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ReishiMax – Compendium of Abstracts

Journal reference:
Loganathan J[1], Jiang J[1], Smith A[1], Jedinak A[1], Thyagarajan-Sahu A[1], Sandusky GE[2], Nakshatri H[3], Sliva D[1].
The mushroom Ganoderma lucidum suppresses breast-to-lung cancer metastasis through the inhibition of pro-invasive genes. Int J Oncol. 2014 Jun;44(6):2009-15.

[1] Cancer Research Laboratory, Methodist Research Institute, Indiana University Health, Indianapolis, IN 46202, USA.
[2] Department of Pathology, Indiana University School of Medicine, Indianapolis, IN 46202, USA.
[3] Department of Biochemistry and Molecular Biology, Indiana University School of Medicine, Indianapolis, IN 46202, USA.

Reishi mushroom extract used by Loganathan *et al.* in their 2014 publication is identified in the Materials and Methods Section of their publication as follows: GLE was supplied by Pharmanex (Provo, UT). GLE is a standardized Ganoderma lucidum extract containing 6% triterpenes and 13.5% polysaccharides;

The reishi extract supplied by Pharmanex was ReishiMax^{GLp}

The mushroom Ganoderma lucidum suppresses breast-to-lung cancer metastasis through the inhibition of pro-invasive genes.

ABSTRACT

Breast cancer metastasis is one of the major reasons for the high morbidity and mortality of breast cancer patients. In spite of surgical interventions, chemotherapy, radiation therapy and targeted therapy, some patients are considering alternative therapies with herbal/natural products. In the present study, we evaluated a well-characterized extract from the medicinal mushroom Ganoderma lucidum (GLE) for its effects on tumor growth and breast-to-lung cancer metastasis. MDA-MB-231 human breast cancer cells were implanted into the mammary fat pads of nude mice. GLE (100 mg/kg/every other day) was administered to the mice by an oral gavage for 4 weeks, and tumor size was measured using microcalipers. Lung metastases were evaluated by hematoxylin and eosin (H&E) staining. Gene expression in MDA-MB-231 cells was determined by DNA microarray analysis and confirmed by quantitative PCR. Identified genes were silenced by siRNA, and cell migration was determined in Boyden chambers and by wound-healing assay. Although an oral administration of GLE only slightly suppressed the growth of large tumors, the same treatment significantly inhibited the number of breast-to-lung cancer metastases. GLE also downregulated the expression of genes associated with invasive behavior (HRAS, VIL2, S100A4, MCAM, I2PP2A and FN1) in MDA-MB-231 cells. Gene silencing of HRAS, VIL2, S100A4, I2PP2A and FN1 by siRNA suppressed migration of MDA-MB-231 cells. Our study suggests that an oral administration of GLE can inhibit breast-to-lung cancer metastases through the downregulation of genes responsible for cell invasiveness. The anti-metastatic benefits of GLE warrant further clinical studies.

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The below abstract is available at the following internet link:
http://www.plosone.org/article/info%3Adoi%2F10.1371%2Fjournal.pone.0047873

Journal reference:
Daniel Sliva[1,2,4]*, Jagadish Loganathan[1], Jiahua Jiang[1], Andrej Jedinak[1], John G. Lamb[5], Colin Terry[1], Lee Ann Baldridge[3], Jiri Adamec[6], George E. Sandusky[3], Shailesh Dudhgaonkar[1] Mushroom *Ganoderma lucidum* Prevents Colitis-Associated Carcinogenesis in Mice. PLoS ONE 7(10): e47873. doi:10.1371/journal.pone.0047873

[1] Cancer Research Laboratory, Methodist Research Institute, Indiana University Health, Indianapolis, Indiana, United States of America,
[2] Department of Medicine, Indiana University School of Medicine, Indianapolis, Indiana, United States of America, [3] Department of Pathology, Indiana University School of Medicine, Indianapolis, Indiana, United States of America, [4] Indiana University Cancer Center, Indiana University School of Medicine, Indianapolis, Indiana, United States of America
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Reishi mushroom extract used by Silva *et al.* in their 2012 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

Mushroom *Ganoderma lucidum* Prevents Colitis-Associated Carcinogenesis in Mice

ABSTRACT

Background: Epidemiological studies suggest that mushroom intake is inversely correlated with gastric, gastrointestinal and breast cancers. We have recently demonstrated anticancer and anti-inflammatory activity of triterpene extract isolated from mushroom Ganoderma lucidum (GLT). The aim of the present study was to evaluate whether GLT prevents colitis-associated carcinogenesis in mice.
Methods/Principal Findings: Colon carcinogenesis was induced by the food-borne carcinogen (2-Amino-1-methyl-6-phenylimidazol[4,5-b]pyridine [PhIP]) and inflammation (dextran sodium sulfate [DSS]) in mice. Mice were treated with 0, 100, 300 and 500 mg GLT/kg of body weight 3 times per week for 4 months. Cell proliferation, expression of cyclin D1 and COX-2 and macrophage infiltration was assessed by immunohistochemistry. The effect of GLT on XRE/AhR, PXR and rPXR was evaluated by the reporter gene assays. Expression of metabolizing enzymes CYP1A2, CYP3A1 and CYP3A4 in colon tissue was determined by immunohistochemistry. GLT treatment significantly suppressed focal hyperplasia, aberrant crypt foci (ACF) formation and tumor formation in mice exposed to PhIP/DSS. The anti-proliferative effects of GLT were further confirmed by the decreased staining with Ki-67 in colon tissues. PhIP/DSS-induced colon inflammation was demonstrated by the significant shortening of the large intestine and macrophage infiltrations, whereas GLT treatment prevented the shortening of colon lengths, and reduced infiltration of macrophages in colon tissue. GLT treatment also significantly downregulated PhIP/DSS-dependent expression of cyclin D1, COX-2, CYP1A2 and CYP3A4 in colon tissue.
Conclusions: Our data suggest that GLT could be considered as an alternative dietary approach for the prevention of colitis-associated cancer.

