell motility is directly linked to the inhibition of the signaling pathway for constitutively active NF-kappaB in breast and prostate cancer cells, we determined how different samples of Ganoderma lucidum inhibit constitutively active NF-kappaB in a reporter gene assay. RESULTS: Some of the samples of Ganoderma lucidum demonstrated strong inhibition of cancer cell migration comparable to the inhibition of constitutively active NF-kappaB, whereas other samples showed less or no activity in highly invasive estrogen receptor-negative breast cancer cells or androgen receptor-negative prostate cancer cells, respectively. Interestingly, we did not find any correlation between the purity and composition (spores versus powder) of Ganoderma lucidum and biologic activity. CONCLUSIONS: Ganoderma lucidum has demonstrated strong activity against breast and prostate cancer cells. Nevertheless, the composition of samples did not correlate with their ability to inhibit cell migration and activation of NF-kappaB in vitro.

Analysis of genetic variation in Ganoderma lucidum after space flight.:Adv Space Res. 2003;31(6):1617-22.Qi JJ, Ma RC, Chen XD, Lan J.Institute of Medicinal Plants, Chinese Academy of Medical Sciences, Peking Union Medical College, Xibeiwang, Beijing, China

A modified CTAB method was used in the extraction of total cellular DNA of Ganoderma lucidum. Four strains Cx, Ch, C3 and C4, and their counterparts, four space flown strains Sx, Xh, S3 and S4, were analysed by amplified fragment length polymorphism (AFLP) with several primer combinations. Polymorphic bands were detected between Sx and Cx, S3 and C3, respectively. Somatic incompatibility tests further confirmed their heterogeneity. However, no disparity between Sh and Ch, S4 and C4 was detectable. The results suggest that spaceflight may be used to accelerate breeding of Ganoderma lucidum strains for commercial cultivation.

In vitro and in vivo protective effect of Ganoderma lucidum polysaccharides on alloxan-induced pancreatic islets damage.:Life Sci. 2003 Sep 19;73(18):2307-19.Zhang HN, He JH, Yuan L, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Peking University Health Science Center, 38 Xueyuan Road, Beijing 100083, PR China.

This study was undertaken to investigate the protective effect against alloxan-induced pancreatic islets damage by Ganoderma lucidum Polysaccharides (GI-PS) isolated from the fruiting body of Ganoderma lucidum (Leyss. ex Fr.) Karst. In vitro, alloxan caused dose-dependent toxicity on the isolated pancreatic islets. Pre-treatment of islets with GI-PS for 12 h and 24 h significantly reversed alloxan-induced islets viability loss. GI-PS was also found to inhibit the free radicals production induced by alloxan in the isolated pancreatic islets using confocal microscopy. GI-PS dose-dependently increased serum insulin and reduced serum glucose levels when pretreated intragastrically for 10 days in alloxan-induced diabetic mice. It was found that the pancreas homogenates had higher lipid peroxidation products in alloxan-treated mice than in the GI-PS-treated animals. Aldehyde fuchsin staining revealed that alloxan caused nearly all the beta cells disappearing from the pancreatic islets, while GI-PS partly protected the beta cells from necrosis. Alloxan (60 mg/kg) induced NF-kappa B activation in the pancreas at 30 min after injection, pretreatment with GI-PS inhibited alloxan-induced activation of NF-kappa B. These results suggest that GI-PS was useful in protecting against alloxan-induced pancreatic islets damage in vitro and in vivo; one of the mechanisms is through its scavenging ability to protect the pancreatic islets from free radicals-damage induced by alloxan.

Effects of ganopoly (a Ganoderma lucidum polysaccharide extract) on the immune functions in advanced-stage cancer patients.:Immunol Invest. 2003 Aug;32(3):201-15.Gao Y, Zhou S, Jiang W, Huang M, Dai X.Institute of Food, Nutrition and Human Health, Massey University, New Zealand.

Preclinical studies have established that the Ganoderma lucidum polysaccharide (GLPS) fractions have potent anti-tumor activity, which has been associated with the immuno-stimulating effects of GLPS. However, it is unclear whether GLPS has immuno-modulating effects in humans in vivo. This study aimed to investigate the effects of Ganopoly, the polysaccharides fractions extracted from G. lucidum, on the immune function of advanced-stage cancer patients. Thirty-four advance-stage cancer patients were entered onto this study, and treated with 1800 mg Ganopoly, three times daily orally before meals for 12 weeks. Immune parameters (cytokines, T cell subsets, mitotic response to phytohemagglutinin (PHA) and natural killer activity) were compared between baseline and after 12-week treatment. Thirty patients are assessable for their immune functions. Treatment of Ganopoly for 12 weeks resulted in a significant ($P < 0.05$) increase in the mean plasma concentrations of interleukin (IL-2), IL-6, and interferon (IFN)-gamma, whereas the levels of IL-1 and tumor necrosis factor (TNF-alpha) were significantly ($P < 0.05$) decreased. A marked variability among patients with advanced-stage cancer was observed in the numbers of each lymphocyte subset at baseline. The mean absolute number of CD56+ cells was significantly ($P < 0.05$) increased after 12-week treatment of Ganopoly, whereas the numbers of CD3+, CD4+, and CD8+ were just marginally increased compared to baseline levels, with the CD4:CD8 T cell ratios unchanged. PHA responses after 12-week treatment with Ganopoly were enhanced in most patients, when compared to pretreatment baselines ($P < 0.05$). In addition, Ganopoly treatment resulted in a significant increase ($P < 0.05$) in the mean NK activity compared to baselines (34.5 +/- 11.8% vs 26.6 +/- 8.3%). The present study indicates that Ganopoly enhanced the immune responses in patients with advanced-stage cancer. Clinical evaluations of response and toxicity are ongoing.

Purification and characterization of thermostable alpha-galactosidase from Ganoderma

lucidum.:Biosci Biotechnol Biochem. 2003 Jul;67(7):1485-91.Sripuan T, Aoki K, Yamamoto K, Tongkao D, Kumagai H.Department of Chemistry, Faculty of Science, Chiang Mai University, Thailand. thidach@yahoo.com

Alpha-galactosidase was purified from a fresh fruiting body of Ganoderma lucidum by precipitation with ammonium sulfate and column chromatographies with DEAE-Sephadex and Con A-Sepharose. The purified enzyme was homogeneous on polyacrylamide gel electrophoresis. Its N-terminal amino acid sequence was similar to that of Mortierella vinacea alpha-galactosidase. The molecular mass of the enzyme was about 56 kDa by SDS-polyacrylamide gel electrophoresis, and about 249 kDa by gel filtration column chromatography. The optimum pH and temperature were 6.0 and 70 degrees C, respectively. The enzyme was fully stable to heating at 70 degrees C for 30 min. It hydrolyzed p-nitrophenyl-alpha-D-galactopyranoside (Km=0.4 mM) but hydrolyzed little o-nitrophenyl-alpha-D-galactopyranoside. It also hydrolyzed melibiose, raffinose, and stachyose. The enzyme catalyzed the transgalactosylation reaction which synthesized melibiose. The product was confirmed by various analyses.

Natural products of the medicinal fungus Ganoderma lucidum: occurrence, biological activities, and pharmacological functions.:Chem Rec. 2003;3(3):172-80.Shiao MS.Department of Medical Research and Education, Taipei Veterans General Hospital, Taiwan 11217. msshia@ughtpe.gov.tw

Ganoderma lucidum, a fungus used in traditional Chinese medicine, produces polysaccharides and oxygenated triterpenoids with a very broad spectrum of biological activities and pharmacological functions. Among the Ganoderma triterpenoids, many pairs of C-3 alpha/beta stereoisomers and C-3/C-15 positional isomers have been identified. Biosynthetic study has indicated that the C-3alpha series of oxygenated triterpenoids is derived from the C-3beta series via an oxidation-reduction pathway. The interaction of Ganoderma triterpenoids with human platelets in the induction of aggregation and inhibition of agonist-induced aggregation and signal transduction has been elucidated. Reduction of cellular mevalonate content to a stage in which cholesterol synthesis is strongly inhibited and cell growth is marginally arrested sensitizes hepatoma cells to the oxygenated triterpenoids. A combination treatment of lovastatin and Ganoderma triterpenoids in animal studies has exhibited a potential anticancer effect.

Comparison of the effects of polysaccharides from wood-cultured and bag-cultured Ganoderma lucidum on murine spleen lymphocyte proliferation in vitro.:Yao Xue Xue Bao. 2003 Feb;38(2):92-7.Cao LZ, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Health Science Center, Peking University, Beijing 100083, China.

AIM: To compare the influences of wood-cultured Ganoderma lucidum polysaccharides (GI-PS-WC) and bag-cultured Ganoderma lucidum polysaccharides (GI-PS-BC) on the proliferation activities of murine spleen lymphocytes in vitro, and investigate whether GI-PS-BC can be substituted for GI-PS-WC. METHODS: Mixed lymphocyte culture (MLC) reaction, lymphocyte proliferation induced by concanavalin A (Con A, 1 mg.L-1) or lipopolysaccharide (LPS, 5 mg.L-1), MLC reactions inhibited by immunosuppressive drugs, cyclosporine A (CsA, 0.1 mg.L-1), mitomycin (Mit C, 0.1 mg.L-1), or antitumor drug, etoposide (VP-16, 0.1 mg.L-1), were detected in the presence or absence of GI-PS-WC and GI-PS-BC in the concentration range of 0.2-12.8 mg.L-1. RESULTS: Two kinds of polysaccharides were shown to promote MLC in the range of 0.2-12.8 mg.L-1, increase lymphocyte proliferation induced by Con A or LPS and antagonize the inhibitory effects of CsA, Mit C or VP-16 on MLC. No significant difference was observed between these two kinds of polysaccharides in selected concentrations. CONCLUSION: GI-PS-WC and GI-PS-BC showed similar effects on the proliferation activities of murine spleen lymphocytes in vitro.

Determination of nucleosides in siweilingzhi mixture by HPCE:Zhongguo Zhong Yao Za Zhi. 2002 Sep;27(9):665-8.Dai J, Lu J, Lin RC, Liu WY.Hebei Provincial Institute for Drug Control, Shijiazhuang 050011, Hebei, China.

OBJECTIVE: To establish a method for determining nucleosides (adenoside and guanoside) in Siweilingzhi Mixture by HPCE. METHOD: Adenoside and guanoside were separated within 25 min using an 20 mmol.L-1 borate buffer with 30 mmol.L-1 SDS and 5% Ethanol (adjusted to pH

10.0 with sodium hydroxide solution), with an operation voltage of 10 kV, temperature of 20 degrees C and a hydrodynamic injection time of 15 s. Seperations were carried out in a fused-silica capillary 75 microns id x 57 cm (effective length 50 cm) with peak detection by direct UV at 254 nm. RESULT: Regression equation of adenoside and that of guanoside were Y = 0.0705 + 0.01707X (r = 0.9995) and Y = 0.0232 + 0.01864X (r = 0.9999) respectively. The average recovery rate was 99.22% (RSD = 3.66%) and 104.3% (RSD = 1.91%) respectively. Nine samples were determined with the method. CONCLUSION: The method is simple, rapid and accurate with good repeatability and it can be used to determine nucleosides.

Antioxidant effect of Ganoderma polysaccharide peptide.:Yao Xue Xue Bao. 2003 Feb;38(2):85-8.You YH, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Health Science Center, Peking University, Beijing 100083, China.

AIM: To study the antioxidant effect of Ganoderma polysaccharide peptide (GLPP) and its mechanism. METHODS: Copper was used as oxidant to induce low lipoprotein (LDL) oxidative modification, and alloxan was given i.v. to induce reactive oxygen species (ROS) injury in mice. RESULTS: GLPP decreased oxidation of LDL and the relative electrophoretic mobility (REM) of oxidative product of LDL. After GLPP was given i.p. for 20 days, the concentration of malondialdehyde(MDA) in serum and heart of mice was decreased. The GSHpx enzyme activity was increased, while the SOD level was decreased. The catalase(CAT) levels were not significantly changed by GLPP. CONCLUSION: GLPP showed antioxidant effect by scavenging ROS or enhancing the enzyme activity of GSHpx in vivo and in vitro.

Signaling mechanisms of enhanced neutrophil phagocytosis and chemotaxis by the polysaccharide purified from Ganoderma lucidum.:Br J Pharmacol. 2003 May;139(2):289-98.Hsu MJ, Lee SS, Lee ST, Lin WW.Department of Pharmacology, College of Medicine, National Taiwan University, Taipei, Taiwan.

1 The polysaccharide from Ganoderma lucidum (PS-G) has been reported to enhance immune responses and to elicit antitumor effects. In our previous study, we found that PS-G efficiently inhibited spontaneously and Fas-enhanced neutrophil apoptosis when cultured in vitro. Since phagocytosis and chemotaxis play essential roles in host defense mediated by neutrophils, it is of great interest to know the effect of PS-G on these two cell functions, and the molecular events leading to these actions. 2 Using latex beads and heat-inactive Escherichia coli serving as particles for neutrophil engulfment, we found that PS-G is able to enhance phagocytic activity of human primary neutrophils and neutrophilic-phenotype cells differentiated from all trans retinoic acid-treated HL-60 cells. 3 Chemotactic assay using Boyden chamber also revealed the ability of PS-G to increase neutrophil migration. 4 Exposure of neutrophils to PS-G time dependently caused increases in protein kinase C (PKC), p38 mitogen-activated protein kinase (MAPK), Hck, and Lyn activities. 5 Results with specific kinase inhibitors indicate that phagocytic action of PS-G was reduced by the presence of wortmannin (Phosphatidylinositol 3-kinase, PI3K inhibitor), pyrazolpyrimidine 2 (Src-family tyrosine kinase inhibitor), Ro318220 (PKC inhibitor), and SB203580 (p38 MAPK inhibitor), but not by PD98059 (mitogen-activated protein/ERK kinase inhibitor). Moreover, chemotactic action of PS-G requires the activities of PI3K, p38 MAPK, Src tyrosine kinases and PKC. 6 All these results demonstrate the abilities of PS-G to enhance neutrophil function in phagocytosis and chemotaxis, and further provide evidence to strengthen the beneficial remedy of G. lucidum in human to enhance defense system.

Submerged cultivation of Ganoderma lucidum biomass and immunostimulatory effects of fungal polysaccharides.:J Biotechnol. 2003 Jun 12;103(1):77-86.Berovic M, Habijanic J, Zore I, Wraber B, Hodzar D, Boh B, Pohleven F.National Institute of Chemistry, Hajdrihova 19, Ljubljana 1001, Slovenia. marin.berovic@ki.si.

Original Ganoderma lucidum strain MZKI G97 isolated from Slovenian forests was cultivated in a liquid substrate based on potato dextrose and olive oil. The influences of inoculum and oxygen partial pressure in batch and fed batch cultivation in a 10-l laboratory stirred tank reactor were studied. Fungal biomass was found to be oxygen and shear sensible. Using a 17% (wet weight) 6 days old vegetative inoculum, 9.6 g l(-1) of dry biomass in batch cultivation and 15.2 g l(-1) in fed batch process were obtained. Extracellular (9.6 g l(-1)) and intracellular (6.3 g l(-1)) polysaccharide fractions were isolated. Extracellular polysaccharide fraction and four intracellular

polysaccharide fractions were obtained. Polysaccharides were further separated by ion-exchange, gel and affinity chromatography. The isolated polysaccharides were mainly beta-D-glucanes. Immunostimulatory effects of isolates were tested on induction of cytokine (tumour necrosis factor alpha (TNF-alpha) and interferon gamma (IFN-gamma)) synthesis in primary cultures of human peripheral blood mononuclear cells (PBMC) isolated from a buffy coat. The TNF-alpha inducing activity is comparable with romurtide, which has been used as a supporting therapy in cancer patients treated with radiotherapy and/or chemotherapy.

Clinical observation on treatment of Russula subnigricans poisoning patients by Ganoderma lucidum decoction.:Zhongguo Zhong Xi Yi Jie He Za Zhi. 2003 Apr;23(4):278-80.Xiao GL, Liu FY, Chen ZH.Xiangya Hospital, Central South University, Changsha 410008.

OBJECTIVE: To observe the effect of Ganoderma lucidum decoction in treating Russula subnigricans poisoning (RSP) patients. METHODS: The 14 patients of RSP in the treated group were treated with GLD (GLD, one dose was prepared by 100 g of Ganoderma lucidum decocted with water to 600 ml), on the base of conventional treatment, and 11 patients received conventional therapy in the previous year were taken as control. The clinical efficacy and parameters in them were compared, including the urine N-acetyl-D-glucosaminidase (NAG, which reflects the injury of kidney), the red blood cell and protein in urine, the alanine transaminase (ALT, which reflects the injury of liver), and the aspartate aminotransferase (AST, which reflects the injury of heart). RESULTS: A better clinical cure-markedly improving rate was showed in the treated group as compared with the control group, $P < 0.01$. In the treated group, red blood cell in urine disappeared after 24 hrs treatment in the majority of patients, urinary protein reduced obviously and the other three parameters reached the peak at the 3rd day then lowered gradually. In the control group, all the parameters increased continuously. Comparison between the parameters at corresponding time in the two groups showed significant difference ($P < 0.01$), those in the treated group were markedly lower than those in the control group respectively. CONCLUSION: GLD has good effect in treating RSP, could obviously lower the fatat rate of RSP.

Regulatory effect of Ganoderma lucidum polysaccharides on cytotoxic T-lymphocytes induced by dendritic cells in vitro.:Acta Pharmacol Sin. 2003 Apr;24(4):321-6.Cao LZ, Lin ZB. Department of Pharmacology, Health Science Center, Peking University, Beijing 100083, China. linzb@public3.bta.net.cn

AIM: To study the regulatory effects of Ganoderma lucidum polysaccharides (GI-PS) on cytotoxicity and mechanism of specific cytotoxic T-lymphocytes (CTL) induced by dendritic cells (DC) in vitro during the stage of antigen presentation. METHODS: Cultured murine bone marrow-derived DC were pulsed with P815 tumor cell lysates and co-incubated with or without various concentrations of GI-PS (0.8, 3.2, or 12.8 mg/L) at the same time. P815 specific CTL were induced by spleen lymphocytes stimulated with mature DC. Non-adherent cells and culture supernatants were harvested on d 5 for analysis of specific cytotoxicity with lactate dehydrogenase (LDH) activity assay, mRNA expression of IFNgamma, granzyme B with RT-PCR assay, and protein expression of IFNgamma, granzyme B with ELISA or Western blot assay, respectively. RESULTS: Three concentrations of GI-PS promoted LDH activities released into culture supernatants ($P<0.01$). It also increased mRNA expression of IFNgamma in CTL (GI-PS 12.8 mg/L vs RPMI medium 1640, $P<0.05$) and granzyme B in CTL ($P<0.01$). Protein production of IFNgamma in culture supernatants ($P<0.05$) and protein expression of granzyme B in CTL (GI-PS 12.8 mg/L vs RPMI medium 1640, $P<0.05$) were also augmented by GI-PS. CONCLUSION: GI-PS is shown to promote the cytotoxicity of specific CTL induced by DC which were pulsed with P815 tumor antigen during the stage of antigen presentation, and the mechanism of cytotoxicity is believed to be going through IFNgamma and granzyme B pathways.

Triterpene-enriched extracts from Ganoderma lucidum inhibit growth of hepatoma cells via suppressing protein kinase C, activating mitogen-activated protein kinases and G2-phase cell cycle arrest.:Life Sci. 2003 Apr 11;72(21):2381-90.Lin SB, Li CH, Lee SS, Kan LS.Graduate Institute of Medical Technology, College of Medicine, National Taiwan University, 10016, Taipei, Taiwan, ROC. sblin@ha.mc.ntu.edu.tw

The medicinal mushroom Ganoderma lucidum (G. lucidum) has been used in the Orient for the

prevention and treatment of various diseases including cancer. Except for the immune enhancing properties of its polysaccharide constituent, very little is known about the anticancer activity of another major constituent, triterpenes. In this report, we studied the anticancer mechanism of triterpene-enriched extracts from G. lucidum. The triterpene-enriched fraction, WEES-G6, was prepared from mycelia of G. lucidum by sequential hot water extraction, removal of ethanol-insoluble polysaccharides and then gel-filtration chromatography. We found that WEES-G6 inhibited growth of human hepatoma Huh-7 cells, but not Chang liver cells, a normal human liver cell line. Treatment with WEES-G6 caused a rapid decrease in the activity of cell growth regulative protein, PKC, and the activation of JNK and p38 MAP kinases. The changes in these molecules resulted in a prolonged G2 cell cycle phase and strong growth inhibition. None of these effects were seen in the normal liver cells. Our findings suggest that the triterpenes contained in G. lucidum are potential anticancer agents.

