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)]

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/cgi/content/meeting_abstract/21/6/A1100-a?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=ganoderma&andorexactfulltext=and&searchid=1&FIRSTINDEX=0&sortspec=relevance&resourcetype=HWCIT

Publication reference:
Chen W[1], Zhang Y[1], Tan N[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.

The following study was presented at the 15th World Congress of Pharmacology, in Beijing China, July 2006.
A PDF copy of this same abstract is available at the following internet link with paid subscription:

http://www.blackwell-synergy.com/doi/abs/10.1111/j.1745-7254.2006.00453.x

Publication reference:
Sliva, D, and Thyagararjan, 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.

Keywords: G. lucidum, tea, cancer.
Acknowledgment: This work was supported by Pharmanex LLC.

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)]

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.

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/cgi/content/meeting_abstract/20/5/A1012-c?maxtoshow=&HITS=10&hits=10&RESULTFORMAT=&fulltext=ganoderma&searchid=1&FIRSTINDEX=0&volume=20&issue=5&resourcetype=HWCIT

Publication 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.

[1] Cancer Research Laboratory, Methodist Research Institute, 1800 N Capitol Ave, E504, Indianapolis, Indiana, 46202,
[2] Department of Medicine, Indiana University School of Medicine, 545 Barnhill Drive, Indianapolis, Indiana, 46202

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., Harvey, V., Valachovicova, T., and 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*, 695–703.

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

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:
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)]

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.

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)]

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.

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.

[a]Center for Human Nutrition, Department of Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA 90095, USA
[b]Department of Pathology and Laboratory Medicine, David Geffen School of Medicine, University of California, Los Angeles, CA 90095, USA
[c]Department of Epidemiology, School of Public Health, University of California, Los Angeles, CA 90095, USA
[d]Dana-Farber Cancer Institute, Boston, MA 02115, USA

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

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

Keywords: Ganoderma lucidum; Chemoprevention; Bladder cancer; Actin polymerization

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.

Publication 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.

(Supported by a research grant from Pharmanex.).

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, 2003, 24: 1093-1099

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

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.

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.

Publication 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.

http://www.ncbi.nlm.nih.gov/pubmed/11836115?ordinalpos=2&itool=EntrezSystem2.PEntrez.Pubmed.Pubmed_ResultsPanel.Pubmed_RVDocSum

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

Reishi extract used by Wang *et al.* in their 2002 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

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.

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.

Reishi mushroom extract used by Ma *et al.* in their 2002 publication: ReishiMax^{GLp} [Pharmanex (Provo, UT)]

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