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The below abstract is available at the following internet link:
http://www.fasebj.org/doi/10.1096/fasebj.26.1_supplement.373.2

Journal reference:
Yang J[1], Wu Z[1], Yao Y[1], Zhang Y[1], Zhao C[1], Dong Y[1], Tan NZ[1], Zhu JS[2,3]. ReishiMax improves antioxidant capacity in an oxidative stress model and extends lifespan in a natural aging model. *FASEB J. April 2012 (26): 373.2*

[1] Pharmanex Beijing Pharmacology Center, Beijing, China, People's Republic of
[2] Nu Skin Center for Anti-Aging Research, Provo, UT
[3] Hong Kong Polytechnic University, Hong Kong, Hong Kong

Reishi mushroom extract used by Yang *et al.* in their 2012 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

ReishiMax improves antioxidant capacity in an oxidative stress model and extends lifespan in a natural aging model

ABSTRACT

We reported that ReishiMax (RM, a *Ganoderma lucidum* extract) improved immune functions and inhibited cancer malignancy. We further studied its effect on antioxidant and lifespan extension in mice. (1)Antioxidant study: 2-mo male mice were randomized to receive 60 days of vehicle or RM at a dose of 175, 350 or 700 mg/kg, and given a dose of 11 Gy ^{60}Co on Day 60 and sacrificed on Day 64. Compared to radiation controls, 60 days of RM increased plasma GSH by 34–42% ($p<0.05$) and liver CAT by 19–30% ($p<0.01$) in the 3 dose groups. RM increased liver GSH-Rd by 9% ($p=0.03$, 175 and 350 mg/kg), liver GSH-Px by 10% and plasma thiol groups by 12% ($p<0.01$, 700m/kg). (2)Lifespan study: Male and female ICR mice (12-mo) were randomized to receive vehicle or RM at a dose of 175, 350 or 700 mg/kg prior mixed with forage. Calorie intake was adjusted twice a week to match the levels for controls. Compared to controls, the median lifespan was extended with RM by 35–69 days, lifespan of the longest surviving mice by 186–262 days, and the maximal lifespan (average of the longest 10% lifespan) by 124–191days ($p<0.05$). Kaplan-Meier Survivor analysis showed significantly extended lifespan and reduced death risks with RM, with the best survivor curve observed in mice at RM 175 mg/kg ($p=0.02$). In conclusion, RM extends lifespan in natural aging mice and improves antioxidant capacity in oxidative stress mice, supporting in general the anti-aging activity of RM.

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The below abstract is available at the following internet link:
http://www.fasebj.org/doi/10.1096/fasebj.25.1_supplement.601.2

Journal reference:
Wu Z[1], Zhang Y[1], Tan NZ[1], Zhao C[1], Zhu JS[1,2]. ReishiMax extends the lifespan of mice: A preliminary report FASEB *J*, 2011 25:Abstract #601.2

[1] Pharmanex Beijing Pharmacology Center, Beijing, China, People's Republic of
[2] Nu Skin Center for Anti-Aging Research, Provo, UT

Reishi mushroom extract used by Wu *et al.* in their 2011 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

ReishiMax extends the lifespan of mice: *A preliminary report*

ABSTRACT

Ganoderma lucidum (Reishi) has long been used as a medicinal herb for immune enhancement and cancer prevention and adjuvant therapy. We previously reported that ReishiMax (RM), a Reishi extract enriched in Reishi polysaccharides and triterpenes, enhanced proliferations of macrophages, B, T and NK lymphocytes, increased serum IgA, IgG, IgM & secretion of IL2 and Interferon, decreased IL5 secretion, and inhibited cancer malignancy (*FASEB J* 2007, 21:A1100; 2008, 22:1136.2). In this study, we examined the effect of RM in lifespan extension in mice. Male and female ICR mice (12 months of age) were randomized to receive either mouse chaw alone or prior mixed with RM at a dose of 175, 350 or 700 mg/kg. Calorie intake was adjusted twice a week to match the levels for the male or female controls. RM treatment (88 wks so far) showed: (1) no significant differences in body weight and calorie intake among the groups; (2) compared to controls, lifespan was extended 30–66 days at 50% survival, 46–110 days at 20% survival and 61 to >148 days at 10% survival (the study is ongoing). Kaplan-Meier Survivor analysis showed significantly extended lifespan with RM and reduced death risks, with the best survivor curve observed in mice receiving RM supplementation at 175 mg/kg (equivalent to the human dose) (p=0.023). Our data thus far indicates that ReishiMax extends the lifespan of normal aging mice.