Antiperoxidative, anti-inflammatory, and antimutagenic activities of ethanol extract of the mycelium of Ganoderma lucidum occurring in South India.:Teratog Carcinog Mutagen. 2003;Suppl 1:85-97.Lakshmi B, Ajith TA, Sheena N, Gunapalan N, Janardhanan KK.Amala Cancer Research Centre, Thrissur, Kerala, India.

Free radical mediated genetic instability is widely thought to be a major etiological factor for initiation of carcinogenesis. Mushrooms represent a largely untapped source of powerful new pharmaceutical products. In the present study, we examined the antiperoxidative, anti-inflammatory, and antimutagenic activities of the ethanol extract of the mycelium of a medicinal mushroom, Ganoderma lucidum, occurring in south India. Antiperoxidative activity was evaluated using Fe(2+)-ascorbate-induced lipid peroxidation in rat liver homogenate and a phorbol ester (croton oil)-induced lipid peroxidation in mouse skin. Antiinflammatory activity was evaluated against carrageenan-induced acute and formalin-induced chronic inflammatory paw edema in mouse and phorbol ester-induced mouse skin inflammation. Antimutagenic activity was determined by the Ames mutagenicity assay using histidine mutant of Salmonella typhimurium strains TA 98, TA100, and TA102. Sodium azide (NaN(3)), N-methyl-N-nitro-N-nitrosoguanidine (MNNG), 4-nitro-o-phenylenediamine (NPD), and benzo[a]pyrene (B[a]P) were used as the mutagens. The extract showed significant inhibition of Fe(2+)-induced peroxidation of lipid in rat liver (IC(50) 510 +/- 22 microg/ml) and 37% inhibition of croton oil-induced peroxidation on the mouse skin at 20 mg/0.1 ml/skin. Carrageenan-induced acute and formalin-induced chronic inflammatory edema were inhibited by 56 and 60%, respectively, by the extract at 1,000 mg/kg body wt (i.p). The extract at a concentration of 5 mg/plate showed inhibition of mutagenicity elicited by direct acting mutagens, NaN(3) (55.5 and 75.7%) and MNNG (50.0 and 57.5%) for S. typhymurium strains TA100 and TA102, respectively. The extract at the same concentration also inhibited mutagenicity elicited by NPD (52.4 and 64.2%) and B[a]P (60.7 and 59.6%) for TA98 and TA100 strains, respectively. The B[a]P was activated in the presence of rat liver microsomal (S9) fraction. The results of our study revealed that ethanol extract of Ganoderma lucidum mycelium possessed significant antiperoxidative, antiinflammatory, and antimutagenic activities. The findings suggest a medicinal use for the ethanol extract of the mycelium of G. lucidum occurring in South India.

Effect of lugu Ganoderma lucidum on low-density lipoprotein oxidation and monocyte adhesion to endothelium.:Zhongguo Zhong Xi Yi Jie He Za Zhi. 2002 Jul;22(7):534-7.Zhang HM, Yao WJ, Tian HK.Department of Pharmacology, School of Basic Medical Sciences, Peking University, Beijing 100083.

OBJECTIVE: To study the effect of Lugu Ganoderma Lucidum (LGL) on low-density lipoprotein (LDL) oxidation and monocyte adhesion to endothelium (AdM-E) induced by oxydative LDL and advanced glycosylation endproducts (AGE) by using serum pharmacological technique. METHODS: LDL oxidation was determined by measuring the thiobarbituric acid reactive substances in the supernatants, and AdM-E was determined by measuring myeloperoxidase activity of adherent monocyte. RESULTS: Serum derived from rats 0.5 hrs, 1 hr, 2 hrs, 3 hrs after LGL administering 0.12 g/kg once and 0.5 hrs, 1 hr after LGL administering twice showed no significant effect on LDL oxidation, but the serum from rats 2 hrs, 3 hrs after LGL 0.12 g/kg administering twice or from rats after 10 successive days LGL administering in dose of 0.12 g/kg, 0.24 g/kg and 0.72 g/kg, all could lower the LDL oxidation ($P < 0.05$). Besides, the serum from rats with 10 days LGL administering of all dosages also could inhibit AdM-E induced by AGE ($P < 0.05$), and those of 0.24 g/kg and 0.72 g/kg could inhibit AdM-E induced by oxydative LDL ($P < 0.05$). CONCLUSION: LGL could decrease LDL oxidation and AdM-E induced by AGE or

oxydative LDL.

Isolation, purification and structural characterization of active polysaccharides from the mycelium of Ganoderma lucidum:Zhong Yao Cai. 2002 Apr;25(4):252-4.Zhao C, He Y.School of Pharmaceutical Sciences, Peking University, 100083.

The active polysaccharides from the mycelium of Ganoderma lucidum were fractioned by DEAE-Sephadex and DEAE-Cellulose. Through repeated isolation and purification, two polysaccharides, GLMB0 and GLMB1, were finally obtained. Their structures were characterized by chemical and spectral methods.

A new triterpene from the fruiting bodies of Ganoderma lucidum.:Yao Xue Xue Bao. 2001 Aug;36(8):595-8.Luo J, Lin ZB.Department of Pharmacology, School of Basic Medical Science, Peking University, Beijing 100083, China.

AIM: To study the chemical constituents of the fruiting bodies of Ganoderma lucidum. METHODS: Individual constituents, isolated and repeatedly purified on silica gel column, were identified by physicochemical constants and structurally elucidated by spectral methods. RESULTS: From the alcohol extract, compound 2 was obtained and identified as 3 beta,7 beta-dihydroxy-4,4,14 alpha-trimethyl-11,15-dioxo-5 alpha-chol-8-en-24-oic acid. In addition, two known compounds, lucidenic acid A (1) and C (3) were obtained. CONCLUSION: Compound 2 is a new triterpene compound.

A water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia suppresses azoxymethane-induction of colon cancers in male F344 rats.:Oncol Rep. 2003 Mar-Apr;10(2):375-9.

The present study was designed to investigate the protective effect of a dietary water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi or Mannentake) mycelia (designated as MAK) on the induction and development of azoxymethane (AOM)-induced colon tumors in male F344/Du Crj rats. A total of 80 animals were divided into five groups at six weeks of age, groups 2, 3 and 4 being given weekly subcutaneous injections of AOM (15 mg/kg body weight) for the initial 3 weeks to induce colon tumors. Rats in group 1 and 5 were injected with the vehicle, 0.9% (w/v) saline, following the same schedule. Rats in groups 1, 2, 3, 4 and 5 were fed MF, MF, 1.25% MAK, 2.5% MAK and 2.5% MAK diets, respectively, starting 1 week before AOM treatment and throughout the six-month experimental period. There were no significant differences in number of ACF, total AC and AC per site among groups 2 to 4, but the tumor incidence was significantly lower, and tumor size was smaller in group 4 (AOM + 2.5% MAK) than in group 2 (AOM + MF). Additionally, beta-catenin positive tumor cell nuclei were significantly decreased in the MAK-fed rats (groups 3 and 4), which also demonstrated lowering of the PCNA labeling index and a shortened germinal region in the colon. The present results thus indicate that dietary MAK could act as a potent chemopreventive agent for colon carcinogenesis.

Effects of places and stages on the contents of ganoderic acid B from Ganoderma lucidum.:Zhong Yao Cai. 1999 Jun;22(6):271-2.Ding P, Zhen Y, Lai X, Xu H.Guangzhou University of Traditional Chinese Medicine, 510407.

The paper reports the assay of ganoderic acid B from Ganoderma lucidum in different places and stages by means of HPLC. The results show that contents of ganoderic acid B from different cultured places have differnces, different stages have effect on the amount too.

Comparison of the components of Ganoderma lucidum and Ganoderma japonicum.:Zhong Yao Cai. 1999 Sep;22(9):433-5.Ding P, Cai H, Liu Y, Lin L, Xu H.Guangzhou University of Traditional Chinese Medicine, Guangzhou 510407.

By means of spectrophotometric methods, the contents of polysaccharides about Ganoderma

lucidum (including mycelia) and Ganoderma japonicum are determined, HPLC and TLC methods for idntification of their triterpenic acids are given.

Resources and utilization of anticarciogenic medical fungi.:Zhong Yao Cai. 1999 Dec;22(12):614-8.Lan J, Yang J, Xu J.Institute of Medicinal Plant, CAMS, PUMC, Beijing 100094.

This paper summarizes the resources of anticarcinogenic medical fungi, and the information of distribution, eco-environment. It outlines the present statuts of the exploitation and utilization of some species of common anticarcinogenic medical fungi such as Ganoderma lucidum, Coriolus versicolor, Polyporus frondosus etc. The anticarcinogenic mechanism of medical fungi is discussed. Suggestions on how to development and utilize rationally these resources are offered as well.

The study on the fermentation medium of Ganoderma lucidum.:Zhong Yao Cai. 1998 Aug;21(8):379-81.Li G, Li B.Biotechnology Research Center, Zhongshan University, Guangzhou 510275.

This study has explored the fermentation medium of Ganoderma lucidum including inorganic salts, carbon source, nitrogen source and vitamins. Then a suitable formula of fermented medium was obtained by comparing different production slats of Gandoerma powder during fermentation.

Isolation, purification and bioactivities of exopoly saccharides from fermented broth of Ganoderma lucidum.:Wei Sheng Wu Xue Bao. 2000 Apr;40(2):217-20.Li P, Zhang K.School of Biotechnology, Wuxi University of Light Industry, Wuxi 214036.

The exopolysaccharides of Ganoderma lucidum(GLEP) extracted from the fermentation broth after removing protein by Sevage and protease digestion procedures, were applied to a column of DEAE-cellulose(OH- form), and eluted stepwise with distilled water, sodium hydrogen carbonate (0.1 mol/L, 0.3 mol/L, 0.5 mol/L successively) and 0.1 mol/L sodium hydroxide. Five fractions were obtained, and the main fraction was known as GLEP-I, furthermore subjected to chromatography on a column of SepharoseC1-6B, eluted at a flow rate of 30 mL/(cm2.h), the relative viscosity of sample solution of 1.5. Two fractions, GLEP-IFr1 and GLEP-IFr2 with a ratio of 3.8:1, were obtained. Molecular weight of GLEP-IFr1 and GLEP-IFr2 was estimated to be 38,000 and 22,000 Dalton respectively by Membrane Osmometer. The animal test showed that GLEP-IFr1 could inhibited the growth of Sarcoma 180 tumor in mice. The average inhibition ratio was 57.4% (i.p. 10 mg/kg for 10 days). The result of immunological activity showed that GLEP-IFr1 could significantly improve macrophage cytophagy.

Antitumor and antimetastatic effects on liver of triterpenoid fractions of Ganoderma lucidum: mechanism of action and isolation of an active substance.:Anticancer Res. 2002 Nov-Dec;22(6A):3309-18.

The triterpenoid fraction (100 and 200 mg/kg) of the fruit bodies of Ganoderma lucidum inhibited primary solid-tumor growth in the spleen, liver metastasis and secondary metastatic tumor growth in the liver in intrasplenic Lewis lung carcinoma (LLC)-implanted mice. In addition, the triterpenoid fraction (800 micrograms/mL) inhibited angiogenesis induced by Matrigel (a soluble basement membrane extract of the Engelbreth-Holm-Swam (EHS) tumor) supplemented with vascular endothelial growth factor (VEGF) and heparin in an in vivo model. This suggested that the antitumor and antimetastatic activities of the triterpenoid fraction of G. lucidum might be due to the inhibition of tumor-induced angiogenesis. Next, we attempted to isolate the active substance(s) using the in vivo assay system of Matrigel-induced angiogenesis. The acidic fraction of the triterpenoid fraction inhibited the Matrigel-induced angiogenesis. Compound I was isolated from the acidic fraction as an active substance that inhibited the Martigel-induced angiogenesis. Compound I was identified as ganoderic acid F based on the data of IR, 1H- and 13C-NMR and MS analyses.

Studies on difference between sporoderm-broken and nonbroken spores of Ganoderma lucidum (Leyss. ex Fr.) Karst. by polysaccharide analysis.:Zhongguo Zhong Yao Za Zhi. 2001 May;26(5):326-8.Bao XF, Fang JN.Shanghai Institute of Materia Medica, Academia Sinica, Shanghai 200031, China.

OBJECTIVE: To compare the release ability of water-soluble polysaccharides in sporoderm-broken and nonbroken spores of Ganoderma lucidum, and establish a comparatively correct method for the determination and analysis of polysaccharide contents in Chinese herbs. METHOD: The release ability of water-soluble polysaccharides was determined on the basis of phenol-sulfuric acid modification in different conditions. RESULT: The release ability of polysaccharides of sporoderm-broken spores was much greater than that of nonbroken spores; and the phenol-sulfuric acid modified cation method proved excellent in accuracy and reproducibility, with a relative error less than 1.5%. CONCLUSION: The spores should be wall-wracked if used as a nutriment, or for extraction and analysis of their effective components. The method can be successfully used for the determination of polysaccharide contents in Chinese herbs or nutriments.

Extraction and separation of antitumor components from Ganoderma lucidum (Leyss. ex Fr.) Karst.:Zhongguo Zhong Yao Za Zhi. 2000 May;25(5):288-90.Zhao DX, Yang XL, Chen L, Wang BW, Xu JL, Zhu HS.Research Center of Material Sciences, Beijing Institute of Technology, Beijing 100081, China.

OBJECTIVE: To examine the variation of alcohol extraction rates of Ganoderma lucidum spores with different rates of wall-wrack, and analyze the antitumor components of alcohol extract by chromatography. METHOD: The G. lucidum spores were soaked and extracted with absolute alcohol. The alcohol extract was chromatographed on a silica gel column and HPLC in proper order, and the antitumor activity of every eluted fraction was represented by its cytotoxicity towards Hela cells. RESULT: Extraction rates 5%, 25% and 33% corresponded to wall-wrack rates 0%, 60%-80% and 99% respectively. The alcohol extract from spores with the highest wall-wrack rate was chromatographed on a silica gel column, eluting successfully with CHCl3, EtOAc and CH3OH in order. The CHCl3 fraction had not any antitumor activity, while this activity of CH3OH fraction was 34 times greater than that of EtOAc fraction. HPLC analysis found out that two mixtures(II1 and II3) possess significant antitumor activity in vitro. CONCLUSION: The weight of alcohol extract from spores with wall-wrack was far greater than that of spores without. The antitumor components of G. lucidum spores could be analyzed with methanol-water on a reverse HPLC.

Themes for mushroom exploitation in the 21st century: Sustainability, waste management, and conservation.:J Gen Appl Microbiol. 2000 Dec;46(6):269-282.Chiu SW, Law SC, Ching ML, Cheung KW, Chen MJ.Department of Biology and Environmental Science Programme, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong, China.

Because many natural resources are limited, sustainability becomes an important concept in maintaining the human population, health, and environment. Mushrooms are a group of saprotrophic fungi. Mushroom cultivation is a direct utilization of their ecological role in the bioconversion of solid wastes generated from industry and agriculture into edible biomass, which could also be regarded as a functional food or as a source of drugs and pharmaceuticals. To make the mushroom cultivation an environmentally friendly industry, the basic biology of mushrooms and the cultivation technology must be researched and developed. This is very true for Lentinula edodes, Volvariella volvacea, and Ganoderma lucidum, which are commonly consumed in Asian communities but are now gaining popularity worldwide. Besides the conventional method, strain improvement can also be exploited by protoplast fusion and transformation. Biodiversity is the key contribution to the genetic resource for breeding programs to fulfill different consumer demands. The conservation of these mushrooms becomes essential and is in immediate need not only because of the massive habitat loss as a result of human inhabitation and deforestation, but also because of the introduced competition by a cultivar with the wild germ plasm. Spent mushroom compost, a bulky solid waste generated from the mushroom industry, however, can be exploited as a soil fertilizer and as a prospective bioremediating agent.

Mechanism of the antiulcerogenic effect of Ganoderma lucidum polysaccharides on indomethacin-induced lesions in the rat.:Life Sci. 2002 Dec 27;72(6):731-45.Gao Y, Zhou S, Wen J, Huang M, Xu A.New Zealand Institute of Natural Medicines, Auckland, New Zealand.

Many cytokines, in particular tumor necrosis factor (TNF)-alpha have been known to play an important role in the pathogenesis of gastric mucosal lesions caused by various factors such as drugs and Helicobacter pylori infection. Our previous studies have shown that the polysaccharide fractions isolated from the fruiting bodies of Ganoderma lucidum (GLPS) prevented indomethacin- and acetic acid-induced gastric mucosal lesions in the rat. However, the mechanisms remain unclear. This study aimed to investigate whether GLPS had a direct mucosal healing effect in the indomethacin-treated rat, and to explore the possible mechanisms by determining the gastric mucosal mRNA and protein levels of TNF-alpha and ornithine decarboxylase (ODC) activity. In addition, the effects of GLPS on the cellular proliferation, ODC and c-Myc protein expression and mucus synthesis in the rat gastric cell culture (RGM-1) were examined. The present study demonstrated that GLPS at 250 and 500 mg/kg by intragastric input caused ulcer-healing effect in the rat; this was accompanied with a significant suppression of TNF-alpha gene expression, but with an increased ODC activity. In RGM-1 cells, GLPS at 0.05, 0.25 and 1.0 mg/ml significantly enhanced [3H]thymidine incorporation and ODC activity in a concentration-dependent manner. However, these effects were abrogated by the addition of the ODC inhibitor, DL-alpha-difluoromethyl-ornithine (DFMO). GLPS at 0.25-1.0 mg/ml also increased mucus synthesis, as indicated by the increased D-[6-3H]glucosamine incorporation in RGM-1 cells. Furthermore, GLPS at 0.05-1.0 mg/ml increased the c-Myc protein expression. These findings indicated that GLPS produced a mucosal healing effect in the rat model, perhaps due partly to the suppression of TNF-alpha and induction of c-myc and ODC gene.

Antioxidant properties of several medicinal mushrooms.:J Agric Food Chem. 2002 Oct 9;50(21):6072-7.Mau JL, Lin HC, Chen CC.Department of Food Science, National Chung-Hsing University, 250 Kuokuang Road, Taichung 402, Taiwan, Republic of China. jlmau@dragon.nchu.edu.tw

Three species of medicinal mushrooms are commercially available in Taiwan, namely, Ganoderma lucidum (Ling-chih), Ganoderma tsugae (Sung-shan-ling-chih), and Coriolus versicolor (Yun-chih). Methanolic extracts were prepared from these medicinal mushrooms and their antioxidant properties studied. At 0.6 mg/mL, G. lucidum, G. lucidum antler, and G. tsugae showed an excellent antioxidant activity (2.30-6.41% of lipid peroxidation), whereas C. versicolor showed only 58.56%. At 4 mg/mL, reducing powers were in the order G. tsugae (2.38) approximately G. lucidum antler (2.28) > G. lucidum (1.62) > C. versicolor (0.79). At 0.64 mg/mL, scavenging effects on the 1,1-diphenyl-2-picrylhydrazyl radical were 67.6-74.4% for Ganoderma and 24.6% for C. versicolor. The scavenging effect of methanolic extracts from G. lucidum and G. lucidum antler on hydroxyl radical was the highest (51.2 and 52.6%) at 16 mg/mL, respectively. At 2.4 mg/mL, chelating effects on ferrous ion were in the order G. lucidum antler (67.7%) > G. lucidum (55.5%) > G. tsugae (44.8%) > C. versicolor (13.2%). Total phenols were the major naturally occurring antioxidant components found in methanolic extracts from medicinal mushrooms. Overall, G. lucidum and G. tsugae were higher in antioxidant activity, reducing power, scavenging and chelating abilities, and total phenol content.

