

How Lingzhi Combats Aging

By Emily Steiner

Over the past several decades, scientific research has intensified and focused on analyzing the hundreds of unique bio-active compounds found in the medicinal Lingzhi Mushroom. Just this year alone, three new compounds were discovered. With each new finding, intriguing medical applications for Lingzhi have emerged.

There is now a wealth of impressive data that demonstrates Lingzhi's life extending properties, but also its significant ability to stimulate brain neurons search and destroy cancer cells and prevent the development of new fat cells in obese individuals. As an example of growing science supporting Lingzhi, researchers using laboratory mice have detailed life span extension of 9% to more than 20% —the equivalent of seven to nearly sixteen years in human terms.

As if these targeted benefits were not sufficient, Lingzhi's numerous compounds show a therapeutic effect on asthma, ⁸ allergies, ⁹ autoimmune diseases, ¹⁰ 11 12 13 14 15 Alzheimer's ¹⁶ and Parkinson's diseases, ¹ diabetes, ¹⁷ 18 19 20 21 22 pancreatic issues ²³ ²⁴ ²⁵ ²⁶, liver disease, ²⁷ ²⁸ ²⁹ ³⁰ ³¹ ³² ³³ ³⁴³⁵ ³⁶ and more.

Given Lingzhi's complex composition of bioactive compounds, there is still more to discover. In this report, we will bring you up to date on how Lingzhi successfully targets a broad spectrum of deleterious factors of aging.

Multiple Components in Lingzhi Target Aging Mechanisms

Lingzhi mushrooms have been used for medicinal purposes for at least 2,000 years.³⁷ The mushrooms were known to the ancients as "the mushroom of immortality" ³⁷—and for good reason. They had the reputation of promoting health and longevity, boosting the immune system, and reducing the risk of life-shortening conditions such as cardiovascular disease and cancer.³⁸ ³⁹ ⁴⁰ ⁴¹ Science has finally validated this traditional wisdom.

Originally, Lingzhi mushrooms were rare and expensive, ^{38 42} but now advances in cultivation techniques have made these medicinal mushrooms more available which has led to an explosion of research on their properties and components. ^{38 42}

Studies have shown that Lingzhi mushrooms can contribute to longer life spans. ^{1 2} They can help manage some of today's most troubling age-related conditions, including autoimmune diseases, neurodegenerative disorders, diabetes, liver disease, cancer, and more.

How is it that this simple mushroom can have such wide-ranging health effects? Keep in mind that there isn't one single cause of aging and disease. Numerous factors contribute to these conditions—meaning that in order to combat them, you need to fight them from a multi-targeted approach. That's exactly what makes Lingzhi mushrooms so powerful. The mushroom itself contains hundreds of biologically active molecules—all of which work together to have such broad-reaching health benefits. 37

Researchers have identified three specific compounds that are essential to Lingzhi's powerful antioxidant and anti-aging effects:

- **Polysaccharides** have anticancer effects based on their ability to prevent abnormal blood vessel formation, and to boost immune system function. 40 42
- **Triterpenes** protect the liver, lower blood pressure and cholesterol, prevent platelet clumping that leads to heart attack and stroke, fight allergic responses triggered by histamine, and also possess anticancer activity.
- Ganoderma lucidum peptide is a unique protein that has remarkably potent antioxidant characteristics that are still being unraveled.⁴³

But what makes Lingzhi mushroom beneficial to so many varied aspects of your health is its actions on many different targets in your body. The actions triggered by Lingzhi mushrooms produce important changes that may contribute to their promotion of longevity.

Lingzhi extracts are known to:

- Protect cellular DNA from oxidant damage that causes aging and cancer.⁴⁴
- Protect mitochondrial DNA and the mitochondria themselves from oxidant damage that weakens their energy-producing abilities and makes them inefficient, another major cause of aging. 45 46 47
- Increase levels and activity of a large suite of natural intracellular antioxidant molecules, resulting in reduced oxidation of cell membranes and organelles that lead to aging and its related diseases. 38 48
- Protect kidney tubule cells from oxidant damage that leads to kidney failure.
- Increase expression of a key longevity gene and promote an increased life span in species ranging from yeasts, to primitive worms, to mammals such as mice. I 2 50 5 I

Several studies have shown that Lingzhi is one of the most powerful mushrooms with regard to antioxidant characteristics. ^{52 53} Lingzhi mushrooms boost total antioxidant capacity, an important measure of the vigor with which they fight oxidant damage. ^{52 54}

In a human study, Lingzhi mushrooms were given to healthy volunteers as a single 1100mg dose.⁵⁴ Plasma antioxidant capacity rose rapidly to a peak at ninety minutes, while urine antioxidant capacity (a measure of what has been in the body) rose by 29% after three hours. Neither study showed any evidence of toxicity or side effects.³⁹

Lingzhi's many mechanisms of action are what allow it to have such a dramatic impact on such a wide array of age-related health threats. Let's now look at some of the most promising areas of research.