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The below abstract is available at the following internet link:
http://www.fasebj.org/doi/10.1096/fasebj.24.1_supplement.738.5

Journal reference:
Tan NZ[1], Zhang Y[1], Yang J[1], Zhao C[1], Zhu JS[2,3]. ReishiMax extends the lifespan in an aging model: A preliminary report. FASEB *J.* April 2010 (24): Abstract #738.5

[1] Pharmanex Beijing Pharmacology Center, Beijing, China, People's Republic of
[2] Pharmanex Research Institute, Provo, UT
[3] School of Pharmacy, Xinjiang Shihezi University, Shihezi, China, People's Republic of

Reishi mushroom extract used by Tan *et al.* in their 2010 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

ReishiMax extends the lifespan in an aging model: *A preliminary report*

ABSTRACT

Ganoderma lucidum (Reishi) has long been used as a medicinal herb in China for immune enhancement and cancer prevention and adjuvant therapy. ReishiMax (RM), a proprietary extract of Reishi enriched in Reishi triterpenes and polysaccharides showed immune enhancement (enhanced proliferations of macrophages, B, T and NK lymphocytes, increases in serum IgA, IgG, IgM & secretion of IL2 and Interferon, and decreases in IL5 secretion) and inhibition of cancer malignancy (FASEB J 2007, 21:A1100; 2008, 22:1136.2). We further examined the RM's effect in lifespan extension in mice. ICR mice (12 m of age; 25 males & 25 females) were randomized into 4 groups, receiving either rat chaw alone or the forage prior mixed with RM at a dose of 175, 350 or 700 mg/kg. Calorie intake was monitored twice a week and adjusted to match the calorie intake of controls. RM treatment (36 wks so far) showed: (1) no significant differences in body weight and calorie intake among the groups; (2) compared to controls, the 90% survival time extends 20, 56 and 44 days in the 3 RM dose groups, and the 75% survival time extends 21, 70 and 24 days, respectively. Kaplan-Meier Survivor analysis showed significantly extended lifespan and reduced death risks by RM: p=0.048 (Wk28), p=0.045 (Wk32), p=0.022 (Wk36), with the best survivor curve for the RM 350 mg/kg therapy (equivalent to the human dose). The data thus far indicates that RM extends the lifespan in mice.

Journal reference:
Thyagarajan-Sahu A, Lane B, Sliva D. ReishiMax, mushroom based dietary supplement, inhibits adipocyte differentiation, stimulates glucose uptake and activates AMPK. BMC Complement Altern Med. 2011 Sep 19;11:74

Reishi mushroom extract used by Thyagarajan-Sahu *et al.* in their 2011 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] are identified by name in the title, and in several places throughout the study.

ReishiMax, mushroom based dietary supplement, inhibits adipocyte differentiation, stimulates glucose uptake and activates AMPK

ABSTRACT

Background: Obesity is a health hazard which is closely associated with various complications including insulin resistance, hypertension, dyslipidemia, atherosclerosis, type 2 diabetes and cancer. In spite of numerous preclinical and clinical interventions, the prevalence of obesity and its related disorders are on the rise demanding an urgent need for exploring novel therapeutic agents that can regulate adipogenesis. In the present study, we evaluated whether a dietary supplement ReishiMax (RM), containing triterpenes and polysaccharides extracted from medicinal mushroom Ganoderma lucidum, affects adipocyte differentiation and glucose uptake in 3T3-L1 cells.
Methods: 3T3-L1 pre-adipocytes were differentiated into adipocytes and treated with RM (0-300 μg/ml). Adipocyte differentiation/lipid uptake was evaluated by oil red O staining and triglyceride and glycerol concentrations were determined. Gene expression was evaluated by semi-quantitative RT-PCR and Western blot analysis. Glucose uptake was determined with [3H]-glucose.
Results: RM inhibited adipocyte differentiation through the suppresion of expression of adipogenic transcription factors peroxisome proliferator-activated receptor-γ (PPAR- γ), sterol regulatory element binding element protein-1c (SREBP-1c) and CCAAT/enhancer binding protein-α (C/EBP-α). RM also suppressed expression of enzymes and proteins responsible for lipid synthesis, transport and storage: fatty acid synthase (FAS), acyl-CoA synthetase-1 (ACS1), fatty acid binding protein-4 (FABP4), fatty acid transport protein-1 (FATP1) and perilipin. RM induced AMPactivated protein kinase (AMPK) and increased glucose uptake by adipocytes. **Conclusion:** Our study suggests that RM can control adipocyte differentiation and glucose uptake. The health benefits of ReishiMax warrant further clinical studies.

Journal reference:
Thyagarajan A, Jedinak A, Nguyen H, Terry C, Baldridge LA, Jiang J, Sliva D. Triterpenes from Ganoderma Lucidum induce autophagy in colon cancer through the inhibition of p38 mitogen-activated kinase (p38 MAPK). Nutr Cancer. 2010;62(5):630-40.

Reishi extract used by Thyagarajan *et al.* in their 2010 publication: is identified as "GLT" (Ganoderma lucidum triterpene extract) from Pharmanex (Provo, UT; batch number 050607; Shanghai R&D, Pharmanex) in the materials and methods section of the study (see page 631 of the full-length study).

Triterpenes from Ganoderma Lucidum induce autophagy in colon cancer through the inhibition of p38 mitogen-activated kinase (p38 MAPK)

ABSTRACT

Medicinal mushroom Ganoderma lucidum is one of the most esteemed natural products that have been used in the traditional Chinese medicine. In this article, we demonstrate that G. lucidum triterpene extract (GLT) suppresses proliferation of human colon cancer cells HT-29 and inhibits tumor growth in a xenograft model of colon cancer. These effects of GLT are associated with the cell cycle arrest at G0/G1 and the induction of the programmed cell death Type II-autophagy in colon cancer cells. Here, we show that GLT induces formation of autophagic vacuoles and upregulates expression of Beclin-1 (1.3-fold increase) and LC-3 (7.3-fold increase) proteins in colon cancer cells and in tumors in a xenograft model (Beclin-1, 3.9-fold increase; LC-3, 1.9-fold increase). Autophagy is mediated through the inhibition of p38 mitogen-activated protein kinase (p38 MAPK) because p38 MAPK inhibitor, SB202190, induces autophagy and expression of Beclin-1 (1.2-fold increase) and LC-3 (7.4-fold increase), and GLT suppresses phosphorylation of p38 MAPK (approximately 60% inhibition) in colon cancer cells. Taken together, our data demonstrate a novel mechanism responsible for the inhibition of colon cancer cells by G. lucidum and suggest GLT as natural product for the treatment of colon cancer.