Protective effects of Ganoderma lucidum polysaccharides peptide on injury of macrophages induced by reactive oxygen species.:Acta Pharmacol Sin. 2002 Sep;23(9):787-91.You YH, Lin ZB.Department of Pharmacology, School of Basic Medical Science, Peking University Health Science Center, Beijing 100083, China.

AIM: To study the protective effects of Ganoderma lucidum polysaccharides peptide (GLPP) on the mice peritoneal macrophages injured by reactive oxygen species (ROS), derived from tert-butylhydroperoxide (tBOOH) in vitro and in vivo. METHODS: Mice peritoneal macrophages were injured by ROS, derived from tBOOH. The survival rate of macrophages was measured by MTT assay, and the morphological changes of macrophages were observed under light and electron microscopes. RESULTS: GLPP (50, 100, 200 mg/kg, ip for 5 d) could inhibit the foam cell formation and necrosis of macrophages. The survival rate of macrophages was increased. GLPP (3.125, 12.5, 50, 200 mg/L) given to the cultured macrophages brought the same protective effects. Under the electron microscope it was found that GLPP (100 mg/kg, ip, for 5 d) could protect the organelle such as mitochondria against injury by tBOOH. CONCLUSION: GLPP had

significant scavenging ROS and antioxidant effects.

Regression of prostate cancer following administration of Genistein Combined Polysaccharide (GCP), a nutritional supplement: a case report.:J Altern Complement Med. 2002 Aug;8(4):493-7.Ghafar MA, Golliday E, Bingham J, Mansukhani MM, Anastasiadis AG, Katz AE.Department of Urology, College of Physicians and Surgeons of Columbia University, New York, NY, USA.

PURPOSE: It has been reported that genistein, an isoflavone used in soybeans, has antiprostate cancer effects. Genistein Combined Polysaccharide (GCP trade mark; AMino Up, Sapporo, Japan), a nutritional supplement manufactured in Japan, is composed of genistein and a polysaccharide obtained from basidiomycetes (mycelia) that grows in a variety of mushrooms. METHODS: We report a case of a patient with a biopsy proven prostate cancer showing clinical and pathologic evidence of regression following administration of GCP. The patient was enrolled in an Institutional Review Board (IRB)-approved protocol and received GCP for 6 weeks prior to radical prostatectomy. RESULTS: The patient's prostate-specific antigen (PSA) decreased from an initial value of 19.7 to 4.2 ng/mL after 44 days of low-dose GCP. No cancer was identified in the radical prostatectomy specimen and no side effects were observed in this patient. CONCLUSION: This case suggests that GCP, which has shown potent inhibitory effects against prostate cancer in vitro, may have some potential activity in the treatment and prevention of prostate cancer.

Effect of Ganoderma polysaccharides on cAMP in murine peritoneal macrophages.:Zhongguo Zhong Yao Za Zhi. 2000 Jan;25(1):41-3.Li MC, Liang DS, Xu ZM, Lei LS, Yang SQ.Department of Pharmacy, Navy 401 Hospital, Shandong, Qingdao 266071, China.

OBJECTIVE: Investigating the effect of GLB7 on cAMP in murine peritoneal macrophages to provide a scientific evidence for the immunomodulatory mechanism. METHOD: Cell culture and radio-immunological assay of cAMP were used. RESULT: GLB7 increased the production of cAMP in a concentration and time dependent manner in murine peritoneal macrophages. CONCLUSION: The immunopotentiating effect of GLB7 may be due to the activation of macrophages that leads to the increase of cAMP.

Hepatoprotective role of Ganoderma lucidum polysaccharide against BCG-induced immune liver injury in mice.:World J Gastroenterol. 2002 Aug;8(4):728-33.Zhang GL, Wang YH, Ni W, Teng HL, Lin ZB.Department of Pharmacology, School of Basic Medical Sciences, Beijing University, Beijing 100083, China. yuankui@public.bta.net.cn

AIM: To examine the effect of ganoderma lucidum polysaccharide (GLP) on the immune liver injury induced by BCG infection, and investigate the relationship between degrees of hepatic damage and NO production in mice. METHODS: Immune hepatic injury was markedly induced by BCG-pretreatment (125 mg.kg(-1), 2-week, iv) or by BCG-pretreatment plus lipopolysaccharide (LPS, 125 microg.kg(-1), 12-hour,iv) in mice in vivo.Hepatocellular damage induced by BCG-pretreated plus inflammatory cytokines mixture (CM), which was included TNF-alpha, IL-1beta, IFN-gamma and LPS in culture medium in vitro. Administration of GLP was performed by oral or incubating with culture medium at immune stimuli simultaneity. Liver damage was determined by activity of alanine aminotransferase (ALT) in serum and in hepatocytes cultured supernatant, by liver weight changes and histopathological examination. NO production in the cultured supernatant was determined by the Griess reaction. Moreover, inducible nitric oxide synthase (iNOS) protein expression was also examinated by immunohistochemical method. RESULTS: Immune hepatic injury was markedly induced by BCG or BCG plus inflammatory cytokines in BALB/c mice in vivo and in vitro. Under BCG-stimulated condition, augment of the liver weight and increase of the serum/supernatant ALT level were observed, as well as granuloma forming and inflammatory cells soakage were observed by microscopic analysis within liver tissues. Moreover, NO production was also increased by BCG or/and CM stimuli in the culture supernatant, and a lot of iNOS positive staining was observed in BCG-prestimulated hepatic sections. Application of GLP significantly mitigated hepatic tumefaction, decreased ALT enzyme release and NO production in serum/supernatant, improved the pathological changes of chronic and acute inflammation induced by BCG-stimuli in mice. Moreover, the immunohistochemical result showed that GLP inhibited iNOS protein expression in

BCG-immune hepatic damage model. CONCLUSION: The present study indicates that NO participates in immune liver injury induced by Mycobacterium bovis BCG infection. The mechanisms of protective roles by GLP for BCG-induced immune liver injury may be due to influence NO production in mice.

Is the widely used medicinal fungus the Ganoderma lucidum (Fr.) Karst. sensu stricto? (A short review).:Acta Microbiol Immunol Hung. 2002;49(2-3):235-43.Szedlay G.Department of Plant Anatomy, E?tv?s Lor¨¢nd University, P¨¢zm¨¢ny P¨¦ter s¨¦t¨¢ny 1/C H-1117 Budapest, Hungary.

The identification of Ganoderma species is usually based on classical morphological criteria. The objectives of this review were to collect available information on Ganoderma lucidum and to utilize them in exact identification of Ganoderma lucidum (Fr.) Karst. sensu stricto. A lot of taxonomical confusion has always been associated with G. lucidum and allied species. Species circumscription, phylogenetic relationships, host range and distribution of species of the G. lucidum complex are unclear even among the few taxa living in temperate climate. Several methods have been proposed to identify the species as examination of cultural characteristics, isozymes, secondary metabolites, DNA sequences and interfertility. Although G. lucidum sensu stricto has been reported world-wide accumulated evidence supported the suggestion that it seems restricted to Europe. The strains used in the medicine are usually collected in Asia. There is little likelihood that any one belongs to the G. lucidum sensu stricto. The strains labelled as G. lucidum in the medicinal and pharmacological literature encompass a broad range of species which produce different medicinally active compounds and have significantly different pharmacological effects.

Polysaccharide purified from Ganoderma lucidum inhibits spontaneous and Fas-mediated apoptosis in human neutrophils through activation of the phosphatidylinositol 3 kinase/Akt signaling pathway.: J Leukoc Biol. 2002 Jul;72(1):207-16.Hsu MJ, Lee SS, Lin WW.Department of Pharmacology, College of Medicine, National Taiwan University, No. 1 Sec. 1, Jen-Ai Road, Taipei, Taiwan, ROC.

Ganoderma lucidum has been widely used as a remedy to promote health and longevity in China. The polysaccharide component with a branched (1-->3)-beta-D-glucan moiety from G. lucidum (PS-G) has shown evidence of enhancement of immune responses and of eliciting anti-tumor effects. In this study, we investigated the effect of PS-G on neutrophil viability, which is manifested by spontaneous apoptosis. Annexin V staining and MTT assays reveal that PS-G is able to inhibit spontaneous and Fas-induced neutrophil apoptosis, and this effect of PS-G is enhanced by the presence of zVAD (a caspase inhibitor) and GM-CSF. The antiapoptotic effect of PS-G is diminished by the presence of wortmannin and LY294002 (two PI-3K inhibitors), but is not altered by PD98059 (a MEK inhibitor). Western blotting indicates the stimulating effect of PS-G on Akt phosphorylation and its inhibition of procaspase 3 degradation, which occurs in neutrophils undergoing spontaneous apoptosis or triggered death by Fas. Taken together, PS-G elicitation of antiapoptotic effects on neutrophils primarily relies on activation of Akt-regulated signaling pathways.

Regulation on maturation and function of dendritic cells by Ganoderma lucidum polysaccharides.:Immunol Lett. 2002 Oct 1;83(3):163-9.Cao LZ, Lin ZB.Department of Pharmacology, Peking University Health Science Center, 38 Xueyuan Road, Beijing 100083, People's Republic of China.

Ganoderma lucidum polysaccharides (GI-PS) exhibits a variety of immunomodulatory activities, and dendritic cells (DC) are professional antigen presenting cells, which are pivotal for initiation of primary immune response. In this study, the regulatory effects of GI-PS on maturation and function of cultured murine bone marrow derived DC were investigated in vitro. GI-PS (0.8, 3.2, or 12.8 microg/ml) could increase the co-expression of CD11c and I-A/I-E molecules on DC surface, promote mRNA expression of cytokine IL-12 p40 in DC and augment protein production of IL-12 P40 in culture supernatants. The lymphocyte proliferation of mixed lymphocyte culture (MLC) induced by mature DC was enhanced by GI-PS, either. GI-PS was shown to promote not only the maturation of cultured murine bone marrow derived DC in vitro, but also the immune response initiation induced by DC.

Effects of Ganoderma lucidum (Leyss ex Fr) Karst compound on the proliferation and differentiation of K562 leukemic cells.:Hunan Yi Ke Da Xue Xue Bao. 1999;24(6):521-4.Zhong L, Jiang D, Wang Q.Research Laboratory of Blood Physiology, Hunan Medical University, Changsha 410078.

A series of experiments including cell culture and benzidine staining test were undertaken to investigate the effects of Ganoderma lucidum(Leyss ex Fr) Karst Compound(GLC) on the proliferation and differentiation of K562 leukemic cells. The results showed that different concentrations of GLC(from 4 mg.ml-1 to 12 mg.ml-1) could promote human bone marrow granulocyte-macrophage colony forming unit (CFU-GM) proliferation, but suppressed the growth of K562 leukemic cell colonies, and IC50 was 9.2 mg.ml-1. The data from liquid culture demonstrated that GLC could suppress K562 cells proliferation in a dose-dependent(from 4 mg.ml-1 to 20 mg.ml-1) and time-dependent(from 1-5 days) manner. K562 cells could be induced to differentiate into more mature erythrocytic cells by 4 mg.ml-1 and 8 mg.ml-1 GLC. It is concluded that GLC may be a good medicine for leukemia therapy.

Activation of B lymphocytes by GLIS, a bioactive proteoglycan from Ganoderma lucidum.:Life Sci. 2002 Jun 28;71(6):623-38.Zhang J, Tang Q, Zimmerman-Kordmann M, Reutter W, Fan H.Institut f¨¹r Molekularbiologie und Biochemie, Freie Universit?t Berlin, Arnimallee 22, D-14195 -Dahlem, Berlin, Germany.

A bioactive fraction (GLIS) was isolated from the fruiting body of the fungus Ganoderma lucidum using successive chromatographic steps. GLIS is a proteoglycan and has a carbohydrate: protein ratio of 11.5 : 1. The carbohydrate portion is composed of seven different monosaccharides, predominantly D-glucose, D-galactose and D-mannose in the molar ratio of 3.0 : 1 : 1.GLIS stimulated the proliferation of mouse spleen lymphocytes, resulting in a three to four-fold increase in the percentage of B cells. GLIS also activated mouse spleen lymphocytes, and most of the activated cells were B cells. The B cells were enlarged, expressed CD71 and CD25 on the cell surface, and showed an increase in the secretion of immunoglobulin. Lymphocytes also showed a slightly increased production of IL-2, whereas the secretion of IL-4 was not influenced by GLIS. Furthermore, GLIS did not influence the intracellular Ca2+ concentration of lymphocytes, but it enhanced the expression of protein kinase C alpha and protein kinase C gamma in B cells. According to our results GLIS is a new B cell-stimulating factor.

A new lanostane-type triterpene from the fruiting bodies of Ganoderma lucidum.:J Asian Nat Prod Res. 2002 Jun;4(2):129-34.Luo J, Zhao YY, Li ZB.Department of Pharmacology, School of Basic Medical Science, Peking University, Beijing, China.

A new lanostane-type triterpene, named ganoderic acid LM2 (5), was isolated from the fruiting bodies of Ganoderma lucidum. Its structure was characterized as (23S) 7beta, -dihydroxy-3, 11, 15-trioxo-5alpha-lanosta-8, 24-dien-26-oic acid by 1D- and 2D-NMR spectra. In addition, a known triterpene, ganoderic acid epsilon (4), was obtained. Both of them exhibited potent enhancement of ConA-induced mice splenocytes proliferation in vitro.

Structure and Conformation Behavior of a Glucan from Spores of Ganoderma lucidum (Fr.) Karst.:Sheng Wu Hua Xue Yu Sheng Wu Wu Li Xue Bao (Shanghai). 2000;32(6):557-561.Bao XF, Dong Q, Fang JN.Shanghai Institute of Meteria Medica, the Chinese Academy of Science, Shanghai 200031, China. jnfang@mail.shcnc.ac.cn

A novel polysaccharide designated as beta-D-glucan LB-NB, [alpha](D)(21) -24.52(0)(c =0.81, H(2)O)and Mr 4.7x10(4), was isolated and purified from a 0.5 mol/L sodium hydroxide extract of the sporoderm-broken spores of Ganoderma lucidum. The results of NMR experiments, total hydrolysis, methylation analysis and Smith degradation of LB-NB showed that it possesses a backbone consisting of(1right curved arrow 3)- beta-D-glucosyl residues, about two out of nine glucosyl residues being substituted at O-6 by single glucosyl groups. The conformational behavior of LB-NB was studied. Measurements by specific rotations and viscometry showed that the glucan LB-NB takes an ordered structure in water or lower concentration(<0.05 mol/L)alkaline solution and dissolves as random coil in higher concentration(>0.1 mol/L)alkaline solution or in

dimethyl sulfoxide(Me(2)SO). The ordered conformation melts into flexible chains with the increase of the concentration of alkali or the V(DMSO)(v/v)of H(2)O-Me(2)SO mixture. The former dissociation is reversible and the later is irreversible. The complex-formation with Congo red indicated that the LB-NB takes neither triple-stranded helical nor randomly coiled conformation in neutral or slightly alkaline solution, and most probably, it should contain single helical structure in aqueous solution. According to immunological test, the LB-NB showed remarkable activity of stimulating the proliferation of T-Cells in vitro, giving a good example for Kulicke's statement.

Antitumor activity of the sporoderm-broken germinating spores of Ganoderma lucidum.:Cancer Lett. 2002 Aug 28;182(2):155-61.Liu X, Yuan JP, Chung CK, Chen XJ.Food Engineering Research Center of State Education Ministry, Zhongshan University, Guangzhou 510275, People's Republic of China

The inhibitory effects of the dormant spores, the germinating spores, the sporoderm-broken germinating spores (SBGS), and the lipids extracted from the germinating spores of Ganoderma lucidum on the growth of mouse hepatoma, sarcoma S-180, and reticulocyte sarcoma L-II cells were investigated, respectively. The dormant spores could be activated by germination, and thus the bioactivities of the spores might be enhanced. The sporoderm-broken spores could show much higher bioactivities than the whole spores. Both the lipids extracted from the germinating spores and the SBGS of G. lucidum had remarkable antitumor effects in a dose-dependent manner, and could significantly inhibit three tumors with an inhibition of 80-90%.

New triterpene aldehydes, lucialdehydes A-C, from Ganoderma lucidum and their cytotoxicity against murine and human tumor cells.:Chem Pharm Bull.2002 Jun;50(6):837-40.

Three new lanostante-type triterpene aldehydes, named lucialdehydes A-C (1-3), were isolated from the fruiting bodies of Ganoderma lucidum, together with ganodermanonol (4), ganodermadiol (5), ganodermanondiol (6), ganodermanontriol (7), ganoderic acid A (8), ganoderic acid B8 (9), and ganoderic acid C1 (10). The structures of the new triterpenes were determined as (24E)-3 beta-hydroxy-5 alpha-lanosta-7,9(11),24-trien-26-al (1), (24E)-3,7-dioxo-5 alpha-lanosta-8,24-dien-26-al (2), and (24E)-3 beta-hydroxy-7-oxo-5 alpha-lanosta-8,24-dien-26-al (3), respectively, by spectroscopic means. The cytotoxicity of the compounds isolated from the ganoderma mushroom was tested in vitro against Lewis lung carcinoma (LLC), T-47D, Sarcoma 180, and Meth-A tumor cell lines. Lucialdehydes B, C (2, 3), ganodermanonol (4) and ganodermanondiol (6) showed cytotoxic effects on tested tumor cells. Of the compounds, lucialdehyde C (3) exhibited the most potent cytotoxicity against LLC, T-47D, Sarcoma 180, and Meth-A tumor cells with ED(50) values of 10.7, 4.7, 7.1, and 3.8 microg/ml, respectively.

Mechanism of action of herbal supplement PC-SPES: elucidation of effects of individual herbs of PC-SPES on proliferation and prostate specific gene expression in androgen-dependent LNCaP cells.:Int J Oncol. 2002 Mar;20(3):583-8.Hsieh TC, Wu JM.Department of Biochemistry and Molecular Biology, New York Medical College, Valhalla, NY 10595, USA. tze-chen_hsieh@nymc.edu

PC-SPES is a herbal mixture used by prostate cancer patients as an alternative form of treatment. Since PC-SPES is derived from eight individual herbs, each with distinct as well as overlapping properties, it is of interest to investigate whether a particular herb in the formulation principally accounts for the biological properties of PC-SPES. We tested the ability of extracts from individual herbs, using amounts estimated to be equivalent to that present in the herbal mixture, to suppress LNCaP cell growth and/or lower PSA expression, in comparison with cells treated with PC-SPES. Cells were incubated with 0, 1, and 5 microl/ml of single herbal extract for 72 h and proliferation/viability was measured by trypan blue exclusion. LNCaP cells treated with 5 microl/ml ethanol extracts of PC-SPES showed a 72-80% reduction in cell growth, and had a similar decrease in cell viability. These results contrasted with cells incubated with 5 microl/ml of individual herbal extract, which suppressed growth in the following order: Dendranthema morifolium Tzvel (85.2% reduction) > Panax pseudo-ginseng (80.9%) > Glycyrrhiza uralensis Fisch (73%) > Rabdosia rubescens Hara (70.8%) > Scutellaria baicalensis Georgi (66.5%) > Ganoderma lucidum Karst (63.5%) > Isatis indigotica Fort (50.0%) > Serenoa repens (14.5%). Analysis of efficacy of individual herbs to control intracellular/secreted PSA levels and the

expression of AR and PSA revealed that only Glycyrrhiza uralensis Fisch, Scutellaria baicalensis Georgi and Serenoa repens lowered intracellular and secreted PSA, while the remaining herbs actually increased PSA expression. Also, no uniform response in AR/PSA was observed in individual herb treated cells, contrary to PC-SPES, which elicited a coordinated change in AR/PSA. Lack of concordance between changes in prostate cell growth and prostate specific gene expression makes it unlikely that the activity of a single herb can account for the overall effects of PC-SPES.

Purification, characterization, and modification of T lymphocyte-stimulating polysaccharide from spores of Ganoderma lucidum.:Chem Pharm Bull. 2002 May;50(5):623-9.Bao XF, Zhen Y, Ruan L, Fang JN.Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, PR China.