Breaking News on Lingzhi Mushrooms and Cancer Prevention

New compounds are being discovered within extracts of Lingzhi mushroom on a regular basis; at least 3 were identified in late 2012 alone. These discoveries are shedding light on Lingzhi extracts' remarkable, multitargeted anti-cancer properties.

Most intriguing are findings that add to our knowledge about Lingzhi and the phenomenon of immune surveillance. New cancer cells appear in your body every day, but your healthy immune system normally searches these out, quickly activating killer cells to destroy developing cancers before they can form tumors.

Lingzhi's many mechanisms of action are what allow it to have such a dramatic impact on such a wide array of age-related health threats.

Advancing age, coupled with the onset of other chronic illnesses, and exposure to various environmental toxins (and even some medications), means that your immune system's ability to carry out immune surveillance wanes. And, if just one abnormal, cancer-prone cell escapes detection and destruction, it can develop into a full-blown malignancy with tremendous swiftness.

Meta-analysis conducted on Lingzhi for Cancer Treatment

An evaluation of all available clinical trials on the use of Lingzhi in cancer treatment was published in June 2012.

While there was insufficient data to demonstrate efficacy Lingzhi by itself, when Lingzhi was given alongside radiation and/or chemotherapy, patients were 50% more likely to respond positively compared to those given chemo/radiation alone. The results in cancer patients receiving Lingzhi showed the expected increases in immune cells known to enhance tumor response and stimulate host immunity.⁸²

There's an abundance of data on ways that Lingzhi extracts boost immune surveillance and enhance detection and elimination of emerging cancer cells from the body. ⁵⁶ And in late 2012, several new studies revealed that these mushrooms have substantially deeper and more advanced mechanisms than had been previously suspected. The mechanisms of how Lingzhi identifies and then attacks cancer cells are extremely sophisticated and effective. We know that cancer cells evade immune system surveillance by "hiding" their abnormal surface markers. ⁴ These types of molecular changes not only permit primary cancer to arise, but also contribute to relapses of cancer following chemotherapy. ⁵⁷

Lingzhi extracts force cancer cells to reveal their telltale markers, flagging them for destruction by immune killer cells.⁴ At the same time, Lingzhi extracts induce the production of specific molecules that the immune system needs to complete the killing process.⁴ Ultimately, Lingzhi extracts enhance the killing of cancer cells by normal

immune killer cells, and reduce the amount of chemotherapy drugs required to finish the job. 5758

In addition to their impressive immune-surveillance-boosting properties, Lingzhi extracts have numerous other ways of attacking cancer:

- Lingzhi compounds, particularly the triterpenes and polysaccharides, limit tumors' growth rate by blocking the abnormal reproductive cycles of cancer cells.⁵⁹
- Some of these compounds are directly toxic to cancer cells, while sparing healthy tissue. 60 61
- Lingzhi compounds inhibit metastatic processes and decrease the expression of genes involved in cancer cell survival, proliferation, invasion, and metastasis.⁶¹
- Lingzhi compounds also trigger the programmed cell death called apoptosis that's suppressed in malignant cells. 55 60 61 62

Together, all of these effects of Lingzhi mushrooms are shown to reduce the size and growth rates of human tumors, both in animals and in human clinical trials.

The most dramatic impact has been shown in colorectal cancer, which is the second leading cause of cancer death among cancers that affect both men and women.⁶³

Clinical studies show that Lingzhi extracts suppress the development of adenomas, which are pre-malignant masses found in the large intestine.⁶⁴

Remarkable Benefits of Lingzhi

Recent studies show that Lingzhi mushrooms have hundreds of components in three distinct classes of bioactive molecules, making them ideal for combating the complex and multifactorial diseases we face with advancing age.

Together, all of these effects of Lingzhi mushrooms are shown to reduce the size and growth rates of human tumors.

Lingzhi extracts prolong life spans in animal experiments by 9 to more than 20%.

Lingzhi boosts the immune system's vigilance against cancer cells, potentially reducing the risk of developing a detectable and deadly tumor.