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Journal reference:
Adamec J, Jannasch A, Dudhgaonkar S, Jedinak A, Sedlak M, Sliva D. Development of a new method for improved identification and relative quantification of unknown metabolites in complex samples: determination of a triterpenoid metabolic fingerprint for the in situ characterization of Ganoderma bioactive compounds. J Sep Sci. 2009 Dec;32(23-24):4052-8.

Reishi extract used by Adamec *et al.* in their 2009 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the abstract (see below), and the materials and methods section of the study.

Development of a new method for improved identification and relative quantification of unknown metabolites in complex samples: determination of a triterpenoid metabolic fingerprint for the in situ characterization of Ganoderma bioactive compounds

ABSTRACT

Ganoderma lucidum is a mushroom with a long history of medical applications. Research has demonstrated chemotherapeutic effects of G. lucidum in tissue culture, and bioactive fractions of the mushroom have been shown to contain high levels of triterpenoids and polysaccharides. In this study, we developed a new method for the detection of ganoderic acids and other triterpenes in Ganoderma mushroom extracts based on a post-biosynthetic stable isotope encoding technique. Overall, 57 doublets were identified as potential ganoderic acids and 11 of those matched with the database. Ganoderic acid A, F and H were confirmed by standards and their absolute concentrations were measured in GLT (GA A: 3.88 mg/g; GA F: 0.95 mg/g and GA H: 1.74 mg/g) and ReishiMax (GA A: 2.32 mg/g; GA F: 0.43 mg/g and GA H: 0.85 mg/g) extracts. The method was also used for the evaluation of bioavailability of triterpenes after an oral application and demonstrated the presence of G. lucidum triterpenes in plasma.

Journal reference:
Dudhgaonkar S, Thyagarajan A, Sliva D. Suppression of the inflammatory response by triterpenes isolated from the mushroom Ganoderma lucidum. Int Immunopharmacol. 2009 Oct;9(11):1272-80.

Reishi extract used by Dudhgaonkar *et al.* in their 2009 publication: is identified as "GLT" (Ganoderma lucidum triterpene extract) from Pharmanex (Provo, UT, USA) in the materials and methods section of the study (see page 1273 of the full-length study).

Suppression of the inflammatory response by triterpenes isolated from the mushroom Ganoderma lucidum

ABSTRACT

Ganoderma lucidum is a popular medicinal mushroom, which has been used in the Traditional Chinese medicine for the prevention or treatment of a variety of diseases. In the present study we evaluated the anti-inflammatory effects of the triterpene extract from G. lucidum (GLT) in LPS-stimulated macrophages. Here we show that GLT markedly suppressed the secretion of inflammatory cytokine tumor necrosis factor-alpha (TNF-alpha) and interleukin-6 (IL-6), and inflammatory mediator nitric oxide (NO) and prostaglandin E(2) (PGE(2)) from lipopolysaccharide (LPS)-stimulated murine RAW264.7 cells. GLT also down-regulated LPS-dependent expression of inducible nitric oxide synthase (iNOS) and cyclooxygenase 2 (COX-2) in RAW264.7 cells. The anti-inflammatory effects of GLT were mediated by the inhibition of transcription factor NF-kappaB as demonstrated by decreased NF-kappaB-DNA binding activity, and the suppression of p65 phosphorylation in LPS-stimulated macrophages treated with GLT. Moreover, GLT inhibited LPS-dependent AP-1-DNA binding activity and down-regulated expression of AP-1 subunit c-Jun. In addition, GLT suppressed the activity of MAP kinases as observed by the down-regulation of LPS-induced phosphorylation of ERK1/2 and JNK but not p38. In vivo experiments clearly demonstrated that GLT also inhibited the production of TNF-alpha and IL-6 in LPS-induced endotoxemic mice. Apart from its anti-inflammatory activity, GLT suppressed cell proliferation of RAW264.7 cells through cell cycle arrest at G0/G1-G2M, which was mediated by the down-regulation of expression of cell cycle regulatory proteins cyclin D1, CDK4 and cyclin B1, respectively. In conclusion, the anti-inflammatory and anti-proliferative effects of GLT on macrophages are mediated through the inhibition of NF-kappaB and AP-1 signaling pathways.

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The below abstract is available at the following internet link:
http://www.fasebj.org/doi/10.1096/fasebj.22.1_supplement.1136.2

Journal reference:
Zhang Y[1], Zhang L[2], Tan NZ[1], Qi Y[2], Gao L[1], Zhu JS[3]. Combined use of Ganoderma lucidum ReishiMax and tea polyphenols Tegreen inhibits tumor growth synergistically in cancer-bearing mice. *FASEB J. March 2008 22 (Meeting Abstract Supplement) 1136.2*

[1] Pharmanex BJ Clinical Pharmacology Center, Beijing, China, People's Republic of
[2] Pharmanex Shanghai R&D Center, Shanghai, China, People's Republic of
[3] Clinical Pharmacology, Pharmanex Research Institute, Provo, UT

Reishi mushroom extract and green tea extract used by Zhang *et al.* in their 2008 publication:
ReishiMax[GLp], and Tegreen 97, [Pharmanex (Provo, UT)].