The hot-water extract of the spores of Ganoderma lucidum was shown to have a stimulating effect on concanavalin A-induced mitogenic activity of T lymphocytes. Bioassay-guided separation led to the isolation of a polysaccharide with potent T lymphocyte-stimulating activity by ethanol fractionation, anion-exchange, and size-exclusion chromatography. Based on the composition and methylation analyses, periodate oxidation, Smith degradation, and NMR spectroscopy, the native polysaccharide was shown to be a beta-D-(1-->3)-glucan with branches of terminal glucosyl residues substituted at C-6 of the glucose residues in the main chain. The branching ratio is approximately 20%. A series of sulfated or carboxymethylated derivatives were prepared and their structural features were elucidated by chemical and spectral analyses. The solution conformation and T lymphocyte proliferation effect of the glucans before and after derivatization were compared and discussed. The data obtained indicate that the introduction of ionic groups would significantly affect the original conformation of the native glucan in aqueous solution and further affect T lymphocyte-stimulating activity. The triple-helical structure of the glucans, the nature of the ionic groups, and the density of negative charge were considered to be closely related to this activity.

Studies on the immuno-modulating and antitumor activities of Ganoderma lucidum (Reishi) polysaccharides: functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities.:Bioorg Med Chem. 2002 Apr;10(4):1057-62.Wang YY, Khoo KH, Chen ST, Lin CC, Wong CH, Lin CH.Laboratory of Bioorganic Chemistry, Institute of Chemistry, Academia Sinica, Taipei, Taiwan.

A fucose-containing glycoprotein fraction which stimulates spleen cell proliferation and cytokine expression has been identified from the water-soluble extract of Ganoderma lucidum. Proteomic analysis of mouse spleen cells treated with this glycoprotein fraction showed approximately 50% change of the proteome. Further studies on the activities of this glycoprotein fraction through selective proteolysis and glycosidic cleavage indicate that a fucose containing polysaccharide fraction is responsible for stimulating the expression of cytokines, especially IL-1, IL-2 and INF-gamma.

Two-stage culture process for improved production of ganoderic acid by liquid fermentation of higher fungus Ganoderma lucidum.:Biotechnol Prog. 2002 Jan-Feb;18(1):51-4.Fang QH, Zhong JJ.State Key Laboratory of Bioreactor Engineering, East China University of Science and Technology, 130 Meilong Road, Shanghai 200237, China.

Investigations on the impact of pellet size on the cellular oxygen uptake and accumulation of ganoderic acid (GA) suggested the favorable effect of oxygen limitation on GA formation by the higher fungus Ganoderma lucidum. A two-stage fermentation process was thus proposed for enhanced GA production by combining conventional shake-flask fermentation with static culture. A high cell density of 20.9 g of DW/L (DW = dry cell weight) was achieved through a 4-day shake-flask fermentation followed by a 12-day static culture. A change in the cell morphology and a decrease in the sugar consumption rate were observed during the static culture. The GA production in the new two-stage process was considerably enhanced with its content increased from 1.36 (control) to 3.19 mg/100 mg of DW, which was much higher than previously observed.

Structural features of immunologically active polysaccharides from Ganoderma

lucidum.:Phytochemistry. 2002 Jan;59(2):175-81.Bao XF, Wang XS, Dong Q, Fang JN, Li XY.Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 294 Tai-yuan Road, Shanghai 200031, People's Republic of China.

Three polysaccharides, two heteroglycans (PL-1 and PL-4) and one glucan (PL-3), were solubilized from the fruit bodies of Ganoderma lucidum and isolated by anion-exchange and gel-filtration chromatography. Their structural features were elucidated by glycosyl residue and glycosyl linkage composition analyses, partial acid hydrolysis, acetolysis, periodate oxidation, 1D and 2D NMR spectroscopy, and ESI-MS experiments. The data obtained indicated that PL-1 had a backbone consisting of 1,4-linked alpha-D-glucopyranosyl residues and 1,6-linked beta-D-galactopyranosyl residues with branches at O-6 of glucose residues and O-2 of galactose residues, composed of terminal glucose, 1,6-linked glucosyl residues and terminal rhamnose. PL-3 was a highly branched glucan composed of 1,3-linked beta-D-glucopyranosyl residues substituted at O-6 with 1,6-linked glucosyl residues. PL-4 was comprised of 1,3-, 1,4-, 1,6-linked beta-D-glucopyranosyl residues and 1,6-linked beta-D-mannopyranosyl residues. These polysaccharides enhanced the proliferation of T- and B-lymphocytes in vitro to varying contents and PL-1 exhibited an immune-stimulating activity in mice.

New lanostanoids from the mushroom Ganoderma lucidum.:J Nat Prod. 2002 Jan;65(1):72-5.Ma J, Ye Q, Hua Y, Zhang D, Cooper R, Chang MN, Chang JY, Sun HH.Pharmanex, Inc., 75 West Center Street, Provo, Utah 84601, USA.

From a lipophilic extract of the fruiting body of Ganoderma lucidum, three new lanostanoids, 8beta,9alpha-dihydroganoderic acid J (1), methyl 8beta,9alpha-dihydroganoderate J (2), and 20-hydroxylganoderic acid G (3), along with 12 known lanostanoids and two ergostane sterols were isolated. The structures of 1-3 were determined by interpretation of their spectroscopic data.

Structural characterization and immunomodulating activity of a complex glucan from spores of Ganoderma lucidum.:Biosci Biotechnol Biochem. 2001 Nov;65(11):2384-91.Bao X, Fang J, Li X.Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, People's Republic of China.

A polysaccharide with a molecular weight of 1.26 x 10(5), obtained from the sporoderm-broken spores of Ganoderma lucidum, was purified by anion-exchange and gel-permeation chromatography. This polysaccharide had a strong effect on suppressing the antibody production and the Con A or LPS induced lymphocyte proliferation in mice. Chemically, the structure of the polysaccharide was identified by methylation analysis, 1 D, 2 D NMR and ESI-MS spectroscopic studies of the native one and of the oligosaccharide fragments generated by partial acid hydrolysis, Smith degradation, and acetolysis. It was concluded that the intact polysaccharide was a complex beta-D-glucan consisting of a (1-->6)-linked backbone chain, in which every other glucosyl residue was substituted at C-3 or C-4 with mono-, di- and trisaccharide branches.

Evaluation of the hepatic and renal-protective effects of Ganoderma lucidum in mice.:Am J Chin Med. 2001;29(3-4):501-7.Shieh YH, Liu CF, Huang YK, Yang JY, Wu IL, Lin CH, Li SC.Department of Family Medicine, Taipei Medical University Hospital, Taiwan.

The antioxidative effect of hot water extract of the mushroom Ganoderma lucidum on ethanol-induced free radical generation had been studied. In order to further investigate the hepatic and renal protective mechanism of Ganoderma lucidum, rates of lipid peroxidation were determined. The hot water extract of Ganoderma lucidum dose-dependently exhibited antioxidative effect on mouse liver and kidney lipid peroxidation; our results indicated that hepatic and renal homogenates have a higher malonic dialdehyde level in an ethanol administered group than in the Ganoderma lucidum treated group. It was concluded that the hepatic and renal protective mechanism of Ganoderma lucidum, might be due at least in part to its prominent superoxide scavenging effect. Ganoderma extract could protect the liver and kidney from superoxide induced hepatic and renal damages.

Prevention of development of N,N'-dimethylhydrazine-induced colon tumors by a water-

soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia in male ICR mice.:Int J Mol Med. 2002 Feb;9(2):113-7.

The protective effects of a dietary water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi or Mannentake) mycelia (designated as MAK) against development of colon tumors were investigated in male ICR mice. The animals were given weekly injections of N,N'-dimethylhydrazine (DMH, 10 mg/kg body weight) for the initial 10 weeks to induce colon carcinogenesis, and then fed on diet with or without 5% MAK for 10 weeks. There were no significant differences in incidence and the total number of colon tumors between the groups. However, the MAK diet group demonstrated significantly reduced sizes of tumors in comparison with the MF diet group. Moreover, this was linked to a lowered PCNA positive index and shortening of the germinal region in the colon. beta-catenin positive tumor cell nuclei were also significantly decreased in the MAK group. The present results thus indicate that dietary MAK could act as a potent chemopreventive agent for colon carcinogenesis.

Anticomplement activity of terpenoids from the spores of Ganoderma lucidum.:Planta Med. 2001 Dec;67(9):811-4.

A new lanostane-type terpenoid, lucidenic acid SP1 (1), was isolated from a CHCl(3)-soluble fraction of Ganoderma lucidum spores together with four other known compounds (2 - 5). The structure of lucidenic acid SP1 was determined to be 3 beta,7 beta-dihydroxy-4,4,14 alpha-trimethyl-11,15-dioxo-5 alpha-chol-8-en-24-oic acid by spectroscopic means including 2D-NMR. Twelve triterpenes (1-12) isolated from G. lucidum spores were investigated in vitro for their anticomplementary activity. Compounds 1 - 5 were inactive, whereas ganoderiol F (8), ganodermanondiol (9) and ganodermanontriol (10) showed a strong anticomplement activity against the classical pathway (CP) of the complement system with IC(50) values of 4.8, 41.7, and 17.2 microM, respectively. The potency of these triterpene alcohols (8-10) in inhibiting CP activity was improved when the number of hydroxymethyl groups on the side chain moiety is increased. On the other hand, the ganoderic acids 1-7, which contain a carboxyl group in the side chain, and lucidumols A and B (11, 12) had little activity on this system.

Purification and characterization of laccase isozymes from the white-rot basidiomycete Ganoderma lucidum.:Appl Microbiol Biotechnol. 2001 Oct;57(1-2):98-102.Ko EM, Leem YE, Choi HT.Division of Life Sciences, Kangwon National University, Chunchon, South Korea.

Ganoderma lucidum, a medicinal white-rot basidiomycete, produces many laccase isozymes in liquid culture. Three laccase isozymes (GaLc 1, 2, 3) have been purified 32.4-fold from the crude enzyme protein through anion exchange chromatography, preparative gel electrophoresis, and electroelution. Their estimated molecular weights are 65-68 kDa, and they contain 7-10% N-linked carbohydrates. The three isozymes have identical N-terminal amino acid sequences: G-I-G-P-T. The optimum pH and temperature both for each isozyme singly and the isozyme mixture are pH 3.5 and 20 degrees C, respectively. One isozyme (GaLc 3) is quite stable at pH 4.0-10.0, and shows good stability when incubated at temperatures lower than 40 degrees C. The Km values of GaLc 3 for o-tolidine and 2,2'-azino-bis-(3-ethylthiazoline-6-sulfonate) (ABTS) are 401.6 microM and 3.7 microM respectively, and the Vmax of GaLc 3 for these substrates is 0.0198 OD min(-1) unit(-1) and 0.0142 OD min(-1) unit(-1), respectively.

Chemical modifications of the (1-->3)-alpha-D-glucan from spores of Ganoderma lucidum and investigation of their physicochemical properties and immunological activity.:Carbohydr Res. 2001 Nov 8;336(2):127-40.Bao X, Duan J, Fang X, Fang J.Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, 294 Tai-Yuan Road, 200031, P.R., Shanghai, China.

A linear (1-->3)-alpha-D-glucan was isolated from the spores of Ganoderma lucidum (Fr.) Karst. Six different functionalized derivatives of the (1-->3)-alpha-D-glucan-aminopropylated, hydroxyethylated, sulfated, carboxymethylated, carboxymethylated and sulfated, and benzylamidated-carboxymethylated-with varying degrees of substitution were synthesized. The structural features and physicochemical properties of all derivatives were investigated by means of chemical and spectral analyses, and their effects on lymphocyte proliferation and antibody

production were tested in vitro and in vivo. In general, the structural and physicochemical properties, and lymphocyte proliferation activity of all samples varied with the functionalized groups and the degree of substitution. The results of immunological assays indicated that some modified derivatives had potent stimulating effects on lymphocyte proliferation and antibody production and the introduction of carboxymethyl group with low degree of substitution (DS<0.28) was the best choice on the improvement of the immunostimulating activity.

Assay of trace elements and heavy metals in different growth stages of Ganoderma lucidum:Zhong Yao Cai. 2001 Jul;24(7):469-70.Xing Z, Zhou C, Zhang J, Tang Q, Pan Y.Food Sciences College, Nanjing Agricultural University, Nanjing Shanghai 210095.

The trace elements and heavy metals in the different growth stages of Ganoderma lucidum were analyzed by ICP-MS, AFS and AAS. The fermented mycelia, fruiting bodies and spore contained all kinds of detected trace elements and heavy metals, the contents of which were higher in spore. The content of Se was same in different growth stages. Ganoderma lucidum had the ability of bio-enrichment of Ge.

Prevention of the development of preneoplastic lesions, aberrant crypt foci, by a water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi) mycelia in male F344 rats.:Oncol Rep. 2001 Nov-Dec;8(6):1341-5.

The modifying effects of a dietary water-soluble extract from cultured medium of Ganoderma lucidum (Rei-shi or Mannentake) mycelia (MAK) on the development of azoxymethane (AOM)-induced colonic aberrant crypt foci (ACF) were investigated in male F344 rats. Rats were given subcutaneous injections of AOM (20 mg/kg body weight) once a week for three weeks to induce ACF and fed on diets containing 0, 1.25, 2.5 and 5.0% MAK for five weeks, starting one week before the first dose of carcinogen. MAK significantly and dose-dependently prevented the development of ACF, decreasing the total number of AC and inhibiting cyst formation. MAK (2.5 and 5.0%) also significantly reduced the longitudinal-cross section areas of colon epithelium. MAK in all doses significantly reduced the PCNA positive index, area of the germinal region and number of cells per half crypt. In an additional in vitro experiment, MAK inhibited anchorage-independent growth of several colon carcinoma cell lines. The present results thus indicate that dietary MAK could act as a preventive agent for colon carcinogenesis.

Cytotoxicity of Ganoderma lucidum triterpenes.:J Nat Prod. 2001 Aug;64(8):1121-2.Wu TS, Shi LS, Kuo SC.Department of Chemistry, National Cheng Kung University, Tainan, Taiwan, 701, Republic of China. tswu@mail.ncku.edu.tw

Two new triterpenoids, lucidenic acid N (1) and methyl lucidenate F (2), together with four known compounds, lucidenic acid A, lucidenolactone, lucidenic acid C, and ganoderic acid E, were isolated from the dried fruiting bodies of Ganoderma lucidum. Their structures were elucidated by spectral and chemical transformation studies. Among them, lucidenic acid N (1), lucidenic acid A, and ganoderic acid E showed significant cytotoxic activity against Hep G2, Hep G2,2,15, and P-388 tumor cells.

Structural and immunological studies of a major polysaccharide from spores of Ganoderma lucidum (Fr.) Karst.:Carbohydr Res. 2001 May 8;332(1):67-74.Bao X, Liu C, Fang J, Li X.Shanghai Institute of Materia Medica, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, People's Republic of China.

A polysaccharide isolated from spores of the fungus, Ganoderma lucidum, was found to be a complex glucan. On the basis of compositional and methylation analyses, periodate oxidation, Smith degradation, 1D and 2D NMR, and ESIMS experiments of the native polysaccharide and its degraded products, the polysaccharide was shown to have a backbone of beta-(1-->3)-linked D-glucopyranosyl residues, with branches of mono-, di- and oligosaccharide side chains substituting at the C-6 of the glucosyl residues in the main chain. Conformational analysis in aqueous solution and immunological activities of the native and degraded glucans were also investigated. The results suggested that the degree of substitution on the main chain and the

length of side chains may be very important factors in determining the conformation and the biological activities of beta-(1-->3)-linked glucans.

Inhibition of lipid peroxidation and oxidative DNA damage by Ganoderma lucidum.:Phytother Res. 2001 May;15(3):245-9.Lee JM, Kwon H, Jeong H, Lee JW, Lee SY, Baek SJ, Surh YJ.College of Pharmacy, Seoul National University, Seoul 151-742, South Korea.

Reactive oxygen species (ROS), such as superoxide anions and hydroxyl radicals, are associated with carcinogenesis and other pathophysiological conditions. Therefore, elimination or inactivation of ROS or inhibition of their excess generation may be beneficial in terms of reducing the risk for cancer and other diseases. Ganoderma lucidum has been used in traditional oriental medicine and has potential antiinflammatory and antioxidant activities. In the present study, we tested the amino-polysaccharide fraction (designated as 'G009') from Ganoderma lucidum for the ability to protect against oxidative damage induced by ROS. G009 significantly inhibited iron-induced lipid peroxidation in rat brain homogenates and showed a dose-dependent inactivation of hydroxyl radicals and superoxide anions. It also reduced strand breakage in phiX174 supercoiled DNA caused by UV-induced photolysis of hydrogen peroxide and attenuated phorbol ester-induced generation of superoxide anions in differentiated human promyelocytic leukaemia (HL-60) cells. These findings suggest that G009 from Ganoderma lucidum possesses chemopreventive potential.

Identification and quantification of base and nucleoside markers in extracts of Ganoderma lucidum, Ganoderma japonicum and Ganoderma capsules by micellar electrokinetic chromatography.:J Chromatogr A. 2001 Mar 9;911(1):119-26.Cheung HY, Ng CW, Hood DJ.Department of Biology and Chemistry, City University of Hong Kong, Kowloon Tong, Hong Kong. bhhonyun@cityu.edu.hk

The present paper describes the development of a micellar electrokinetic chromatographic method for the determination of nucleoside (adenosine, uridine) and base (uracil) markers in aqueous extracts of Ganoderma medicinal preparations. The markers were successfully separated within 10 min using an 80 mM borate buffer, with 25 mM sodium dodecyl sulfate adjusted to pH 9.0, an operating voltage of 22 kV, temperature of 20 degrees C and a hydrodynamic injection time of 5 s. Separations were carried out in a fused-silica capillary with peak detection by direct UV at 254 nm. Following semi-validation of the method, with each analyte showing a good linear relationship over a 0.2 to 20 ppm concentration range (correlation coefficients from 0.9986 to 0.9998), the amounts of the three markers in the various forms of Ganoderma were easily determined using a relatively simple extraction procedure.

Solution properties of antitumor sulfated derivative of alpha-(1-->3)-D-glucan from Ganoderma lucidum.:Biosci Biotechnol Biochem. 2000 Oct;64(10):2172-8.Zhang L, Zhang M, Zhou Q, Chen J, Zeng F.Department of Chemistry, Wuhan University, China. lnzhang@public.wh.hb.cn

Four fractions of a water-insoluble alpha-(1-->3)-D-glucan GL extracted from fruiting bodies of Ganoderma lucidum were dissolved in 0.25 M LiCl/DMSO, and then reacted with sulfur trioxide-pyridine complex at 80 degrees C to synthesize a series of water-soluble sulfated derivatives S-GL. The degree of substitution of DS was measured by using IR infrared spectra, elemental analysis, and 13C NMR to be 1.2-1.6 in the non-selective sulfation. Weight-average molecular weight Mw and intrinsic viscosity [eta] of the sulfated derivatives S-GL were measured by multi-angle laser light scattering and viscometry. The Mw value (2.4 x 10(4)) of sulfated glucan S-GL-1 was much lower than that (44.5 x 10(4)) of original alpha-(1-->3)-D-glucan GL-1. The Mark-Houwink equation and average value of characteristic ratio C(infinity) for the S-GL in 0.2 M NaCl aqueous solution at 25 degrees C were found to be: [eta] = 1.32 x 10(-3) Mw(1.06) (cm3 g(-1)) and 16, respectively, in the Mw range from 1.1 x 10(4) to 2.4 x 10(4). It indicated that the sulfated derivatives of the alpha-(1-->3)-D-glucan in the aqueous solution behave as an expanded chain, owing to intramolecular hydrogen bonding or interaction between charge groups. Interestingly, two sulfated derivatives synthesized from the alpha-(1-->3)-D-glucan and curdlan, a beta-(1-->3)-D-glucan, all had significant higher antitumor activity against Ehrlich ascites carcinoma (EAC) than the originals. The effect of expanded chains of the sulfated glucan in the aqueous solution on the improvement of the antitumor activity could not be negligible.