Lingzhi extracts can suppress an overly vigorous immune response, helping to quell symptoms of allergies, asthma, and autoimmune diseases.

Independent of their immune-modulating effects, Lingzhi mushrooms' active molecules are showing promise in the battle against neurodegenerative diseases, obesity and diabetes, and liver disease.

If there is such a thing as the "ideal" supplement, capable of attacking multiple complex diseases each with multiple causative factors, Lingzhi mushrooms are surely an outstanding candidate.

Lingzhi Balances the Immune System

Lingzhi mushrooms have a well-known ability to beneficially modulate the immune system.⁶⁵ ⁶⁶ ⁶⁷ The mushrooms' ability to boost immunity is the source of their advanced cancer- and infection-fighting properties. But it is equally important to keep your immune system from overreacting and turning on itself, as is the case with autoimmune diseases such as allergies. Lingzhi mushrooms have demonstrated the ability to modulate the delicate balance necessary for a healthy immune system. Studies have shown that Lingzhi mushrooms can reduce the overactive immune response that occurs in conditions such as allergies, asthma, and autoimmune diseases.

The polysaccharides and triterpenes found in Lingzhi mushrooms act at multiple targets in the cascade of events leading to inflammation and excessive immune response. 17 67 68

Lingzhi extracts inhibit the release of histamine from specialized immune cells called "mast cells." They have the ability to reduce the activity in nerves that transmit the itch sensation to the brain after a mosquito bite or similar itchy stimulus. 69 70

Lingzhi extracts were able to sharply reduce the symptoms associated with allergies.

In animal models, Lingzhi extracts were able to sharply reduce the symptoms associated with allergies, such as rhinitis (watery, itchy nose) and mosquito bites. Studies also show that Lingzhi extracts can reduce "airway hyper-responsiveness," the "twitchy" smooth muscle responses in the lung bronchi that trigger an asthma attack.

Lingzhi extracts also show promise for the management of the underlying immune imbalance that leads to autoimmune diseases. ¹⁰⁻¹⁵

Lingzhi Promotes Neuro-protection

Lingzhi extracts were found to stimulate the production of nerve growth factor, which in turn supports the rapid development of healthy neurons and enhances their mitochondrial function.³

Lingzhi's powerful antioxidant and anti-inflammatory properties make these mushrooms attractive candidates for preventing neurodegenerative diseases such as Alzheimer's and Parkinson's. Both of these diseases are driven by oxidative stress and inflammation.

The triterpenes and polysaccharides from the mushrooms reduce the oxidative impact of destructive proteins such as Amyloid-beta, the chief trigger of Alzheimer's disease ¹⁶ and they protect brain cells from the inflammation known to cause Parkinson's disease. ¹⁷⁻²¹

Studies reveal that supplementing with Lingzhi mushrooms has beneficial effects for stroke victims. First, it can limit the size of the stroke-damaged area in the brain, which helps limit behavioral and functional damage caused by the stroke. Second, Lingzhi mushrooms protect brain tissue from hypoxia/reperfusion injury, the "one-two" punch of oxygen starvation followed by excessive oxidation that produces most of the damage in the brains of stroke victims.

But as valuable as these benefits are, nowhere are the effects of Lingzhi mushroom extracts more clear than in their impact on diabetes-related cognitive disorders. In animal studies, Lingzhi spores alleviated diabetes-induced oxidative stress and mitochondrial dysfunction in the hippocampus, one of the brain's chief memory-processing areas.²²

Lingzhi and Diabesity

Obesity is a health hazard sweeping the globe in epidemic proportions—and chief among its complications is type II diabetes. The conditions are so often found hand-in-hand that researchers refer to them as a single disease called *diabesity*—diabetes plus obesity. Lingzhi mushrooms are especially valuable in the fight against this epidemic because they've been shown to have benefits across the entire spectrum of diabesity. ²³⁻²⁶

Laboratory studies show that the polysaccharides and triterpenes in Lingzhi extracts can prevent the development of new fat cells from pre-adipocytes, helping to limit excessive fat storage seen in obese people.⁵ The extracts also have favorable effects on lipid profiles (cholesterol and triglycerides), which are frequently elevated in those with obesity and/or diabetes—and are risk factors for cardiovascular disease. ²³

Diabesity-

Diabetes caused by overweight or obesity.