Combined use of Ganoderma lucidum (ReishiMax) and tea polyphenols (Tegreen) inhibits tumor growth synergistically in cancer-bearing mice

ABSTRACT

Ganoderma lucidum (Reishi) and green tea are commonly used in China for cancer prevention and adjuvant therapy. A screening revealed superior anti-malignancy activities of ReishiMax (RM) among commercial Reishi products (JACM 9:491, 2003). Synergy of RM and Tegreen (TG; containing >98% tea polyphenols) was found in anti-cancer in human breast and prostate cancer cells (Itnl J Oncol 30:963, 2007). Further screening showed that fucose-containing polysaccharides are highly enriched in RM (0.34%), the class of polysaccharides demonstrating high immune enhancing activities (Bioorg Med Chem 10:1050, 2002). They are much less (0.04–0.20%) in other Reishi products. In addition to the survival studies in cancer mice (FASEB J 21:A1100, 2007), we tested synergy of RM and TG in inhibiting tumor growth in sarcoma-bearing mice. After 28-day treatment, RM+TG significantly decreased tumor weight by 45% in S180-innoculated mice, compared to controls ($p<0.05$). The data further confirmed the previous finding of synergy of RM and TG in anti-malignancy, indicating their therapeutic values in cancer prevention and adjuvant treatment.

Journal reference:
Thyagarajan A, Zhu J, Sliva D. Combined effect of green tea and *Ganoderma lucidum* on invasive behavior of breast cancer cells. International Journal of Oncology. 2007 Apr;30(4):963-9.

Reishi mushroom extract and green tea extract used by Thyagarajan *et al.* in their 2007 publication:
ReishiMax^{GLP}, and Tegreen 97, [Pharmanex (Provo, UT)] are identified by name in the materials and methods section of the study.

Combined effect of green tea and *Ganoderma lucidum* on invasive behavior of breast cancer cells

ABSTRACT

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.

The following study was presented at the Experimental Biology Meeting, Washington, DC. May 1, 2007. This same abstract is available at the following internet link: http://www.fasebj.org/doi/10.1096/fasebj.21.6.A1100-a

Journal reference:

Chen W[1], Zhang Y[1], Tan NZ[1], Qi Y[2], Zhu JS[3],. Synergy of *Ganoderma lucidum* extract ReishiMax and green tea polyphenols Tegreen in anti-cancer in a S180-inoculation model. *FASEB J.* Meeting Abstracts, 2007, 21(6): Abstract# 852.3.

[1] Pharmanex Beijing Pharmacology Center, 2 Xinkang Street, Beijing, 100088, China, People's Republic of,
[2] Pharmanex Shanghai R&D Center, 572 Bipo Road, 116-11, Shanghai, 201203, China, People's Republic of,
[3] Clincial Pharmacology, Pharmanex Research Institute, 2 Xinkang Street, Beijing, 0, 84601

Reishi mushroom extract and green tea extract used by Chen *et al.* in their 2007 publication:

ReishiMax^{GLp}, and Tegreen 97, [Pharmanex (Provo, UT)]

Synergy of *Ganoderma lucidum* extract ReishiMax and green tea polyphenols Tegreen in anti-cancer in a S180-inoculation model

ABSTRACT

Ganoderma lucidum (GL, or Reishi) and green tea have been used as folk medicines in China for cancer prevention and adjuvant therapy. Screening of commercial GL products showed that ReishiMax (RM) is superior to other commercial products in inhibiting cancer malignancy (Sliva, J Altern Compl Med 2003, 9:491). RM or Tegreen (TG; containing >98% tea polyphenols) inhibits the proliferation, colony formation, migration and invasive behaviors of human breast cancer cells (Sliva, Acta Pharmacol Sinica 2006, suppl.1:338). The inhibitory effects were enhanced profoundly by combining RM & TG. Chemical comparisons showed higher amounts of triterpenes and polysaccharides and more triterpene species in RM. Immune profiling demonstrated that RM enhances proliferations of macrophages, B, T and NK lymphocytes. It increases serum IgA, IgG & IgM, and IL2 secretion, but decreases IL5 secretion. In vivo studies were conducted to confirm the synergistic effects of the 2 anti-cancer herbs in cancer mice inoculated with S180 sarcoma cells. Treatment with RM+TG for 12 days delayed the death of S180-innoculated mice and reduced the death risk in this early malignant phase after S180-inoculation, compared to controls. The data demonstrates synergy in vivo of RM and TG in anti-sarcoma, suggesting potential therapeutic values for cancer prevention and adjuvant cancer treatment in humans.

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The following study was presented at the 15th World Congress of Pharmacology, in Beijing China, July 2006. A full-length study write-up is not available.

Journal reference:
Sliva, D, and Thyagarajan, A., Combined inhibition of invasive behavior of metastatic breast cancer cells by *Ganoderma lucidum* and green tea. Acta Pharmacologica Sinica [Abstracts of the 15th World Congress of Pharmacology, July 2-7, 2006, Beijing, China] 2006 July; Supplement 1:1-489. (pg. 338).

Reishi mushroom extract and green tea extract used by Thyagarajan *et al.* in their 2006 publication:
ReishiMax^{GLp}, and Tegreen 97, [Pharmanex (Provo, UT)]

Combined inhibition of invasive behavior of metastatic breast cancer cells by *Ganoderma lucidum* and green tea.

Daniel Sliva[1,2,3] and Anita Thyagarajan[1]. [1]Cancer Research Laboratory, Methodist Research Institute, 1800 N Capitol Ave, E504, Indianapolis, [2]Department of Medicine, and [3]Indiana University Cancer Center, Indiana University School of Medicine, Indianapolis, IN, USA.