New lanostanoids from Ganoderma lucidum that induce NAD(P)H:quinone oxidoreductase in cultured hepalcic7 murine hepatoma cells.:Planta Med. 2000 Oct;66(7):681-4.Ha TB, Gerh?user C, Zhang WD, Ho-Chong-Line N, Fourast¨¦ I.

Two new lanostanoids were isolated from the basidiocarp of Ganoderma lucidum and were identified as 26,27-dihydroxy-5 alpha-lanosta-7,9(11),24-triene-3,22-dione (1) and 26-hydroxy-5 alpha-lanosta-7,9(11),24-triene-3,22-dione (2) by their respective spectral data. Crude extracts and the isolated compounds were tested for their potential to induce NAD(P)H:quinone oxidoreductase (QR), a phase 2 drug-metabolizing enzyme, as an approach to detect potential cancer chemopreventive activity. Compound 2 doubled the specific activity of QR at a concentration of 3.0 micrograms/ml, whereas compound 1 was significantly less active (1.7-fold induction at 20 micrograms/ml). In addition, both compounds weakly inhibited sheep vesicle cyclooxygenase 1 activity at a test concentration of 40 micrograms/ml.

Constituents from the fruiting body of Ganoderma lucidum (Fr.) Karst.:Zhongguo Zhong Yao Za Zhi. 1997 Sep;22(9):552-3, 576.Chai H, Wang F, Zhang Z, Yang J, Zhang Y.Department of Chemistry, Changchun University of Agricultute and Animal Sciences.

One compounds were isolated from the fruiting body of Ganoderma lucidum. Basis on chemical evidences and spectral analysis (MS, UV, IR, 1HNMR, 13CNMR), its structures were deduced as ergosta-7,22 E-dien-3-one.

Effects of extracts from sporoderm-broken spores of Ganoderma lucidum on HeLa cells..:Cell Biol Toxicol. 2000;16(3):201-6.Zhu HS, Yang XL, Wang LB, Zhao DX, Chen L.Research Center of Materials Science, Beijing Institute of Technology, China. xlyang@bit.edu.cn

The effects of extracts from Ganoderma lucidum spores on the growth of human cervix uteri tumor HeLa cells as well as on the cell cycle and intracellular calcium level were investigated. Alcohol extracts were prepared from sporoderm-broken and sporoderm-nonbroken spores (termed extract I and extract II) of G. lucidum. Extract I was then subjected to silica gel chromatography to obtain extract III. Cytotoxicity was examined by means of trypan blue exclusion and MTT tests. It was found that extract I and extract III, but not extract II strongly inhibited the growth of HeLa cells, and that extract III was more effective than extract I. Moreover, extract III was shown to be capable of blocking the cell cycle at the transition from G1 to S phase and inducing a marked decrease of intracellular calcium level, determined by flow cytometry and the specific fluorescent calcium probe Fura-2, respectively. These results imply that (1) the breaking of G. lucidum spores improves the release of cytotoxic activity and (2) the effective extract might influence the cell cycle and cellular signal transduction by altering the calcium transport system.

On the anti-inflammatory and anti-phospholipase A(2) activity of extracts from lanostane-rich species.:J Ethnopharmacol. 2000 Nov;73(1-2):61-9.Giner-Larza EM, M¨¢?ez S, Giner-Pons RM, Carmen Recio M, R¨¨ªos JL.Departament de Farmacologia, Facultat de Farm¨¤cia, Universitat de Val¨¨ncia, Valencia, Spain.

We have studied extracts from three species rich in lanostane triterpenes for their activity against different in vivo models of inflammation induced by TPA, EPP and PLA(2). The inhibitory effect against PLA(2) in vitro was also studied. When the Poria cocos extract was tested against PLA(2)-induced mouse paw edema, it was active by the oral and parenteral routes. Its effect was greater in both magnitude and duration than that of Pistacia terebinthus and Ganoderma lucidum extracts. P. terebinthus was effective against chronic and acute inflammation, and according to a preliminary chromatographic analysis, its seems to be a good source of lanostane anti-inflammatory agents. G. lucidum was the least effective of the three species studied and, unlike the other two, failed to inhibit the activity of PLA(2) in vitro.

Possible mode of antiviral activity of acidic protein bound polysaccharide isolated from

Ganoderma lucidum on herpes simplex viruses.:J Ethnopharmacol. 2000 Oct;72(3):475-81.Eo SK, Kim YS, Lee CK, Han SS.College of Pharmacy, Chungbuk National University, 361-763, Cheongju, South Korea.

Two protein bound polysaccharides, a neutral protein bound polysaccharide (NPBP) and an acidic protein bound polysaccharide (APBP), were isolated from water soluble substances of Ganoderma lucidum by EtOH precipitation and DEAE-cellulose column chromatography. Their antiviral activities against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) were then investigated by plaque reduction assay. APBP exhibited more potent HSV-1 and HSV-2 antiviral activity than NPBP with 50% effective concentration (EC(50)) of 300-520 microg/ml. In order to examine the possible mode of the antiviral activity of APBP its virucidal effect, antiviral activity in preincubation, attachment and penetration assay were tested with HSV-1 and HSV-2. APBP was found to have a direct virucidal effect on HSV-1 and HSV-2. APBP did not induce IFN or IFN-like materials in vitro and is not expected to induce a change from a normal state to an antiviral state. APBP in concentrations of 100 and 90 microg/ml inhibited up to 50% of the attachment of HSV-1 and HSV-2 to Vero cells and was also found to prevent penetration of both types of HSV into Vero cells. These results show that the antiherpetic activity of APBP seems to be related to its binding with HSV-specific glycoproteins responsible for the attachment and penetration, and APBP impedes the complex interactions of viruses with cell plasma membranes.

Antiherpetic activities of acidic protein bound polysacchride isolated from Ganoderma lucidum alone and in combinations with interferons.:J Ethnopharmacol. 2000 Oct;72(3):451-8.Kim YS, Eo SK, Oh KW, Lee C, Han SS.College of Pharmacy, Chungbuk National University, 361-763, Cheongju, South Korea.

To investigate antiherpetic activity, an acidic protein bound polysaccharide (APBP) was isolated from carpophores of Ganoderma lucidum. This brownish APBP was isolated from water soluble substances of the carpophores by activity-guided isolation method. APBP was tested for its antiviral activity against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) by plaque reduction assay in tissue culture. APBP showed potent antiviral activity against HSV-1 and HSV-2 in Vero cells at its 50% effective concentration (EC(50)) of 300 and 440 microg/ml, respectively. APBP had no cytotoxicity on Vero cells at a concentration of 1x10(4) microg/ml. APBP exhibited a potent antiviral activity with selectivity index (SI) of more than 22.73. The combined antiherpetic effects of APBP with protein antiviral agents, interferon alpha (IFN alpha) and interferon gamma (IFN gamma), were examined on the multiplication of these two strains of herpesviruses in Vero cells by the combination assay. The results of combination assay were evaluated by the combination index (CI) that was calculated by the multiple drug effect analysis. The combinations of APBP with IFN alpha on HSV-1 and HSV-2 showed more potent synergistic effects with CI values of 0.30-0.62 for 50-90% effective levels than those of APBP with IFN gamma with CI values of 0.65-1.10. These results suggest the possibility of developing APBP as a new antiherpetic agent.

Antiherpetic activities of acidic protein bound polysacchride isolated from Ganoderma lucidum alone and in combinations with acyclovir and vidarabine.:J Ethnopharmacol. 2000 Sep;72(1-2):221-7.Oh KW, Lee CK, Kim YS, Eo SK, Han SS.College of Pharmacy, Chungbuk National University, Cheongju 361-763, South Korea.

To investigate antiherpetic activity, an acidic protein bound polysaccharide (APBP) was isolated from carpophores of Ganoderma lucidum. This brownish APBP was isolated from water soluble substances of the carpophores by activity-guided isolation method. APBP was tested for its antiviral activity against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) by plaque reduction assay in tissue culture. APBP showed potent antiviral activity against HSV-1 and HSV-2 in Vero cells at its 50% effective concentration (EC(50)) of 300 and 440 microg/ml, respectively. APBP had no cytotoxicity on Vero cells at a concentration of 1 x 10(4) microg/ml. APBP exhibited a potent antiviral activity with selectivity index (SI) of more than 22.73. The combined antiherpetic effects of APBP with nucleoside antiherpetic agents, acyclovir (ACV) and vidarabine (ara-A), were examined on the multiplication of these two strains of herpesviruses in Vero cells by the combination assay. The results of combination assay were evaluated by the combination index (CI) that was calculated by the multiple drug effect analysis. CI values were in the range 0.47-0.51 for a combination of APBP with ACV, and in the range of 1.02-1.18 for a combination of APBP with ara-A. The combinations of APBP with ACV on HSV-1 and HSV-2 showed potent

synergistic effects, and these results suggest that the possibility of developing APBP as a new antiherpetic agent.

Potentiation of ganodermic acid S on prostaglandin E(1)-induced cyclic AMP elevation in human platelets.:Thromb Res. 2000 Jul 15;99(2):135-45.Su C, Shiao M, Wang C.Department of Life Science, National Tsing Hua University, 300, Hsinchu, Taiwan.

Ganodermic acid S (GAS), isolated from the Chinese medicinal fungus Ganoderma lucidum (Fr.) Karst (Polyporaceae), exhibits inhibitory effects on platelet responses to various aggregating agonists. Our study demonstrated that GAS also participated in potentiating the response of human gel-filtered platelets to prostaglandin (PG) E(1). GAS at <20 microM did not show any significant change of basal cyclic AMP level in gel-filtered platelets. However, GAS potentiated the PGE(1)-evoked cyclic AMP level in a bell-shaped, concentration-dependent manner. The agent at 7.5 microM enhanced the level up to 1.8-fold of that evoked by PGE(1) alone. Collagen did not inhibit the PGE(1)-induced cyclic AMP level in platelets pretreated with GAS at 6 to 7.5 microM. In the presence of 7.5 microM GAS, the agent enhanced the inhibition of PGE(1) on platelet response to collagen in: phosphorylation of myosin light chain and pleckstrin; alpha-granule secretion; cell aggregation and protein-tyrosine phosphorylation. In addition, the agent along with PGE(1) almost abolished the dense-granule secretion and thromboxane (TX) B(2) formation. The results suggest that GAS played an additional role in potentiating the PGE(1)-induced cyclic AMP synthesis. GAS and PGE(1) inhibited additively the platelet response to collagen.

Triterpenes from the spores of Ganoderma lucidum and their cytotoxicity against meth-A and LLC tumor cells.:Chem Pharm Bull. 2000 Jul;48(7):1026-33.

Six new highly oxygenated lanostane-type triterpenes, called ganoderic acid gamma (1), ganoderic acid delta (2), ganoderic acid epsilon (3), ganoderic acid zeta (4), ganoderic acid eta (5) and ganoderic acid theta (6), were isolated from the spores of Ganoderma lucidum, together with known ganolucidic acid D (7) and ganoderic acid C2 (8). Their structures of the new triterpenes were determined as (23S)-7beta,15alpha,23-trihydroxy-3,11-dioxolanosta-8, 24(E)-diene-26-oic acid (1), (23S)-7alpha,15alpha23-trihydroxy-3,11-dioxolanosta-8, 24(E)-diene-26-oic acid (2), (23S)-3beta3,7beta, 23-trihydroxy-11,15-dioxolanosta-8,24(E)-diene-26-oic acid (3), (23S)-3beta,23-dihydroxy-7,11,15-trioxolanosta-8, 24(E)-diene-26-oic acid (4), (23S)-3beta,7beta,12beta,23-tetrahydroxy-11,15-dioxolanos ta-8,24(E)-diene-26-oic acid (5) and (23S)-3beta,12beta23-trihydroxy-7,11,15-trioxolanosta-8,24(E)-diene-26-oic acid (6), respectively, by chemical and spectroscopic means, which included the determination of a chiral center in the side chain by a modification of Mosher's method. The cytotoxicity of the compounds isolated from the Ganoderma spores was carried out in vitro against Meth-A and LLC tumor cell lines.

Effect of fatty acids on the mycelial growth and polysaccharide formation by Ganoderma lucidum in shake flask cultures.:Enzyme Microb Technol. 2000 Aug 1;27(3-5):295-301.Yang F, Ke Y, Kuo S.Department of Chemical Engineering, Tunghai University, 40704, Taichung, Taiwan, People's Republic of China

Fatty acids were added into the media to investigate their effects on the mycelial growth and polysaccharide formation by Ganoderma lucidum. The experiments were carried out in freely suspended cultures or immobilized cultures using shake flasks. The results indicate that the extent of stimulation or inhibition were associated with the types and levels of fatty acids. Oleic acid at the level of 0.15 g/100 ml led to a significant increase in cell concentration from 0.20 to 0.46 g/100 ml in a suspended culture and palmitic acid was of great advantage to polysaccharide production. In contrast, linoleic acid (0.1 g/100 ml) drastically suppressed both mycelial growth and polysaccharide formation. In immobilized cultures with fatty acids, the stimulation of mycelial growth remained the same level, but the enhancement of polysaccharide production became less. In addition, the growth of G. lucidum in the pattern of immobilization might be beneficial to the production of mycelia and polysaccharide.

Ganoderma lucidum: partial characterization of spore and whole body antigenic extracts.:J Investig Allergol Clin Immunol. 2000 Mar-Apr;10(2):83-9.Gupta SK, Pereira BM, Singh

AB.Centre for Biochemical Technology, Delhi, India

This study focused on the characterization of antigenic/ allergenic profiles of Ganoderma lucidum spore and whole body preparations. Whole body G. lucidum contained higher protein to carbohydrate ratio whereas it was less than one for spore extract. Isoelectric focusing showed 12 and 11 bands in acidic pH range (pI 3.5-6.5) for G. lucidum spore and whole body, respectively, while SDS-PAGE showed 8 and 23 fractions, respectively, in molecular weight range of 12.8-75.0 kD. The prominent protein fractions of G. lucidum spores were 19.4, 22.8 and 23.8 kD, whereas for G. lucidum whole body, 13.2, 14.7, 18. 7, 21.5 and 23.5 constituted major fractions. Immunoblotting with 41 individual serum samples revealed 21.8, 23.8, 19.4 and 20.0 kD to be major allergenic protein fractions of G. lucidum spores. The same using G. lucidum whole body and 26 individual serum samples identified several fractions of 17.0, 17.5, 18.5, 22.0, 23.8, 42.0, 44.0, 56.0 and 69.0 kD as major allergens. The compiled data suggest that there are common as well as specific allergenic components in two G. lucidum extracts studied.

Anti-inflammatory triterpenoids from mysterious mushroom Ganoderma lucidum and their potential possibility in modern medicine.:Acta Medica (Hradec Kralove). 1999;42(4):123-5.Patocka J.Department of Toxicology, Purkyn? Military Medical Academy, Hradec Kr¨¢lov¨¦. patocka@pmfhk.cz

Ganoderma lucidum, a mushroom long used in the East for a broad range of disorders, contains numerous pharmacologically active compounds. Very important of them are highly oxygenated anti-inflammatory triterpenes, which are the aim of this mini-review.

Nutritional value of ganoderma extract and assessment of its genotoxicity and antigenotoxicity using comet assays of mouse lymphocytes.:Food Chem Toxicol. 2000 Feb-Mar;38(2-3):173-8.Chiu SW, Wang ZM, Leung TM, Moore D.Department of Biology, The Chinese University of Hong Kong, Shatin, N. T., Hong Kong, China.

The nutritive composition of a hot aqueous extract of wild Ganoderma fruit bodies was determined. This extract was assessed for cytotoxicity and in vivo genotoxicity by both acute and subchronic exposure of mice (given by mouth at a dose equivalent to extract of 220g fresh Ganoderma fruit body/kg body weight). To test any alleged protection against mutagens by Ganoderma treatments, the mice were injected intraperitoneally with the radiomimetic mutagen ethyl methanesulfonate (EMS), and after 24hr of treatment their lymphocytes were examined using the comet assay. Ganoderma extract consisted of Folin-positive material (68.9% of dry weight), but protein comprised only 7.3% of dry weight. Glucose accounted for 11. 1% and metals 10.2% of dry weight (K, Mg and Ca being the major components with Ge (often touted as being of value in sales literature for Ganoderma preparations) having the fifth highest metal concentration at 489 microg/g). In comparison to rodent chow, Ganoderma extract was a modest dietary supplement. No evidence was found for genotoxic chromosomal breakage nor cytotoxic effects by Ganoderma extract in the mouse, nor did it protect against the effects of ethyl methanesulfonate. We found no support in this study for the extract having any value in protecting against the test mutagen.

Study on certified reference material of germanium in Ganoderma lucidum:Wei Sheng Yan Jiu. 1998 Jul;27(4):283-4.Lu L, Qian Y, Hu Z, Ye Y.Zhejiang Academy of Medical Sciences, Hangzhou, China.

Analytical reference material of Ge in Ganoderma lucidum is designed and prepared for accurete analysis, monitoration and evaluation in trades of farming, forestry, medicine and food hygiene for Ge. It is used in technical training, technical assessing, monitoring, data arbitrating and analytic method verifing for professional supervisors. This reference material has been certified by graphitic oven atomic absorption spectrometry, hydride spectrophotometry, polarography, chemical separation spectrophotometry, atomic fluorescence method and x-ray fluorescence method. According to Grubb's law to judge the data of each group, it is confirmed that all of seven groups certified crude data are normal distribution by checking normality D. The arithmatic mean value of all data is 0.38 microgram/g. Standard deviation is 0.08 microgram/g.

Update from Asia. Asian studies on cancer chemoprevention.:Ann N Y Acad Sci. 1999;889:157-92.Yun TK.Laboratory of Experimental Pathology, Korea Cancer Center Hospital, Seoul, Korea. tkyun@nuri.net

In Asia, nontoxic dietary products are considered desirable primary prevention vehicles for conquering cancer. As early as 1978, investigators in Korea carried out extensive long-term anticarcinogenicity experiments using the mouse lung tumor model and observed an anticarcinogenic effect of Panax ginseng C.A. Meyer extract in 1980. The results showed that natural products can provide hope for human cancer prevention. A newly established nine-week medium-term model using mouse lung tumors (Yun's model) could confirm the anticarcinogenicity of ginseng that varies according to its type and age. Subsequently, the ginseng was shown by epidemiological studies to be a nonorgan-specific cancer preventive agent associated with a dose-response relationship. The anticarcinogenic effects of vegetarian foods common at every dining table in Korea and some synthetics were also studied using Yun's nine-week model. In brief, ascorbic acid, soybean lecithin, capsaicin, biochanin A, Ganoderma lucidum, caffeine, and a novel synthetic 2-(allylthio)pyrazine decrease the incidence of mouse lung tumors, whereas fresh ginseng (4 years old), carrot, spinach, Sesamum indicum, beta-carotene, and 13-cis retinoic acid do not. This result regarding beta-carotene is consistent with the ineffective findings of the ATBC trial, the CARET trial, and the Physicians' Health Study. In 1983, a cancer chemoprevention study group was first established in Japan. Subsequently, (-)-epigallocatechin gallate, cryptoporic acid E, and sarcophytol A from natural products, and synthetic acyclic retinoid and canventol were shown to be anticarcinogenic or chemopreventive in human subjects. Despite the frequent consumption of tea wordwide as a beverage and current experimental evidence of anticarcinogenesis, including controversial results of epidemiological studies, more systematic clinical trials for confirmation of preventive activity of tea against cancer are needed. Placebo-controlled intervention trials of dietary fiber are under study in Japan. In the past decade, new triterpenoids were isolated from various natural sources, and its biological activities were investigated in Asia. In the late 1970s a comprehensive chemoprevention program was established at the Institute of Materia Medica, Chinese Academy of Medical Sciences. Since then, many retinoid compounds have been synthesized and screened in the search for chemopreventive cancer agents. The National Cancer Institute (USA) and China are jointly engaged in the two-nutrition intervention in Linxian, China. The results of joint study of the general population and of dysplasia in China should stimulate further research to clarify the potential benefits of micronutrient supplements. We need to clarify if there is a connection between the lower rates of cancer mortality in Korea and the frequent consumption of anticarcinogenic vegetables or traditional foods, including ginseng and Ganoderma lucidum. The constituents of the nontoxic stable dietary products promise to be the future hope for conquering cancers in the coming years.