Lingzhi extracts work to lower blood sugar by several different mechanisms. ⁵ 23 24 72 73 74 75 76 Lingzhi inhibits alpha-glucosidase, the chief enzyme responsible for digesting starches into sugars. ⁷⁷ This inhibition prevents the sharp after-meal spike in glucose that is so dangerous as we age. ⁷⁸ They also limit the destruction caused by advanced glycation end products (AGEs), the proteins whose malfunction promotes aging and inflammation. ⁷⁹

Studies have shown that reducing blood sugar and glycation with Lingzhi supplements reduces diabetic consequences like kidney disease.⁸⁰ Lingzhi extracts also speed wound healing in diabetic individuals, the result of enhanced antioxidant function.⁸¹

Lingzhi Safeguards Liver Function

Your liver is the direct recipient of toxic threats both from the environment and from destructive molecules produced within your body. While it is well protected with its own antioxidant and detoxification systems, oxidation and inflammation eventually take their toll, leaving the aging liver at risk for decreased function, increased accumulation of toxic injury, fibrosis, and cancer. Fortunately, Lingzhi mushrooms offer direct protection against such threats.²⁷

Studies show, for instance, that pre-treating animals with Lingzhi spores can protect them when they're exposed to cadmium, a highly toxic metal capable of causing massive liver failure. Researchers found the spores decreased the cadmium accumulation in liver, while "pushing" the toxic metal into the liquid matrix of the cells. Once there, the mushroom spores increased the production of a cadmium-binding protein that removes the toxin from the body. 28

Lingzhi mushroom extracts similarly protect liver tissue from the toxic effects of certain bacterial infections. In animals with such infections, Lingzhi polysaccharides inhibit inflammation in liver cells.²⁹ Other studies reveal that

Lingzhi polysaccharides restore natural liver antioxidant systems to normal function following an infection, while inhibiting liver enzymes that produce excessive oxidative stress.^{30 31} Lingzhi mushrooms limit the activity of beta-glucuronidase, an enzyme that is elevated in many liver conditions, including inflammation, cirrhosis, and jaundice.^{31 32}

One of the most exciting potential applications for Lingzhi mushrooms in liver disease is in the condition called liver fibrosis, which is the final stage of non-alcoholic fatty liver disease. Statistics have shown that non-alcoholic fatty liver disease is the most common form of liver disease, ultimately affecting 20 to 30% of the population.³²⁻³⁵ In an animal model of toxin-induced liver fibrosis, treatment with Lingzhi extract reversed the fibrosis even after it was

Lingzhi extract reversed liver fibrosis caused by liver disease, long thought to be irreversible.

well-established.³⁶ This is an exceptional result, because in most cases, liver disease that has advanced to the stage of fibrosis is considered irreversible.

Summary

Lingzhi mushrooms provide a broad-spectrum approach to the treatment and prevention of many of today's age-related diseases. With their diverse molecular makeup, they offer a broad spectrum of actions that attack aging at its root.

This is seen clearly in research demonstrating Lingzhi's ability to prolong the life spans of laboratory mice by 9% to more than 20% —the equivalent of 7 to nearly 16 years in human terms.

This is further demonstrated in research that has uncovered its powerful anti-cancer activity. Lingzhi mushrooms contribute to enhanced immune surveillance that can seek and destroy cancer cells before they can form threatening tumors.

Finally, studies have shown that Lingzhi extracts have a role in the prevention or mitigation of asthma, allergies, and autoimmune disorders, while offering protection against neuro-degeneration, obesity and diabetes, and liver diseases of many kinds.

References

- ¹ Chuang MH, Chiou SH, Huang CH, Yang WB, Wong CH. The lifespan-promoting effect of acetic acid and Reishi polysaccharide. Bioorg Med Chem. 2009 Nov 15;17(22):7831-40.
- ² Wu Z, Zhang Y, Tan N, Zhao C, Yang J, Zhu J-S. ReishiMax extends the life span of mice: A preliminary report. The FASEB Journal. 2011 April;25(601.2).
- ³ Chen LW, Horng LY, Wu CL, Sung HC, Wu RT. Activating mitochondrial regulator PGC-1alpha expression by astrocytic NGF is a therapeutic strategy for Huntington's disease. Neuropharmacology. 2012 May 24.
- ⁴ Sun LX, Lin ZB, Duan XS, et al. Enhanced MHC class I and costimulatory molecules on B16F10 cells by Ganoderma lucidum polysaccharides. J Drug Target. 2012 Aug;20(7):582-92.