ABSTRACT

The objective of the present study was to evaluate the combined effects of dietary supplements consisting of *Ganoderma lucidum* (GL) and green tea (GT) extracts on human breast cancer cells MDA-MB-231. The effect on growth was evaluated by the inhibition of cell proliferation (anchorage-dependent growth) and colony formation (anchorage-independent growth), whereas the effect on invasive behavior was evaluated by the inhibition of cell adhesion to vitronectin, cell migration and cell invasion through matrigel. GL as well as GT inhibited proliferation and colony formation of MDA-MB- 231 cells in a dose-dependent manner, and these effects were profoundly enhanced by the combination of GL/GT. In addition, the combination of GL/GT demonstrated synergism against invasive behavior of breast cancer cells. The inhibition of cell invasiveness (adhesion, migration invasion) is mediated through the urokinaseplasminogen activator (uPA), since GT, GL as well as GT/GL suppressed secretion of uPA. In summary, combination of *G. lucidum* and green tea extracts could be considered in the prevention/therapy of breast cancer.

Journal reference:
Thyagarajan A, Jiang J, Hopf A, Adamec J, Sliva D. Inhibition of oxidative stress-induced invasiveness of cancer cells by *Ganoderma lucidum* is mediated through the suppression of interleukin-8 secretion. International Journal of Molecular Medicine. 2006 Oct;18(4):657-64.

Reishi extract used by Thyagarajan *et al.* in their 2006 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study.

Inhibition of oxidative stress-induced invasiveness of cancer cells by *Ganoderma lucidum* is mediated through the suppression of interleukin-8 secretion

ABSTRACT

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 stressinduced 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-κB. 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.

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The following study was presented at the Experimental Biology (FASEB) meeting in San Francisco, CA. April 1-5, 2006. This same abstract is available at the following internet link:
http://www.fasebj.org/doi/10.1096/fasebj.20.5.A1012-c

Journal reference:
Thyagarajan A[1], Jiang J[1], Stanley G[1], Sliva D[1,2]. *Ganoderma lucidum* inhibits oxidative stress-induced invasiveness of cancer cells through the suppression of interleiken-8 (IL-8) secretion. *FASEB J.*, 2006; 20(5):A1012, Abstract# 652.6.

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Reishi mushroom extract used by Thyagarajan *et al.* in their 2006 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

Ganoderma lucidum inhibits oxidative stress-induced invasiveness of cancer cells through the suppression of interleukin-8 (IL-8) secretion

ABSTRACT

Epidemiological and experimental studies suggest that the intake of natural/nutrient products is inversely related to cancer risk, and dietary antioxidants can reduce the risk of certain cancers. *Ganoderma lucidum* is an Asian medicinal mushroom that has been used for the treatment of various diseases including cancer. We have previously demonstrated that *G. lucidum* suppresses growth, angiogenesis and invasiveness of highly 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. Here, 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 ERK1/2, which resulted in the down-regulation of expression of c-Fos, followed by the inhibition of transcription factor AP-1. The biological effect of *G. lucidum* on cell migration was mediated by the suppression of secretion of interleukin-8 (IL-8) from MCF-7 cells. In summary, our results suggest that *G. lucidum* inhibit oxidative stress-induced invasive behavior of breast cancer cells by modulating of MAPK signaling and could be potentially considered as an antioxidant in adjuvant cancer therapy.

Journal reference:
Jiang J, Slivova V, Sliva D. *Ganoderma lucidum* inhibits proliferation of human breast cancer cells by down-regulation of estrogen receptor and NF-κB signaling. International Journal of Oncology, 2006, 29(3), 695–703.

Reishi extract used by Jiang *et al.* in their 2006 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study.

Ganoderma lucidum suppresses growth of breast cancer cells through the inhibition of Akt/NF-κB signaling

ABSTRACT

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-κB 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-κB signaling. Thus, *G. lucidum* down-regulated the expression of ERα in MCF-7 cells but did not affect the expression of ERβ 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-α-induced (MCF-7) as well as constitutive (MDA-MB-231) activity of NF-κB. The inhibition of ER and NF-κB 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-κB signaling, and implicate *G. lucidum* as a suitable herb for chemoprevention and chemotherapy of breast cancer.

Journal reference:
Stanley G, Harvey K, Slivova V, Jiang J, Sliva D. 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.

Reishi extract used by Stanley *et al.* in their 2005 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study (see page 47 of the full-length study).

Ganoderma lucidum suppresses angiogenesis through the inhibition of secretion of VEGF and TGF-beta1 from prostate cancer cells

ABSTRACT

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.

Journal reference:
Jiang J, Slivova V, Harvey V, Valachovicova T, and Sliva D. *Ganoderma lucidum* suppresses growth of breast cancer cells through the inhibition of Akt/NF-κB signaling. Nutrition and Cancer, 2004, *49*(2), 209–216.

Reishi extract used by Jiang *et al.* in their 2004 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study.

Ganoderma lucidum suppresses growth of breast cancer cells through the inhibition of Akt/NF-κB signaling

ABSTRACT

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.

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Journal reference:
Slivovas, V., Valachoviciva, T., Jiang, J., Sliva, D. *Ganoderma lucidum* inhibits invasiveness of breast cancer cells, Journal of Cancer Integrative Medicine, 2004; 2:1, pp. 25-30.

Reishi extract used by Slivova *et al.* in their 2004 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study.