Antiherpetic activities of various protein bound polysaccharides isolated from Ganoderma lucidum.:J Ethnopharmacol. 1999 Dec 15;68(1-3):175-81.Eo SK, Kim YS, Lee CK, Han SS.College of Pharmacy, Chungbuk National University, Cheongju, South Korea.

To investigate antiherpetic substances from Ganoderma lucidum, various protein bound polysaccharides, GLhw, GLhw-01, GLhw-02, GLhw-03, were isolated by activity-guided isolation from water soluble substances of the carpophores. These substances were examined for their antiviral activities against herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) by plaque reduction assay in vitro. Among them, the acidic protein bound polysaccharide, GLhw-02 of a brownish substance, exhibited the most potent antherpetic activity with 50% effective concentrations (EC50) of 300 approximately 520 microg/ml in Vero and HEp-2 cells, and its selectivity indices (SI) were more than 20. GLhw-02 was identified to consist mainly of polysaccharide (approximately 40.6%) and protein (approximately 7.80%) by anthrone test and Lowry-Folin test, and showed the usual molar ratio (C:H:O = 1:2:1) of carbohydrates by elemental analysis. These results suggest that GLhw-02 possesses the possibility of being developed from a new antiherpetic agent.

Antiviral activities of various water and methanol soluble substances isolated from Ganoderma lucidum.:J Ethnopharmacol. 1999 Dec 15;68(1-3):129-36.Eo SK, Kim YS, Lee CK, Han SS.College of Pharmacy, Chungbuk National University, Cheongju, South Korea.

In order to find antiviral substances from basidiomycetes, two water soluble substances, GLhw and GLlw, and eight methanol soluble substances, GLMe-1-8, were prepared from carpophores of Ganoderma lucidum. These substances were examined for their activities against five strains of pathogenic viruses such as herpes simplex virus types 1 (HSV-1) and 2 (HSV-2), influenza A virus (Flu A) and vesicular stomatitis virus (VSV) Indiana and New Jersey strains in vitro. Antiviral activities were evaluated by the cytopathic effect (CPE) inhibition assay and plaque reduction assay. Five substances, GLhw, GLMe-1, -2, -4 and -7 significantly inhibited the cytopathic effects of HSV and VSV. In the plaque reduction assay, GLhw inhibited plaque formation of HSV-2 with 50% effective concentrations (EC50) of 590 and 580 microg/ml in Vero and HEp-2 cells, and its selectivity indices (SI) were 13.32 and 16.26. GLMe-4 did not exhibit cytotoxicity up to 1000 microg/ml, while it exhibited potent antiviral activity on the VSV New Jersey strain with an SI of more than 5.43. These results indicate the possibility of development of antiviral agents from basidiomycetous fungi.

Lignin-modifying enzymes of the white rot basidiomycete Ganoderma lucidum.:Appl Environ Microbiol. 1999 Dec;65(12):5307-13.D'Souza TM, Merritt CS, Reddy CA.Department of Microbiology and NSF Center for Microbial Ecology, Michigan State University, East Lansing, Michigan 48824-1101, USA.

Ganoderma lucidum, a white rot basidiomycete widely distributed worldwide, was studied for the production of the lignin-modifying enzymes laccase, manganese-dependent peroxidase (MnP), and lignin peroxidase (LiP). Laccase levels observed in high-nitrogen (HN; 24 mM N) shaken cultures were much greater than those seen in low-nitrogen (2.4 mM N), malt extract, or wood-grown cultures and those reported for most other white rot fungi to date. Laccase production was readily seen in cultures grown with pine or poplar (100-mesh-size ground wood) as the sole carbon and energy source. Cultures containing both pine and poplar showed 5- to 10-fold-higher levels of laccase than cultures containing pine or poplar alone. Since syringyl units are structural components important in poplar lignin and other hardwoods but much less so in pine lignin and other softwoods, pine cultures were supplemented with syringic acid, and this resulted in laccase levels comparable to those seen in pine-plus-poplar cultures. Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of concentrated extracellular culture fluid from HN cultures showed two laccase activity bands (M(r) of 40,000 and 66, 000), whereas isoelectric focusing revealed five major laccase activity bands with estimated pIs of 3.0, 4.25, 4.5, 4.8, and 5.1. Low levels of MnP activity (approximately 100 U/liter) were detected in poplar-grown cultures but not in cultures grown with pine, with pine plus syringic acid, or in HN medium. No LiP activity was seen in any of the media tested; however, probing the genomic DNA with the LiP cDNA (CLG4) from the white rot fungus Phanerochaete chrysosporium showed distinct hybridization bands suggesting the presence of lip-like sequences in G. lucidum.

Characterization of an alkali-extracted peptidoglycan from Korean Ganoderma lucidum.:Arch Pharm Res. 1999 Oct;22(5):515-9.Cheong J, Jung W, Park W.IlYang Central Research Institute, Yongin, Kyungki, Korea.

The biologically active peptidoglycan was purified from the alkali fraction of the fruiting bodies of Ganoderma lucidum and the composition of the peptidoglycan was investigated by conventional analyses. The alkali-extracted peptidoglycan showed differences in chemical compositions from the water-extracted. The alkali-extracted peptidoglycan contained 6.9% protein and 75.9% carbohydrates composed mainly of beta-glucose, mannose, and alpha-glucose. The molecular weight range of the peptidoglycan was determined as 2,000 kDa-17 kDa. The peptidoglycan is considered to be a hybrid molecule of polysaccharide chains covalently bound as a side chain to the polypeptide core.

Lucidenic acid O and lactone, new terpene inhibitors of eukaryotic DNA polymerases from a basidiomycete, Ganoderma lucidum.:Bioorg Med Chem. 1999 Sep;7(9):2047-52.

Terpenoids, 1, 2 and 3, which selectively inhibit eukaryotic DNA polymerase activities, were isolated from the fruiting body of a basidiomycete, Ganoderma lucidum, and their structures were determined by spectroscopic analyses. New terpenes, lucidenic acid O (1) and lucidenic lactone (2), prevented not only the activities of calf DNA polymerase alpha and rat DNA polymerase beta, but also these of human immunodeficiency virus type 1 reverse transcriptase. Cerevisterol (3), which was reported to be a cytotoxic steroid, inhibited only the activity of DNA polymerase alpha.

Although these compounds did not influence the activities of prokaryotic DNA polymerases and other DNA metabolic enzymes such as T7 RNA polymerase and deoxyribonuclease

Triterpene antioxidants from ganoderma lucidum.:Phytother Res. 1999 Sep;13(6):529-31.Zhu M, Chang Q, Wong LK, Chong FS, Li RC.Department of Pharmacy, The Chinese University of Hong Kong, Shatin, N.T., Hong Kong, China. minzhu@cuhk.edu.hk

Ganoderma lucidum was studied for its antioxidative activity by bioassay guided isolation in conjunction with in vitro tests. The powdered crude drug was treated with boiling water and the aqueous extract (Ex1) was further separated to obtain terpene and polysaccharide fractions. The two fractions and Ex1 were screened for their antioxidative effect against pyrogallol induced erythrocyte membrane oxidation and Fe (II)-ascorbic acid induced lipid peroxidation. All tested samples showed antioxidative activities in a dose dependent manner and the terpene fraction was found to possess the highest effect compared with the others. Chemical isolation of the terpene fraction resulted in the detection of ganoderic acids A, B, C and D, lucidenic acid B and ganodermanontriol as major ingredients.

In vitro chemopreventive effects of plant polysaccharides (Aloe barbadensis miller, Lentinus edodes, Ganoderma lucidum and Coriolus versicolor).:Carcinogenesis. 1999 Aug;20(8):1637-40.Kim HS, Kacew S, Lee BM.Division of Toxicology, College of Pharmacy, Sungkyunkwan University, Changan-ku, Chunchun-dong, Kyunggi-do, Suwon 440-746, Korea.

A plant polysaccharide, Aloe gel extract, was reported to have an inhibitory effect on benzo[a]pyrene (B[a]P)-DNA adduct formation in vitro and in vivo. Hence, chemopreventive effects of plant polysaccharides [Aloe barbadensis Miller (APS), Lentinus edodes (LPS), Ganoderma lucidum (GPS) and Coriolus versicolor (CPS)] were compared using in vitro short-term screening methods associated with both initiation and promotion processes in carcinogenesis. In B[a]P-DNA adduct formation, APS (180 micrograms/ml) was the most effective in inhibition of B[a]P binding to DNA in mouse liver cells. Oxidative DNA damage (by 8-hydroxydeoxyguanosine) was significantly decreased by APS (180 micrograms/ml) and CPS (180 micrograms/ml). In induction of glutathione S-transferase activity, GPS was found to be the most effective among plant polysaccharides. In screening anti-tumor promoting effects, APS (180 micrograms/ml) significantly inhibited phorbol myristic acetate (PMA)-induced ornithine decarboxylase activity in Balb/3T3 cells. In addition, APS significantly inhibited PMA-induced tyrosine kinase activity in human leukemic cells. APS and CPS significantly inhibited superoxide anion formation. These results suggest that some plant polysaccharides produced both anti-genotoxic and anti-tumor promoting activities in in vitro models and, therefore, might be considered as potential agents for cancer chemoprevention.

Ganoderma lucidum extract protects DNA from strand breakage caused by hydroxyl radical and UV irradiation.:Int J Mol Med. 1999 Sep;4(3):273-7.Kim KC, Kim IG.Department of Radiation Biology, Environmental Radiation Research Group, Korea Atomic Energy Research Institute, Yusong, Taejon 305-600, Korea.

The fruit bodies of Ganoderma lucidum have been used for the prevention and treatment of various diseases in the Orient. Its antitumor and immune enhancing properties, along with no cytotoxicity, raise the possibility that it could be effective in preventing oxidative damage and resulting disease. Using agarose gel electrophoresis, we have evaluated the potential of Ganoderma lucidum extract as a radioprotector and antioxidant defense against oxygen radical-mediated damage. Although the evidence presented here is based on in vitro using isolated DNA, the results clearly demonstrate that the hot-water extract of Ganoderma lucidum shows good radioprotective ability, as well as protection against DNA damage induced by metal-catalyzed Fenton reactions and UV irradiation. We also found that the water-soluble polysaccharide isolated from the fruit body of Ganoderma lucidum was as effective as the hot-water extract in protecting against hydroxyl radical-induced DNA strand breaks, indicating that the polysaccharide compound is associated with the protective properties. Our data suggest that Ganoderma mushroom merits investigation as a potential preventive agent in humans.

Differential effects of ganodermic acid S on the thromboxane A2-signaling pathways in human platelets.:Biochem Pharmacol. 1999 Aug 15;58(4):587-95.Su CY, Shiao MS, Wang CT.Department of Life Science, National Tsing Hua University, Hsinchu, Taiwan, ROC

Ganodermic acid S (GAS) [lanosta-7,9(11),24-triene-3beta,15alpha-diacetoxy-26-oic acid], isolated from the Chinese medicinal fungus Ganoderma lucidum (Fr.) Karst (Polyporaceae), exerted a concentration-dependent inhibition on the response of human gel-filtered platelets (GFP) to U46619 (9,11-dideoxy-9alpha,11alpha-methanoepoxyprostaglandin F2alpha), a thromboxane (TX) A2 mimetic. GAS at 2 microM inhibited 50% of cell aggregation. GAS at 7.5 microM inhibited 80% of Ca2+ mobilization, 40% of phosphorylation of myosin light chain and pleckstrin, 80% of alpha-granule secretion, and over 95% of aggregation. GAS also strongly inhibited U46619-induced diacylglycerol formation, arachidonic acid release, and TXB2 formation. An immunoblotting study of protein-tyrosine phosphorylation showed that GAS inhibited the formation of phosphotyrosine proteins at the steps involving the engagement of integrin alphaIIbbeta3 and aggregation. However, GAS did not inhibit U46619-induced platelet shape change or the inhibitory effect of U46619 on the prostaglandin E1-evoked cyclic AMP level in GFP. It is concluded that GAS inhibits platelet response to TXA2 on the receptor-Gq-phospholipase Cbeta1 pathway, but not on the receptor-G1 pathway.

Basidiocarp and mycelium morphology of Ganoderma lucidum Karst. Strains isolated in Hungary.:Acta Microbiol Immunol Hung. 1999;46(1):41-52.Szedlay G, Jakucs E, Boldizs¨¢r I, B¨®ka K.Department of Plant Anatomy, E?tv?s Lor¨¢nd University, Budapest, Hungary.

Morphological, anatomical and cultural characteristics of 14 Ganoderma lucidum (Fr.) Karst strains isolated in Hungary have been investigated. Macroscopically the basidiocarps of the Hungarian strains are absolutely identical with those of described previously about the Ganoderma lucidum species-complex. Microscopic features of the fruitbodies and basidiospores showed some differences from the typical G. lucidum species. Pilocystidia, forming a homogeneous layer on the surface of the pileus, have smooth heads without protrusions and stalks not ramifying. Cell wall pillar density and width of the basidiospores also differ from that of regarded to be characteristic to G. lucidum. Although according to several authors chlamydospore formation is a characteristic feature of G. lucidum it has not been observed in mycelial cultures of the Hungarian strains. Antagonistic reactions between the Hungarian and Far Eastern G. lucidum isolates were mostly similar to the interspecific reactions between the two species G. lucidum and G. applanatum and corresponded only in a few cases to the interactions within one species. Our results suggest that the Hungarian strains significantly differ from the Far Eastern strains. To determine the taxonomic degree of this divergence genetical examinations should be carried out.

Beta-glucuronidase-inhibitory activity and hepatoprotective effect of Ganoderma lucidum.:Biol Pharm Bull. 1999 Feb;22(2):162-4.Kim DH, Shim SB, Kim NJ, Jang IS.College of Pharmacy, Kyung Hee University, Seoul, Korea.

To prove the relationship between the fluctuation in serum beta-glucuronidase level and hepatotoxicity, an inhibitor of beta-glucuronidase from G. lucidum was isolated and its hepatoprotective activity was investigated. The ether fraction of G. lucidum, which had potent beta-glucuronidase-inhibitory activity, protected against CCl4-induced liver injury. From this ether fraction, ganoderenic acid A, was isolated as the potent inhibitor of beta-glucuronidase. It had a potent hepatoprotective effect against CCl4-induced liver injury. These results suggest that the beta-glucuronidase seems to be closely related to liver injury, which could be prevented by beta-glucuronidase inhibitors.

Therapeutic effects of substances occurring in higher Basidiomycetes mushrooms: a modern perspective.:Crit Rev Immunol. 1999;19(1):65-96.Wasser SP, Weis AL.International Centre for Cryptogamic Plants and Fungi, Institute of Evolution, University of Haifa, Israel.

This review highlights some of the recently isolated and identified substances of higher Basidiomycetes mushrooms origin that express promising antitumor, immune modulating,

cardiovascular and hypercholesterolemia, antiviral, antibacterial, and antiparasitic effects. Medicinal mushrooms have a long history of use in folk medicine. In particular, mushrooms useful against cancers of the stomach, esophagus, lungs, etc. are known in China, Russia, Japan, Korea, as well as the U.S.A. and Canada. There are about 200 species of mushrooms that have been found to markedly inhibit the growth of different kinds of tumors. Searching for new antitumor and other medicinal substances from mushrooms and to study the medicinal value of these mushrooms have become a matter of great significance. However, most of the mushroom origin antitumor substances have not been clearly defined. Several antitumor polysaccharides such as hetero-beta-glucans and their protein complexes (e.g., xyloglucans and acidic beta-glucan-containing uronic acid), as well as dietary fibers, lectins, and terpenoids have been isolated from medicinal mushrooms. In Japan, Russia, China, and the U.S.A. several different polysaccharide antitumor agents have been developed from the fruiting body, mycelia, and culture medium of various medicinal mushrooms (Lentinus edodes, Ganoderma lucidum, Schizophyllum commune, Trametes versicolor, Inonotus obliquus, and Flammulina velutipes). Both cellular components and secondary metabolites of a large number of mushrooms have been shown to effect the immune system of the host and therefore could be used to treat a variety of disease states.

Anti-HIV-1 and anti-HIV-1-protease substances from Ganoderma lucidum.:Phytochemistry. 1998 Nov;49(6):1651-7.

A new highly oxygenated triterpene named ganoderic acid alpha has been isolated from a methanol extract of the fruiting bodies of Ganoderma lucidum together with twelve known compounds. The structures of the isolated compounds were determined by spectroscopic means including 2D-NMR. Ganoderiol F and ganodermanontriol were found to be active as anti-HIV-1 agents with an inhibitory concentration of 7.8 micrograms ml-1 for both, and ganoderic acid B, ganoderiol B, ganoderic acid C1, 3 beta-5 alpha-dihydroxy-6 beta-methoxyergosta-7,22-diene, ganoderic acid alpha, ganoderic acid H and ganoderiol A were moderately active inhibitors against HIV-1 PR with a 50% inhibitory concentration of 0.17-0.23 mM.

Effect of Ganoderma lucidum on postherpetic neuralgia.:Am J Chin Med. 1998;26(3-4):375-81

Administration of hot water soluble extracts of Ganoderma lucidum (GI) (36 to 72 g dry weight/day) decreased pain dramatically in two patients with postherpetic neuralgia recalcitrant to standard therapy and two other patients with severe pain due to herpes zoster infection.

Triterpenes from the spores of Ganoderma lucidum and their inhibitory activity against HIV-1 protease.:Chem Pharm Bull. 1998 Oct;46(10):1607-12.

Two new lanostane-type triterpenes, lucidumol A and ganoderic acid beta, were isolated from the spores of Ganoderma (G.) lucidum, together with a new natural one and seven that were known. The structures of the new triterpenes were determined as (24S)-24,25-dihydroxylanost-8-ene-3,7-dione and 3 beta,7 beta-dihydroxy-11,15-dioxolanosta-8,24(E)-dien-26-oic acid, respectively, by chemical and spectroscopic means. The quantitative analyses of 5 fruiting bodies, antlered form and spores of G. lucidum were performed by high performance liquid chromatography and demonstrated that ganoderic alcohol and acid contents were quite high in the spore. Of the compound isolated, ganoderic acid beta, (24S)-lanosta-7,9(11)-diene-3 beta,24,25-triol (called lucidumol B), ganodermanondiol, ganodermanontriol and ganolucidic acid A showed significant anti-human immunodeficiency virus (anti-HIV)-1 protease activity with IC50 values of 20-90 microM.

A mushroom fruiting body-inducing substance inhibits activities of replicative DNA polymerases.:Biochem Biophys Res Commun. 1998 Aug 10;249(1):17-22.

We found and isolated two natural products in the extract from a basidiomycete, Ganoderma lucidum, as eukaryotic DNA polymerase inhibitors. The compounds were identified as cerebrosides, (4E,8E)-N-D-2'-hydroxypalmitoyl- 1-O-beta-D-glucopyranosyl-9-methyl-4,8-sphingadienine and (4E,8E)-N-D-2'-hydroxystearoyl-1-O-beta-D-glucopyranos yl-9-methyl- 4,8-

sphingadienine and were found to be identical to the mushroom fruiting body-inducing substances (FIS) reported. These cerebrosides selectively inhibited the activities of replicative DNA polymerases, especially the alpha-type, from phylogenetically broad eukaryotic species, whereas they hardly influenced the activities of DNA polymerase beta, prokaryotic DNA polymerases, terminal deoxynucleotidyl transferase, HIV reverse transcriptase, RNA polymerase, deoxyribonuclease I, and ATPase. The inhibition of another replicative polymerase, the delta-type, was moderate. The inhibitions of the replicative polymerases were dose-dependent, and the IC50 for animal or mushroom DNA polymerase alpha was achieved at approximately 12 micrograms/ml (16.2 microM) and for animal DNA polymerase delta at 57 micrograms/ml (77.2 microM). FIS is possibly a DNA polymerase inhibitor specific to the replicative enzyme group, and the fruiting body formation may be required for the suppression of the DNA replication or the vegetative growth of the mycelium.