- ⁵Thyagarajan-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;11:74.
- ⁶ Available at: http://www.census.gov/compendia/statab/cats/births_deaths_marriages_divorces/life_expectancy.html. Accessed July 3, 2012.
- ⁷ Available at: http://web.jhu.edu/animalcare/procedures/mouse.html#biology. Accessed November 2, 2012.
- ⁸ Liu YH, Tsai CF, Kao MC, Lai YL, Tsai JJ. 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.
- ⁹ Mizutani N, Nabe T, Shimazu M, Yoshino S, Kohno S. Effect of Ganoderma lucidum on pollen-induced biphasic nasal blockage in a guinea pig model of allergic rhinitis. Phytother Res. 2012 Mar;26(3):325-32.
- ¹⁰ Jan RH, Lin TY, Hsu YC, et al. Immuno-modulatory activity of Ganoderma lucidum-derived polysaccharide on human monocytoid dendritic cells pulsed with Der p 1 allergen. BMC Immunol. 2011;12:31.
- ¹¹ Ho YW, Yeung JS, Chiu PK, et al. Ganoderma lucidum polysaccharide peptide reduced the production of pro-inflammatory cytokines in activated rheumatoid synovial fibroblast. Mol Cell Biochem. 2007 Jul;301 (1-2):173-9.
- ¹² van der Hem LG, van der Vliet JA, Bocken CF, Kino K, Hoitsma AJ, Tax WJ. Ling Zhi-8: studies of a new immunomodulating agent. Transplantation. 1995 Sep 15;60(5):438-43.
- ¹³ Qi G, Hua H, Gao Y, Lin Q, Yu GY. Effects of Ganoderma lucidum spores on sialoadenitis of non-obese diabetic mice. Chin Med J (Engl). 2009 Mar 5;122(5):556-60.
- ¹⁴ Lin YL, Lee SS, Hou SM, Chiang BL. 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.
- 15 Kohguchi M, Kunikata T, Watanabe H, et al. Immuno-potentiating effects of the antler-shaped fruiting body of Ganoderma lucidum (Rokkaku-Reishi). Biosci Biotechnol Biochem. 2004 Apr;68(4):881-7.
- ¹⁶ Lai CS, Yu MS, Yuen WH, So KF, Zee SY, Chang RC. Antagonizing beta-amyloid peptide neurotoxicity of the anti-aging fungus Ganoderma lucidum. Brain Res. 2008 Jan 23;1190:215-24.
- ¹⁷ Ding H, Zhou M, Zhang RP, Xu SL. Ganoderma lucidum extract protects dopaminergic neurons through inhibiting the production of inflammatory mediators by activated microglia. Sheng Li Xue Bao. 2010 Dec 25;62(6):547-54.
- ¹⁸ Patocka J. Anti-inflammatory triterpenoids from mysterious mushroom Ganoderma lucidum and their potential possibility in modern medicine. Acta Medica (Hradec Kralove). 1999;42(4):123-5.
- ¹⁹ Zhao HB, Lin SQ, Liu JH, Lin ZB. Polysaccharide extract isolated from ganoderma lucidum protects rat cerebral cortical neurons from hypoxia/reoxygenation injury. J Pharmacol Sci. 2004 Jun;95(2):294-8.
- ²⁰ Lee I, Ahn B, Choi J, Hattori M, Min B, Bae K. Selective cholinesterase inhibition by lanostane triterpenes from fruiting bodies of Ganoderma lucidum. Bioorg Med Chem Lett. 2011 Nov 1;21(21):6603-7.
- ²¹ Zhang R, Xu S, Cai Y, Zhou M, Zuo X, Chan P. Ganoderma lucidum protects dopaminergic neuron degeneration through inhibition of microglial activation. Evid Based Complement Alternat Med. 2011;2011:156810.
- ²² Zhou Y, Qu ZQ, Zeng YS, et al. Neuroprotective effect of pre-administration with Ganoderma lucidum spore on rat hippocampus. Exp Toxicol Pathol. 2012 Nov;64(7-8):673-80.
- ²³ Wang CD, Teng BS, He YM, et al. Effect of a novel proteoglycan PTP1B inhibitor from Ganoderma lucidum on the amelioration of hyperglycemia and dyslipidaemia in db/db mice. Br J Nutr. 2012 Mar 27:1-12.
- ²⁴ Zhang HN, He JH, Yuan L, Lin ZB. 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.
- ²⁵ Xue H, Qiao J, Meng G, et al. Effect of *Ganoderma lucidum* polysaccharides on hemodynamic and anti-oxidation in T2DM rats. *Zhongguo Zhong Yao Za Zhi.* 2010 Feb;35(3):339-43.