Ganderma lucidum inhibits invasiveness of breast cancer cells

ABSTRACT

Ganoderma lucidum (Reishi) is a popular Asian medical mushroom, which has been widely used in traditional Chinese medicine to treat a variety of diseases. Although originally used as a mushroom for longevity, the dried powder of *Ganoderma lucidum* was recommended as a cancer chemotherapy agent in ancient China. Recent *in vitro* and animal studies have suggested that *Ganoderma lucidum* exhibits anticancer activity, mainly through stimulation of the host immune system by polysaccharides or by the cytotoxic effects of triterpenes. We have demonstrated that purified spores or fruiting body of *Ganoderma lucidum* down-regulated the expression of urokinase plasminogen activator (uPA) and uPA receptor (uPAR), which resulted in the suppression of cell motility in cancer cells. In this study, we investigated how *Ganoderma lucidum*, in the form of a dietary supplement, can modulate the metastatic behavior of the highly invasive human breast cancer cells MDA-MB-231. Our data demonstrate that *Ganoderma lucidum* inhibits cell adhesion, cell migration, and cell invasion of highly metastatic breast cancer cells. Furthermore, *Ganoderma lucidum* suppressed the anchorage-independent growth (colony formation) of MDA-MB-231 cells. Based on these results, *Ganoderma lucidum* may contribute to reducing invasion and metastasis of breast cancers by inhibiting cancer cell adhesion, cell migration, cell invasion, and growth of cancer cells.

PHARMANEX®

Journal reference:
Sliva, D., Sedlak, M., Slivova, V., Valachovicova, T., Lloyd, F., HO, NW., Biologic activity of spores and dried powder from Ganoderma lucidum for the inhibition of highly invasive human breast and prostate cancer cells. Journal of Alternative and Complementary Medicine, 2003; 9:4, pp. 491-497.

Study focus: Six reishi products were compared for their effects on human breast cancer cells and human prostate cancer cells

Excerpt from the article:

> *Interestingly, the sample containing powdered extract with spores (sample F) was the most potent in inhibiting migration (99%).*

ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified as "sample F" in this *Sliva 2003* investigation.

Biologic activity of spores and dried powder from Ganoderma lucidum for the inhibition of highly invasive human breast and prostate cancer cells

ABSTRACT

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-*k*B in breast and prostate cancer cells, we determined how different samples of *Ganoderma lucidum* inhibit constitutively active NF-*k*B 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-*k*B, 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-*k*B *in vitro*.

Journal reference:
Lu QY[a], Jin YS[b], Zhang Q[a], Zhang Z[c], Heber D[a], Go VL[a], Li FP[d], Rao JY[b]. *Ganoderma lucidum* extracts inhibit growth and induce actin polymerization in bladder cancer cells in vitro. Cancer Letters. 2004;216 (1):9-20.

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[c]Department of Epidemiology, School of Public Health, University of California, Los Angeles, CA 90095, USA
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Reishi extract used by *Lu et al.* in their 2004 publication: Pharmanex (Provo, UT) is identifiedas the provider of *Ganoderma lucidum* fruiting body in the materials and methods section of the study (see page 10 of the full-length study).

Ganoderma lucidum extracts inhibit growth and induce actin polymerization in bladder cancer cells *in vitro*

ABSTRACT

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 mg/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 etalloproteinase-2 and focal adhesion kinase (total and phospholated) were unchanged, which suggests that other mechanisms may be involved.

The following study was presented at the Experimental Biology (FASEB) meeting in Washington DC, April 17-21, 2004. A full-length study write-up is not available; however, the poster presented at this meeting may be viewed at eh following link: http://www.px2.com.tw/poster/No6.ReishiMax%20liver%20poster%20EB04.pdf

Journal reference:
Lin, W.C., Wu, Y.W., Xie, M.C., Zhu, J.S., ReishiMax protects the liver and improves liver functions in an experimental hepatitis model. FASEB J. 2004; 18(4): A999 (Abstract #650.7).

Reishi mushroom extract used by Lin *et al.* in their 2004 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

ReishiMax protects the liver and improves liver functions in an experimental hepatitis model

ABSTRACT

Literature reported that Reishi (*Ganoderma lucidum*) is capable of protecting the liver. This study was to examine the liver-protecting functions of ReishiMax (RM), a proprietary product containing both extract of *G. lucidum* fruit body and cracked spores of *G. lucidum* (Pharmanex). CCl4 (20%, 0.5ml/rat) was used twice a week during the study to induce liver injury in rats. RM was given daily by gavage at a dose of 208, 624, or 1664 mg/kg, started 1 week prior to the CCl4 injection, and continuously after initial CCl4 injection for 8 weeks. In vehicle controls, CCl4 caused liver injuries, featured with increases in serum GPT and GOT, liver collagen, and spleen weight, and decreases in serum albumin and liver total protein. RM treatment reduced serum transaminases ($p<0.050.01$) and liver collagen ($p<0.01$); prevented the reduction of serum albumin ($p<0.05$) and liver total protein ($p<0.05$); reduced spleen weight ($p<0.05$). Histopathology examination showed apparent improvement of liver structure in RM-treated rats. Our results demonstrated that RM improves liver functions and prevents injury-associated liver fibrosis in the chemical-induced liver injury rat model.

Journal reference:
Jiang, J., Slivova, V., Valachovicova, T., Harvey, K., Sliva, D. *Ganderma lucidum* inhibits proliferation and indices apoptosis in human prostate cancer cells PC-3. International Journal of Oncology, 2004, 24: 1093-1099

Reishi extract used by Jiang *et al.* in their 2004 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)] is identified by name in the materials and methods section of the study.

Ganderma lucidum inhibits proliferation and indices apoptosis in human prostate cancer cells PC-3

ABSTRACT

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.