An ergosterol peroxide, a natural product that selectively enhances the inhibitory effect of linoleic acid on DNA polymerase beta.:Biol Pharm Bull. 1998 May;21(5):444-8

As described previously (Mizushina Y., Tanaka N., Yagi H., Kurosawa T., Onoue M., Seto H., Horie T., Aoyagi N., Yamaoka M., Matsukage A., Yoshida S., and Sakaguchi K., Biochim. Biophys. Acta, 1308, 256-262, 1996), linoleic acid (LA) inhibits the activities of mammalian DNA polymerases. We found a natural product from a basidiomycete, Ganoderma lucidum, that enhances this effect of LA in a special manner. The structure was identified to be an ergosterol peroxide, 5,8-epidioxy-5alpha,8alpha-ergosta-6,22E-dien -3beta-ol by spectroscopic analyses. The ergosterol peroxide (EPO) itself scarcely inhibited the activities of calf thymus DNA polymerase alpha (pol. alpha) or rat DNA polymerase beta (pol. beta). However, when EPO at 0.25 mM was present, 10 microM or less of LA almost completely inhibited the pol. beta activity, while almost complete inhibition by LA itself was achieved at 80 microM or higher. Interestingly, under the same conditions, EPO did not affect the LA-effect on pol. alpha. The action mode of the EPO was discussed.

Natural inhibitors for protein prenyltransferase.:Planta Med. 1998 May;64(4):303-8.Lee S, Park S, Oh JW, Yang C.Department of Chemistry, College of Natural Sciences, Seoul National University, Republic of Korea.

Farnesyl protein transferase (FPT) catalyzes the posttranslational farnesylation of the cysteine residue located in the carboxyl-terminal tetrapeptide of the Ras oncoprotein. Prenylation of this residue is essential for membrane association and cell transforming activities of Ras. Inhibitors of FPT have been demonstrated to inhibit Ras-dependent cell transformation and thus represent a potential therapeutic strategy for the treatment of human cancers (1). In the present study, the inhibitory principles for protein prenyltransferases were isolated and identified from Ganoderma lucidum and garlic. The inhibitors from Ganoderma lucidum were identified as ganoderic acid A and ganoderic acid C by comparison with the reported spectral data. Ganoderic acid A has an IC50 value of 100 microM against FPT and its methyl ester (methyl ganoderate A) has an IC50 value of 38 microM for the same enzyme. These inhibitors appear to be competitive with farnesyl pyrophosphate (FPP), and Ki values of ganoderic acid A and methyl ganoderate A are 54 microM and 20 microM, respectively. The inhibitors from garlic were identified as diallyl thiosulfinate (allicin), methyl allyl thiosulfinate, and allyl methyl thiosulfinate. These inhibitors are more effective against geranylgeranyl protein transferase (GGPT) than FPT and IC50 values of allicin, methyl allyl thiosulfinate, and allyl methyl thiosulfinate for GGPT were 43 microM, 57 microM, and 53 microM, respectively. Methyl allyl thiosulfinate appears to be competitive with geranylgeranyl pyrophosphate (GGPP) and its Ki was determined to be 15 microM. The molecular structures of triterpenes and thiosulfinates are expected to be useful in designing lead compounds for new potent antitumour agents.

Chemical studies on peptidepolysaccharides of Ganoderma lucidum (W. Curt. Fr.) Karst.:Zhongguo Zhong Yao Za Zhi. 1997 Aug;22(8):487-9, 512.Li T, He Y, Li R.School of Pharmacy Beijing Medical University.

Seven homogeneous peptidepolysaccharides have been obtained from the fruit-body of Ganoderma lucidum. The main constituents are TGLP-2, TGLP-3, TGLP-6 and TGLP-7, whose molecular weights are 20.9 x 10(4), 4.5 x 10(4), 3.2 x 10(4) and 10 x 10(4) respectively. TGLP-2

is a heteroglycan peptide, TGLP-3 and TGLP-6 are glycan peptides and TGLP-7 is a galactan peptide.

Studies on the ganoderic acid, a new constituents from the fruiting body of Ganoderma lucidum (Fr.) Karst.:Yao Xue Xue Bao. 1997 Jun;32(6):447-50.Wang FS, Cai H, Yang JS, Zhang YM, Hou CY, Liu JQ, Zhao MJ.Department of Chemistry, University of Agriculture and Animal Science, PLA, Chang Chun 130062.

Three compounds have been isolated from the dichloromethane soluble fraction of the fruiting body of Ganoderma lucidum (Fr.) Karst. On basis of spectral analyses (UV, IR, MS, 1HNMR, 13CNMR and 2D-NMR), they were identified as 3, 7-dioxo-lanosta-8, 24(E)-dien-26-oic acid (I), 7 beta-15 alpha-dihydroxy-3, 11, 23-trioxo-5 alpha-lanost-8-en-26-oic acid (II) and 3 beta, 7 beta, 15 alpha-trihydroxy-11, 23-dioxo-5 alpha-lanosta-8-en-26-oic acid (III). Compound I is a new compound named ganoderic acid DM.

Antinociceptive components of Ganoderma lucidum.:Planta Med. 1997 Jun;63(3):224-7.

The antinociceptive effects 134 extracts prepared from 45 species of mushrooms were examined by the acetic acid-induced writhing method. From the CH2Cl2 extract of Ganoderma lucidum among the active extracts, ganoderic acids A, B, G and H and compound C6 were isolated as the antinociceptive components.

Antifibrotic effects of a polysaccharide extracted from Ganoderma lucidum, glycyrrhizin, and pentoxifylline in rats with cirrhosis induced by biliary obstruction.:Biol Pharm Bull. 1997 Apr;20(4):417-20.Park EJ, Ko G, Kim J, Sohn DH.College of Pharmacy, Medicinal Resources Research Center, Wonkwang University, Iksan, Geonbuk, Korea.

For the past few years, we have been investigating polysaccharides from Ganoderma lucidum as antifibrotic agents. In a previous study, we discovered that polysaccharides extracted from G. lucidum lowered the collagen content in liver but had no effect on serum biochemical parameters in rats subjected to bile duct ligation and scission-induced fibrosis. In this study, we changed the extraction method and obtained polysaccharides extracted from G. lucidum. The polysaccharide from G. lucidum reduced the serum aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase (ALP) and total bilirubin and also reduced the collagen content in liver and improved the morphology. Pentoxifylline, which is reported to exhibit an antifibrotic effect in pigs with fibrosis induced by yellow phosphorus, did not have any antifibrotic effects in fibrosis induced by biliary obstruction. Glycyrrhizin, which is used in the treatment of hepatitis, reduced serum ALT and AST values but there was no significance. It had no effect on liver hydroxyproline content which implies that glycyrrhizin has no antifibrotic effect in the rats with fibrosis induced by bile duct ligation and scission. These data suggest that the polysaccharide from Ganoderma lucidum could be a promising antifibrotic agent. However, further study is needed to understand the inhibition mechanism of collagen deposition of polysaccharides from Ganoderma lucidum and its clinical applicability remains to be established.

The anti-tumor effect of Ganoderma lucidum is mediated by cytokines released from activated macrophages and T lymphocytes.:Int J Cancer. 1997 Mar 17;70(6):699-705.Wang SY, Hsu ML, Hsu HC, Tzeng CH, Lee SS, Shiao MS, Ho CK.Department of Medical Research, Veterans General Hospital-Taipei, Taiwan, Republic of China.

The present study was to ascertain the immunomodulating and anti-tumor effects of Ganoderma (G.) lucidum. Polysaccharides (PS) from fresh fruiting bodies of G. lucidum (PS-G) were isolated and used to potentiate cytokine production by human monocytes-macrophages and T lymphocytes. Our results had shown that the levels of interleukin (IL)-1 beta, tumor necrosis factor (TNF)- alpha, and IL-6 in macrophage cultures treated with PS-G (100 micrograms/ml) were 5.1-, 9.8- and 29-fold higher, respectively, than those of untreated controls. In addition, the release of interferon (IFN)- gamma from T lymphocytes was also greatly promoted in the presence of PS-G (25-100 micrograms/ml). Furthermore, these cytokine-containing mononuclear cell-conditioned media (PSG-MNC-CM) were found to suppress the proliferation and

clonogenicity of both the HL-60 and the U937 leukemic cell lines. DNA labeling and gel electrophoresis showed that treatment with PSG-MNC-CM markedly induced leukemic-cell apoptosis. Flow-cytometric analysis revealed that few (2.3 +/- 0.8%) apoptotic cells were seen in the control cultures, while PSG-MNC-CM treatment resulted in a significant increase in the apoptotic population both in the HL-60 (38.3 +/- 4.5%) and in the U937 (44.5 +/- 3.8%) cells. In addition, 40 to 45% of the treated leukemic cells were triggered to differentiate into mature monocytic cells expressing CD14 and CD68 surface antigens. However, PS-G alone had no such effects even at a higher dose of 400 micrograms/ml. Since untreated macrophages and T lymphocytes produced little or no cytokine, and normal MNC-CM did not suppress leukemic cell growth, it was suggestive that the anti-tumor activity of PSG-MNC-CM was derived from the elevated levels of cytokines. Antibody-neutralization studies further revealed that the anti-tumor cytokines in the PSG-MNC-CM were mainly of TNF- alpha and IFN- gamma, and these 2 cytokines acted synergistically on the inhibition of leukemic-cell growth.

Suppressive effects of Ganoderma lucidum on proliferation of peripheral blood mononuclear cells.:Mol Cells. 1997 Feb 28;7(1):52-7.Kim RS, Kim HW, Kim BK.Department of Microbial Chemistry, College of Pharmacy, Seoul National University, Korea

The basidiocarps of Ganoderma lucidum have been used for prevention and treatment of various diseases in the Orient. Methanolic extracts of this mushroom were applied to human peripheral blood mononuclear cell (PBMC) culture systems in the presence of various immunostimulating or immunosuppressive agents. Phytohemagglutinin-induced cell proliferation was reduced to 14% of that of the control by a GLE fraction that is the neutral component of the methanolic extracts of the carpophores. 12-O-tetradecanoylphorbol 13-acetate (TPA)-induced cell proliferation was inhibited by the fractions of GLA, GLC, GLE and GLG. However none of these fractions inhibited proliferation of the PBMCs stimulated with TPA plus ionomycin (IM). Treatment of the PBMCs with cyclosporin A (CsA) led to blockage of the cell proliferation to 9% of that of the control. When the cells were cultured with the methanolic fractions in the presence of CsA, concentration dependent inhibition of the cell proliferation was observed by the addition of GLE and GLG fractions. On the contrary, the GLH fraction recovered the CsA induced inhibition of the cell proliferation. Taken together, among the methanolic fractions, GLE showed the highest inhibitory activity. This fraction might inhibit the protein kinase C signal pathway and accelerate the CsA signal pathway.

A lectin from mycelia of the fungus Ganoderma lucidum.:Phytochemistry. 1997 Jan;44(1):7-10.

A lectin (GLL-M) was isolated from mycelia of Ganoderma lucidum using affinity chromatography on BSM-Toyopearl. GLL-M is a monomer in its native form with a M(r) of 18,000. Another lectin was also purified from fruiting bodies of the same fungus. The two lectins were partially compared with each other.

Ling Zhi-8: studies of a new immunomodulating agent.:Transplantation. 1995 Sep 15;60(5):438-43.van der Hem LG, van der Vliet JA, Bocken CF, Kino K, Hoitsma AJ, Tax WJ.Department of Surgery, University Hospital Nijmegen, The Netherlands.

Ling Zhi-8 (LZ-8) is a protein derived from the fungus Ganoderma lucidum and has immunomodulatory capacities. It was shown to be mitogenic toward mouse splenocytes in vitro and immunosuppressive in vivo by reducing antigen-induced antibody formation and by preventing completely the incidence of autoimmune diabetes in nonobese diabetic mice. In this study, the mitogenic effects of LZ-8 on human mononuclear cells are reported. In accordance to its mitogenic effect on mouse splenocytes, LZ-8 proved to be mitogenic for human PBMC. This mitogenic effect of LZ-8 apparently required the presence of monocytes. We also demonstrated it to be immunosuppressive in vitro in a human MLC performed in the absence of monocytes, using purified T cells and EBV-transformed allogeneic B cells. Furthermore, we tested LZ-8 for its possible suppressive effects in 2 different models of allogeneic tissue transplantation. LZ-8 proved to have a significant effect on cellular immunity, since its administration in an allografted mouse skin model resulted in an increased survival time. In a model of transplanted allogeneic pancreatic rat islets, LZ-8 was effective in delaying the rejection process of allografted islets. More frequent or continuous administration resulted in a further prolongation of survival time. No serious side effects of LZ-8 could be discerned in these experiments.

Radical scavenger and antihepatotoxic activity of Ganoderma formosanum, Ganoderma lucidum and Ganoderma neo-japonicum.:J Ethnopharmacol. 1995 Jun 23;47(1):33-41.Lin JM, Lin CC, Chen MF, Ujiie T, Takada A.Graduate Institute of Natural Products, Kaohsiung Medical College, Taiwan, R.O.C

The free radical scavenging and antihepatotoxic activity from Ganoderma lucidum, Ganoderma formosanum and Ganoderma neo-japonicum were studied. Treatment with the water extract of Ganoderma lucidum, Ganoderma formosanum and Ganoderma neo-japonicum caused a marked decrease in the CCl4-induced toxicity in rat liver, made evident by their effect on the levels of glutamic oxaloacetic transaminase (GOT) and lactic dehydrogenase (LDH) in the serum. The scavenging potency of the water extracts of the crude drugs was evaluated in terms of their ability to reduce the peaks of spin adducts using electron spin resonance (ESR) spin-trapping techniques. The results indicated that Ganoderma formosanum showed the greatest antihepatotoxic activity and the greatest free radical scavenging activity.

Sensitization to Ganoderma lucidum in patients with respiratory allergy in India.:Clin Exp Allergy. 1995 May;25(5):440-7.Singh AB, Gupta SK, Pereira BM, Prakash D.Centre for Biochemical Technology, Delhi, India.

Although human sensitization to basidiomycete Ganoderma has been reported in New Zealand, North America and Europe, hypersensitivity due to this fungi is not known in India, in spite of its prevalence in the atmosphere. We have studied the atmospheric concentration of Ganoderma in different localities within Delhi and the sensitization level to this fungi amongst the Indian population. Aerobiological sampling, using a Burkard personal slide sampler, was carried out in Delhi for 2 consecutive years (October 1989-September 1991). The sampler was operated at 10 day regular intervals for 10 min to trap the spores. The peak season for Ganoderma is recorded from July to September with highest average monthly catch of 336 spores/m3 in September 1991 from south Delhi. Antigenic extracts were prepared from both, the spores and whole body of Ganoderma lucidum. The results of intradermal skin tests conducted on 172 patients revealed that 28.48% and 17.44% of patients showed marked skin reactivity to spore and whole body extracts, respectively. A significant correlation ($r = 0.963$, $P < 0.01$) was found between intradermal and skin-prick tests. More than 80% of the intradermal test positive patients had significantly ($P < 0.01$) elevated IgE antibodies to the fungi in question. Thus, sensitization to Ganoderma lucidum has been reported for the first time in the atopic population of India.

Effects of Ganoderma lucidum and krestin on subset T-cell in spleen of gamma-irradiated mice.:Am J Chin Med. 1995;23(3-4):289-98.Chen WC, Hau DM, Wang CC, Lin IH, Lee SS.Institute of Radiation Biology, National Tsing Hua University, Hsinchu, Taiwan.

Effects of Ganoderma lucidum (Gl) and Krestin (PSK) extracts on spleen, thymus and splenocytes in gamma-irradiated mice were investigated in this study. ICR strain male mice were divided into five groups. Group A was the normal control. Group B, the experimental control, was treated with Gl. Group C, the radiation treatment control, was treated with whole body exposure to 4 Gy gamma-irradiation (RT). Group D was treated with RT and Gl. Group E was treated with RT and PSK. The dosage of Gl was 400 mg/day/kg body weight and PSK was 500 mg/day/kg body weight. Our results indicated that the relative thymus weight in groups D and E were higher than group C on day 28 after gamma-irradiation. Group D was the highest in all the experimental groups. CD4 and CD8 splenocytes in group D were higher than group C on days 7 and 28. Gl was better than PSK in repairing the damage of subset T-cells in the spleen of gamma-irradiated mice.

Effects of Ganoderma lucidum and krestin on cellular immunocompetence in gamma-ray-irradiated mice.:Am J Chin Med. 1995;23(1):71-80.Chen WC, Hau DM, Lee SS.Institute of Radiation Biology, National Tsing Hua University, Hsinchu, Taiwan.

The effects of Ganoderma lucidum (Gl) and Krestin (PSK) extracts on cellular immunocompetence, leukocyte counts and differential count in gamma-irradiated mice were

investigated in this study. ICR strain male mice were used and randomly divided into five groups. Group A is normal control. Group B, the experimental control, was treated with GI. Group C, the radiation treatment control, was treated with whole body exposure to 4 Gy gamma-irradiation (RT). Group D was treated with RT and GI. Group E was treated with RT and PSK. The dosage of GI was 400 mg/day/kg body weight and PSK was 500 mg/day/kg body weight. After irradiation, six mice from each group were sacrificed on day 7 and the other six on day 28. Cellular immunocompetence was measured by means of 3H-thymidine incorporation with splenic cells stimulated through mitogens such as PHA, Con A and LPS. The results revealed that relative splenic weight in Groups D and E were higher than group C on day 28 after gamma-irradiation, Group D was the highest in all the experimental groups. Leukocyte counts were decreased significantly in Groups D and E on day 7, the former was a little higher than the latter. GI administration showed an increase in the leukocyte count in Group D on day 28. The blastogenic response of splenocytes to PHA and Con A in groups D and E were higher than in Group C on days 7 and 28. We suggested that GI and PSK were effective in enhancing the recovery of cellular immunocompetence from gamma-ray irradiation.

Alteration of pulse in human subjects by three Chinese herbs.:Am J Chin Med. 1994;22(2):197-203.Wang WK, Chen HL, Hsu TL, Wang YY.Biophysics Laboratory, Institute of Physics, Academia Sinica, Taipei, Taiwan.

Human subjects were fed with extract of three Chinese herbs, Panax ginseng, Panax quinquefolium roots and Ganoderma lucidum. Pulse of the radial artery was examined. Our results indicate that each herb has a specific effect on the Fourier components of the pulse, and is in agreement with traditional Chinese medical descriptions.

Some characteristics and partial purification of the Ganoderma lucidum cellulase system.:Acta Microbiol Immunol Hung. 1994;41(1):23-31.Jakucs E, R¨¢cz I, L¨¢sztity D.Department of Plant Anatomy, E?tv?s Lor¨¢nd University, Budapest

The extracellular cellulase system of the white-rotting basidiomycete Ganoderma lucidum was characterised while growing in cellulose-containing shaken liquid culture. The protein content of the culture filtrate reached its maximum after 36 days and cellulase activity at about 60 days. Different cellulase activities (endoglucanase, cellobiohydrolase and beta-glucosidase) were determined in a range of pH extending from 6 to 2. All of the three enzyme activities have at least three peaks between pH 6 and 2, although optimum points of the different enzymes are slightly different, showing that the enzyme complex consists of a number of enzymes and isozymes. Partial purification of the enzyme complex was carried out by DEAE-cellulose column chromatography. Using 0-3 M linear urea gradient, protein was eluted in one sharp peak corresponding mainly to beta-glucosidase activity. Comparing crude extracellular protein with that of purified by the column using PAGE indicated that this method was suitable for the separation and partial purification of one type of Ganoderma cellulases.

Recent advances in studies on traditional Chinese anti-aging materia medica.:J Tradit Chin Med. 1993 Sep;13(3):223-6, contd.Chen K, Li C.Institute of Geriatrics, Xiyuan Hospital, China Academy of Traditional Chinese Medicine, Beijing

Presented in this paper is a report of our studies on 386 traditional effective anti-aging medications, the effects of which on cell generation, survival time, immunomodulation, improvement of visceral and metabolic functions, and anti-infection, and their trace element contents were further summarized and analysed. This suggests that the investigations of traditional anti-aging materia medica in China are now well under way and some effective drugs and compound prescriptions have been explored, such as Ginseng, Radix Astragali seu Hedysari, Radix Angelicae Sinensis, Herba Epimedii, Cordyceps, Ganoderma Lucidum seu Japonicum, Radix Polygoni Multiflori, Radix Acanthopanacis Senticosi, Rhizoma Polygonati, Fructus Lycii, and Poria. However, all of these preliminary results remain to be further investigated.