PHARMANEX®

The following study was presented at the Experimental Biology Meeting, San Diego, CA. April 11-15, 2003. A full-length study write-up is not available.

Journal reference:
Zhao, C., Zhang, Y., Yin, W., Zhang, D., Guo, F., Zhu, JS. ReishiMax improves glucose metabolism in normal and STZ-induced diabetic rats. *FASEB J.*, 17: A1099, 2003, Abstract# 689.4

Reishi mushroom extract used by Zhao *et al.* in their 2003 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

ReishiMax improves glucose metabolism in normal and STZ-induced diabetic rats

ABSTRACT

ReishiMax (RM) is made of cracked spores of Reishi (*Ganoderma lucidum*) and extract of Reishi fruit body by use of proprietary manufacturing method, and is standardized to 13.5% Reishi polysaccharides and 6% Triterpenes. We examined its function in improving glucose metabolism in 2 animal models, normal and STZ-induced diabetic rats. (1) 36 SD normal rats were divided into a control and 2 RM (0.15 and 0.5 g/kg by gavage) groups. After 14 days, RM improved oral glucose tolerance ($p<0.01$ AUC at 0.5 and 1 hr), and increased glucose-insulin index ($p=0.049$) indicating improved insulin sensitivity. But fasting blood glucose (FBG) was not altered in the normoglycemic rats. (2) STZ-induced diabetic rats with FBG 16-25 mmol/L were selected and randomized to an STZ-diabetic control, and 2 RM (0.3 and 1.0 g/kg) groups, along with a normal control group. After 28 days, RM decreased FBG ($p=0.022$) and improved oral glucose tolerance (p–0.003~0.04 AUC). We conclude that ReishiMax improves glucose metabolism in both normal and STZ-diabetic animal models.

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Journal reference:
Wang YY, Wong CH, et al. Studies of immuno-modulating and antitumor activities of Ganoderma lucidum (Reishi) polysaccharides: Functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities. Bioorganic & Medicinal Chemistry 2002;10:1057-1062.

Principal investigator: Chi-Huey Wong, Pharmanex Scientific Advisory Board member at the time of publication.

Reishi extract used by Wang *et al.* in their 2002 publication: Pharmanex is named as the provider of the reishi extract in materials section of the study.

Studies of immuno-modulating and antitumor activities of *Ganoderma lucidum* (Reishi) polysaccharides: Functional and proteomic analyses of a fucose-containing glycoprotein fraction responsible for the activities.

ABSTRACT

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.

PHARMANEX®

Journal reference:
Ma J, Ye Q, Hua Y, Zhang D, Cooper R, Chang MN, Chang JY, Sun HH. New lanostanoids from the mushroom Ganoderma lucidum. Journal of Natural Product, 2002 Jan;65(1):72-5.

Study focus: Three new active reishi compounds identified by Pharmanex scientist.

New Lanostanoids from the Mushroom *Ganoderma lucidum*

ABSTRACT

From a lipophilic extract of the fruiting body of *Ganoderma lucidum*, three new lanostanoids, 8β,9α-dihydroganoderic acid J (**1**), methyl 8β,9α-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.

Journal reference:
Li C, Li Y, Sun HH. New ganoderic acids, bioactive triterpenoid metabolites from the mushroom Ganoderma lucidum. Nat Prod Res. 2006 Sep;20(11):985-91.

Study focus: Two new active reishi compounds identified by Pharmanex scientist.

New ganoderic acids, bioactive triterpenoid metabolites from the mushroom Ganoderma lucidum

ABSTRACT

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.

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Journal reference:
Li C, Yin J, Guo F, Zhang D, Sun HH: Ganoderic acid Sz, a new lanostanoid from the mushroom Ganoderma lucidum. *Nat Prod Res.* 2005 July; **19**(5), 461–465.

Study focus: A new active reishi compound is identified by Pharmanex scientist.

Ganoderic acid Sz, a new lanostanoid from the mushroom Ganoderma lucidum

ABSTRACT

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.

Other ReishiMax publications available only in Chinese:

1. Tan N-Z, Chiang B-L, Thyagarajan A, Sliva D, Zhao C-S, Zhang Y, Zhu J-S. Immune modulation functions of ReishiMax and its synergistic anti-cancer effects with Tegreen. Proceedings of The 2011 International Meeting on Ganoderma Research. Aug. 17, 2011 Beijing. pp 44-46. [click here]

2. Yang JY, Zhang Y, Zhao C-S, Tan N-Z, Zhu J-S. Anti-oxidation and lifespan-extension activities of ReishiMax in oxidative stress and aging models. Proceedings of The 2011 International Meeting on Ganoderma Research. Aug. 17, 2011 Beijing. pp 47-49.
[click here]

3. Zhu J-S, Li CL, Sliva D, Tan NZ, Zhang Y. The synergy in anti-cancer by combined use of Ganoderma lucidum extract ReishiMax and green tea polyphenols Tegreen". Proceedings of 2009 International Symposium on Cancer Prevention by Foods and Chemicals April 11, 2009 Taipei, Taiwan. Chinese Society of Oncology Publishing, pp 14-15. [no online abstract available]

4. Tan NZ, Li CL, Thyagarajan A, Sliva D, Zhang Y, Gao L, Zhu J-S. Effects of Ganoderma lucidum extract ReishiMax on anti-cancer in S180 sarcoma-bearing mice and its synergy with green tea polyphenols Tegreen". Proceedings of 2008 Symposium of Chin Asso Med Mycol. Oct 7-9, 2008 Nanchang, Jiangxi. Chinese Association of Medicinal Mycology Publishing, pp 165-171. [no online abstract available]