New techniques of cultivating Ganoderma lucidum (W. Curt.:Fr)Karst.,Rev. with

woodlog.:Zhongguo Zhong Yao Za Zhi. 1993 May;18(5):272-4, 317-8.Cheng TQ, He XJ, Huan JH, Lin CZ, Huang DB.Institute of Plant Protection, Fujian Academy of Agricultural Sciences, Fuzhou.

Imitating wild cultivation of Ganoderma lucidum with short-woodlog is a method of cultivating artificial G. lucidum developed in recent years. The method can be applied to large scale production. This paper shows that section-inoculating and impregnating with steamed shortwoodlog indoors and soil-cover cultivating under large shed are important in the cultivation.

An immunomodulatory protein, Ling Zhi-8, facilitates cellular interaction through modulation of adhesion molecules.:Biochem Biophys Res Commun. 1992 Jul 15;186(1):385-90.

Ling Zhi-8 (LZ-8), a novel immunomodulatory protein, markedly enhanced the expression of CD11b, but not CD11a, CD13, CD14, CD18, CD33 or HLA-DR, on the U937 cell line in a dose-dependent fashion. It also induced ICAM-1 expression on vascular endothelial cells and significantly augmented gamma - interferon-induced cellular binding between vascular endothelial cells and U937. Furthermore, LZ-8 increased the expression of CD2, but not VLA4, VLA5 or LFA3, on MOLT4 and enhanced rosette formation between human T cells and sheep red blood cells. These data suggest that LZ-8 exerts its pharmacological effect by modulating adhesion molecules on immunocompetent cells.

Studies on the triterpenoid constituents of the spores from Ganoderma lucidum karst.:Yao Xue Xue Bao. 1991;26(4):267-73.Chen RY, Yu DQ.Institute of Materia Medica, Chinese Academy of Medical Sciences, Beijing.

Five compounds were isolated from the ether soluble fraction of the spores of Ganoderma lucidum. On the basis of their chemical properties and spectral data (MS, UV, IR, 1H and 13CNMR), they were identified as 3,7,11,12,15,23-hexaoxo-5 alpha-lanosta-8-en-26-oic acid (I), 3 beta,7 beta-dihydroxy-11,15,23-trioxo-5 alpha-lanosta-8-en-26-oic acid (II), 7 beta-hydroxy-3,11,15,23-tetraoxo-5 alpha-lanosta-8-en-26-oic acid (III), 3,7,11,15,23-pentaoxo-5 alpha-lanosta-8-en-26-oic acid (IV), 24,25,26-trihydroxy-5 alpha-lanosta-7,9 (11)-dien-3-one (V), Compound I is a new natural product, named ganosporeric acid A. Compounds II, III, IV and V were obtained for the first time from the spores of Ganoderma lucidum.

Immunomodulator, LZ-8, prevents antibody production in mice.:Int J Immunopharmacol. 1991;13(8):1109-15.

LZ-8, a new and recently discovered immunomodulator from Ganoderma lucidum, has been shown to have immunosuppressive activity in vivo and to be a member of the immunoglobulin superfamily. In this paper we examined the in vivo effect of LZ-8 on antibody production using the hepatitis B surface antigen (HBs Ag) in mice. LZ-8 had mitogenic activity in vitro towards spleen cells of C57BL/10 (B10) and C57BL/10BR (B10BR) as previously shown towards those of DBA/2 mice. B10 and B10BR mice produced anti-HBs Ag antibody by the twice sensitization of the antigen while intraperitoneal administration of LZ-8 twice weekly into the mice (8 and 12 mg/kg) greatly prevented the production of antibody to HBs Ag (83.3-96.8% inhibition). We further examined the effect of LZ-8 administration on mitogen responsibility of spleen cells and on the T-cell subset population in both the spleen and lymph node but no significant differences were observed between the LZ-8 treated and untreated mice. These results suggest that the immunosuppressive activities of LZ-8, previously shown, such as the prevention of systemic anaphylaxis and the Arthus reactions, were caused by the blocking of antigen-specific antibody production.

Application of 2d NMR techniques in the structure determination of ganosporelactone A and B.:o Xue Xue Bao. 1991;26(6):430-6.

Structure and stereochemistry of ganosporelactone A and B isolated from the spores of Ganoderma lucidum have been elucidated by the use of 1H-1H COSY, 1H-13C COSY, 1H-13C COLOC and NOESY 2D NMR spectroscopy. Ganosporelactone A and B are two novel

pentacyclic triterpenoids which may be biogenetically derived from lanostane skeleton through the construction of C16 and C23 bond.

An immunomodulating protein, Ling Zhi-8 (LZ-8) prevents insulitis in non-obese diabetic mice.:Diabetologia. 1990 Dec;33(12):713-8.

Ling Zhi-8 (LZ-8), a novel and recently discovered immunomodulatory protein having in vivo immuno-suppressive activity, was tested for in vivo effect against Type 1 (insulin-dependent) diabetes mellitus in the nonobese diabetic mouse, the disease having immunologically mediated aetiology in this animal. LZ-8 had mitogenic activity in vitro towards spleen cells of the non-obese diabetic mice as previously shown towards those of DBA/2 mice. Intraperitoneal administration of LZ-8 twice weekly into the mice (10.3-12.6 mg/kg body weight) from 4 weeks of age prevented insulitis and an almost normal number of insulin producing cells were observed. Extreme insulitis and reduction of the number of insulin producing cells were observed in the pancreata of the untreated non-obese diabetic mouse. No cumulative incidence of diabetes mellitus was observed in the LZ-8 treated group, while cumulative incidences of 70% and 60% were observed in an untreated group followed up to 42 weeks of age when the incidence of diabetes was defined as a plasma glucose level of greater than 11 mmol/l and as a urine glucose level of greater than 2+, respectively. T cell subset population analysis was performed to further investigate the action of LZ-8 on the non-obese diabetic mouse which revealed that LZ-8 treatment increased in L3T4'/Lyt-2+ ratio.

Cardiovascular effects of mycelium extract of Ganoderma lucidum: inhibition of sympathetic outflow as a mechanism of its hypotensive action.:Chem Pharm Bull. 1990 May;38(5):1359-64.

In an effort to understand the mechanism of cardiovascular actions of Ganoderma lucidum which was cultivated in Korea, the mycelium was isolated for a large-scale culture. Water extract of the mycelia was evaluated for its cardiovascular activity in anesthetized rabbits and rats. The left femoral artery and vein were cannulated for the measurement of arterial pressure and subsequent delivery of drugs. The left kidney was exposed retroperitoneally and a branch of the renal nerve was used to integrate renal efferent or afferent nerve activities. The extract decreased systolic and diastolic blood pressure, which was accompanied by an inhibition of renal efferent sympathetic nerve activity. The extract did not decrease heart rate in these animals, although there was clear hypotension in the extract dose dependent manner. This suggests that the hypotension induced by the treatment of the extract was secondary to the primary effect of the extract in the central nerve system, which suppressed the sympathetic outflow. Therefore we concluded that the mechanism of hypotensive action of Ganoderma lucidum was due to its central inhibition of sympathetic nerve activity.

The lack of antiplatelet effect of crude extracts from ganoderma lucidum on HIV-positive hemophiliacs.:Am J Chin Med. 1990;18(3-4):175-9.Gau JP, Lin CK, Lee SS, Wang SR.Section of Hematology, National Yang-Ming Medical College, Taipei, Taiwan.

Effects of the extracts from Ganoderm lucidum (GL-P) to influence immune status of the hemophiliacs with positive HIV antibody and reversed helper/suppressor T-lymphocyte ratio were studied. Since the extracts from G. lucidum have been reported to contain high levels of adenosine, the untoward antiplatelet effect of the extracts on hemophiliacs were highly concerned. Five patients of hemophilia A voluntarily received the extracts which has been analyzed to contain 150 mg of adenosine in 100 gm of the extracts. Patients were estimated to take 1.35 mg of the adenosine daily. Platelet aggregation tests before and after the trial of the extracts showed no significant change. Our crude extracts of the Ganoderma lucidum was considered not to have untoward antiplatelet effect in vivo despite the high contents of adenosine.

Radioprotective effect of Ganoderma lucidum (Leyss. ex. Fr.) Karst after X-ray irradiation in mice.:Am J Chin Med. 1990;18(1-2):61-9.Hsu HY, Lian SL, Lin CC.School of Technology for Medical Sciences, Department of Radiotherapy, Kaohsiung Medical College,

Taiwan.

Six to seven week old male mice of ICR strain were exposed to 500 or 650 cGy of X-ray during experiments to determine if Ganoderma lucidum could be a factor in modification of radiation damage. Continuous intraperitoneal injection of the extract from Ganoderma lucidum before or after irradiation of 500 and 650 cGy of X-ray was found to improve the 30-day survival fractions of ICR mice, but wasn't significant by statistical analysis. The administration also enhanced the recoveries of the body weights and increased the recovery of hemograms of irradiated mice from radiation damage by injecting before or after radiation exposure, especially for the treatment of 500 cGy irradiation. The 10-day CFUs was significantly higher for Ganoderma lucidum treated groups than for untreated groups. However, the differences of radioprotective effect between the X-ray irradiated groups with Ganoderma lucidum pretreated and post-treated were not significant (p greater than 0.05).

Experimental and clinical studies on inhibitory effect of ganoderma lucidum on platelet aggregation.:J Tongji Med Univ. 1990;10(4):240-3.Tao J, Feng KY.Department of Internal Medicine, Tongji Hospital, Tongji Medical University, Wuhan.

In this study we observed the inhibitory effect of Chinese herbal medicine Ganoderma lucidum (GL) on platelet aggregation in 15 healthy volunteers and 33 patients with atherosclerotic diseases. The results showed that the first and the second phase of aggregation of platelets of the healthy volunteers were obviously inhibited (P less than 0.01) when watery soluble extract of GL of different concentrations was added to the platelets in vitro, i. e., the reaction speed of platelet aggregation was slowed down. The inhibitory effect was related to dosage. Platelet aggregation induced by ADP in final concentration of 2 mumol/L and 3 mumol/L was obviously inhibited, after the patients had taken GL 1 g 3 times a day for 2 weeks, the maximum platelet aggregation inhibition rates were then 31.49% (P less than 0.01) and 17.7% (P less than 0.01) respectively. Length and weights (wet and dry) of the extracorporeal thrombi were reduced from 30.05 +/- 4.38 mm, 103.9 +/- 9.33 mg and 44.89 +/- 4.79 mg to 20.4 +/- 2.33 mm (P less than 0.05), 85.27 +/- 8.77 mg (P less than 0.01) and 35.1 +/- 4.5 mg (P less than 0.01) respectively after oral administration of GL. The results of our experiments suggested that the Chinese herbal medicine GL may be an effective inhibitory agent of platelet aggregation. However, its mechanism and active principles remain to be further investigated.

Mechanisms of hypoglycemic activity of ganoderan B: a glycan of Ganoderma lucidum fruit bodies.:Planta Med. 1989 Oct;55(5):423-8.

Ganoderan B increased the plasma insulin level in normal and glucose-loaded mice but elicited no effect on insulin binding to isolated adipocytes. Administration of ganoderan B elicited significant increases of the activities of hepatic glucokinase, phosphofructokinase and glucose-6-phosphate dehydrogenase, decreased the hepatic glucose-6-phosphate and glycogen synthetase activities and did not affect the activities of hexokinase and glycogen phosphorylase. Ganoderan B reduced the glycogen content in the liver but had no influence on total cholesterol and triglyceride levels in the plasma and liver.

Ganoderic acid and its derivatives as cholesterol synthesis inhibitors.:Chem Pharm Bull. 1989 Feb;37(2):531-3.

Oxygenated lanosterol derivatives, which were isolated from Ganoderma lucidum (Polyporaceae) or their derivatives obtained by chemical conversion, were tested for their effect on cholesterol biosynthesis from 24,25-dihydrolanosterol by rat hepatic subcellular 10,000 x g supernatant fraction. The sterol (VI, 40 microM) with 7-oxo and 15 alpha-hydroxy groups potently inhibited the synthesis of cholesterol from [24,25-3H]-24,25-dihydrolanosterol (18 microM).

Isolation and characterization of a new immunomodulatory protein, ling zhi-8 (LZ-8), from Ganoderma lucidium.:J Biol Chem. 1989 Jan 5;264(1):472-8.

A novel protein with mitogenic activity in vitro and immunomodulating activity in vivo has been isolated from the mycelial extract of an Oriental medicinal fungus, ling zhi (Ganoderma lucidium).

This protein was named ling zhi-8 (LZ-8) and its biochemical and immunological properties are described. LZ-8 was purified by two chromatographic systems, gel filtration and followed by ion-exchange, using an in vitro bioassay measuring blast-formation stimulatory activity toward mouse spleen lymphocytes to monitor purification. Analysis by several types of electrophoresis revealed a single band, with the molecular weight differing slightly depending on the system employed. Under reduced conditions, sodium dodecyl sulfate-polyacrylamide gel electrophoresis using the method of Laemmli, U.K. ((1970) Nature 227, 680-685) indicated an apparent Mr = 17,100, while under nonreduced conditions an apparent Mr = 17,500 was found; and, using Tricine-sodium dodecyl sulfate-polyacrylamide gel electrophoresis, a value of apparent Mr = 13,100 was obtained. LZ-8 has an isoelectric point of 4.4, and sugar analysis indicated a low carbohydrate content (1.3%). Half-cysteine, histidine, and methionine were not detected from the analysis of amino acid composition after further purification of LZ-8 by reversed-phase high performance liquid chromatography. LZ-8 was capable of hemagglutinating sheep red blood cells, but no such activity was observed toward human red blood cells (A, B, AB, and O types). In vivo, LZ-8 prevents the production of systemic anaphylaxis reaction in mice if it has been administered repeatedly, and reduction of antibody production is the suggested mechanism. The mechanisms of hemagglutination of sheep red blood cells and of blast-formation stimulation of mouse spleen cells are also discussed.

Anti-allergic constituents in the culture medium of Ganoderma lucidum. (II). The inhibitory effect of cyclooctasulfur on histamine release.:Agents Actions. 1988 Apr;23(3-4):157-60.

For centuries, Ganoderma lucidum has been used in Oriental medicine for the treatment of chronic bronchitis. Sequential fractions of the culture medium of this plant revealed that one of the active constituents was cyclooctasulfur. The latter effectively inhibited histamine release from rat peritoneal mast cells and impeded 45Ca uptake into these cells without affecting the cyclic AMP content. SDS-PAGE analysis indicated that cyclooctasulfur induced some changes in protein bands obtained from the membrane fraction of mast cells, suggesting that this compound interacts with membrane proteins so as to inhibit 45Ca uptake, and that this may be the main cause of histamine release inhibition.

Anti-allergic constituents in the culture medium of Ganoderma lucidum. (I). Inhibitory effect of oleic acid on histamine release.:Agents Actions. 1988 Apr;23(3-4):153-6.

The chloroform extract from Ganoderma lucidum broth markedly inhibited histamine release from rat peritoneal mast cells. From the active fractions, palmitic acid, stearic acid, oleic acid and linoleic acid were isolated. Oleic acid dose-dependently inhibited the histamine release and 45Ca uptake into mast cells induced by compound 48/80 and A-23187 at concentrations of 5 to 50 microM and 0.5 to 5 microM, respectively. Saturated fatty acids, however, had only a weak inhibitory effect on histamine release. Although linoleic acid and linolenic acid effectively prevented this release, these two compounds caused marked release at concentrations higher than 10 microM and 20 microM, respectively. Oleic acid induces membrane-stabilization in model membrane systems. It was concluded that one of the effective constituents obtainable from the chloroform extract of G. lucidum-cultured broth is oleic acid.

Effect of six edible plants on the development of AFB1-induced gamma-glutamyltranspeptidase-positive hepatocyte foci in rats:Zhonghua Zhong Liu Za Zhi. 1987 Mar;9(2):109-11.Chen ZY, Yan RQ, Qin GZ, Qin LL.Guangxi Cancer Institute, Nanning.

Six edible plants, green tea (GT), black tea (BT), Lentinus edodes (berk) Sing (LE), Hericium erinaceus (Bull. ex Fr.) Pers. (HE), Mixture of Ganoderma Lucidum (Ley ss ex Fr.) Karst et Ganoderma Japanium (Fr.) Lloyd (MGLJ) and mung bean (MB), were tested for the effect on the development of AFB1-induced gamma-glutamyltranspeptidase positive hepatocyte foci (gamma-GT foci) using an in vivo short-term test model in rats. The rats received intraperitoneally 12 doses of initiator AFB1, 400 micrograms/kg per dose for 2 successive weeks. Two weeks after the initiation, the rats were submitted to a modified "Solt-Farber promotion program", i.e., a two weeks' feeding of a diet containing 0.015% acetylaminofluorene plus a two-third partial hepatectomy (PH) on day 7. The rats were sacrificed 10 days after PH and the livers were processed to gamma-glutamyltranspeptidase staining. The tested substances were powdered

and mixed with the basal diet at the concentration level of 30% for MB and 5% for the others. The rats were fed with the diet-containing tested substances from 10 days before the AFB1 initiation to 3 days after the AFB1 conclusion. Consequently, the liver of the rats which had consumed GT showed significantly less and smaller gamma-GT foci, and those which had consumed BT, HE and LE showed somewhat less and significantly smaller foci than the control groups. It is indicated that the four diets have an inhibiting effect on AFB1-induced gamma-GT foci in different degrees. MB and MGLJ show no significant influence on the foci.

Three new lanostanoids from Ganoderma lucidum.:J Nat Prod. 1986 Jul-Aug;49(4):621-5.

Three new lanostanoids--ganodermenonol (1), ganodermadiol (2), and ganodermatriol (3) [isolated as its triacetate derivative (3a)]--were isolated from the MeOH extract of Ganoderma lucidum, together with ergosterol and its peroxide. The new compounds were identified as 26-hydroxy-5 alpha-lanosta-7,9(11),24-trien-3-one (1), 5 alpha-lanosta-7,9(11),24-triene-3 beta, 26-diol (2), and 5 alpha-lanosta-7,9(11),24-triene-3 beta, 26,27-triol (3) by their respective spectral data.

Isolation and Hypoglycemic Activity of Ganoderans A and B, Glycans of Ganoderma lucidum Fruit Bodies1.:Planta Med. 1985 Aug;51(4):339-40.

A water extract of the Oriental crude drug "reishi", the fruit bodies of GANODERMA LUCIDUM, significantly decreased plasma sugar level in mice. Fractionation of the extract by monitoring the hypoglycemic activity afforded two glycans, ganoderans A and B. These glycans elicited remarkable hypoglycemic actions in normal and alloxan-induced hyperglycemic mice.

Scientific References:

1.Ganoderma lucidum:Research update.

Claims & Warning:

Claims: Information this web site presented is meant for Nutritional Benefit and as an educational starting point only, for use in maintenance and promotion good health in cooperation with a common knowledge base reference...Furthermore,it based solely on the traditional and historic use or legend of a given herb from the garden of Adonis. Although every effort has been made to ensure its accurate, please note that some info may be outdated by more recent scientific developments.....

Pharmakon Warning: The order of knowledge is not the transparent order of forms and ideas,as one might be tempted retrospectively to interpret it; it is the antidote....(*Dissemination,Plato's Pharmacy,II.The Ingredients:Phantasms,Festivals,and Paints;138cf. Jacques Derrida.*).

And as it happens,the technique of imitation,along with the production of the simulacrum,has always been in Plato's eyes manifestly magical,thaumaturgical:.....and the same things appear bent and straight to those who view them in water and out,or concave and convex,owing to similar errors of vision about colors, and there is obviously every confusion of this sort in our souls.And so scene painting (skiagraphia) in its exploitation of this weakness of four nature falls nothing short of witchcraft (thaumatopoia), and so do jugglery and many other such contrivances.(*Republic X,602c-d;cf.also 607c*).

t epididymal cells and counteract their apoptosis in diabetic condition.