- ²⁶Yang Q, Wang S, Xie Y, Sun J, Wang J. HPLC analysis of *Ganoderma lucidum* polysaccharides and its effect on antioxidant enzymes activity and Bax, Bcl-2 expression. *Int J Biol Macromol.* 2010 Mar 1;46(2):167-72.
- ²⁷ Shi Y, Sun J, He H, Guo H, Zhang S. Hepatoprotective effects of Ganoderma lucidum peptides against D-galactosamine-induced liver injury in mice. J Ethnopharmacol. 2008 May 22;117(3):415-9.
- ²⁸ Jin H, Jin F, Jin JX, et al. Protective effects of *Ganoderma lucidum* spore on cadmium hepatotoxicity in mice. *Food Chem Toxicol*. 2012 May 29.
- ²⁹ Zhang GL, Wang YH, Ni W,Teng HL, Lin ZB. Hepatoprotective role of *Ganoderma lucidum* polysaccharide against BCG-induced immune liver injury in mice. *World J Gastroenterol.* 2002 Aug;8(4):728-33.
- ³⁰ Wang X, Zhao X, Li D, Lou YQ, Lin ZB, Zhang GL. Effects of *Ganoderma lucidum* polysaccharide on CYP2E1, CYP1A2 and CYP3A activities in BCG-immune hepatic injury in rats. *Biol Pharm Bull.* 2007 Sep;30(9):1702-6.
- ³¹ Kim DH, Shim SB, Kim NJ, Jang IS. Beta-glucuronidase-inhibitory activity and hepatoprotective effect of Ganoderma lucidum. *Biol Pharm Bull*. 1999 Feb;22(2):162-4.
- ³² Basinska A, Florianczyk B. Beta-glucuronidase in disease. Ann Univ Mariae Curie Sklodowska Med. 2003;58(2):386-9.
- ³³ Beaton MD. Current treatment options for nonalcoholic fatty liver disease and nonalcoholic steatohepatitis. *Can J Gastroenterol.* 2012 Jun;26(6):353-7.
- ³⁴ Milic S, Stimac D. Nonalcoholic fatty liver disease/steatohepatitis: epidemiology, pathogenesis, clinical presentation and treatment. *Dig Dis.* 2012;30(2):158-62.
- ³⁵ Paredes AH, Torres DM, Harrison SA. Nonalcoholic fatty liver disease. Clin Liver Dis. 2012 May;16(2):397-419.
- ³⁶ Wu YW, Fang HL, Lin WC. Post-treatment of *Ganoderma lucidum* reduced liver fibrosis induced by thioacetamide in mice. *Phytother Res.* 2010 Apr;24(4):494-9.
- ³⁷ Sanodiya BS,Thakur GS, Baghel RK, Prasad GB, Bisen PS. Ganoderma lucidum: a potent pharmacological macro-fungus. Curr Pharm Biotechnol. 2009 Dec;10(8):717-42
- ³⁸ Wachtel-Galor S, Yuen J, Buswell JA, Benzie IFF. Ganoderma lucidum (Lingzhi or Reishi): A Medicinal Mushroom. In: Benzie IF, Wachtel-Galor S, eds. Herbal Medicine: Biomolecular and Clinical Aspects. 2nd ed. Boca Raton: CRC Press; 2011.
- ³⁹ Wachtel-Galor S, Tomlinson B, Benzie IF. *Ganoderma lucidum* ("Lingzhi"), a Chinese medicinal mushroom: biomarker responses in a controlled human supplementation study. *Br | Nutr.* 2004 Feb;9 I (2):263-9.
- ⁴⁰ Cheng KC, Huang HC, Chen JH, et al. *Ganoderma lucidum* polysaccharides in human monocytic leukemia cells: from gene expression to network construction. *BMC Genomics*. 2007;8:411.
- ⁴¹ Chang YH, Yang JS, Yang JL, et al. *Ganoderma lucidum* extracts inhibited leukemia WEHI-3 cells in BALB/c mice and promoted an immune response in vivo. *Biosci Biotechnol Biochem.* 2009 Dec;73(12):2589-94.
- ⁴² Boh B, Berovic M, Zhang J, Zhi-Bin L. Ganoderma lucidum and its pharmaceutically active compounds. Biotechnol Annu Rev. 2007;13:265-301.
- ⁴³ Sun J, He H, Xie BJ. Novel antioxidant peptides from fermented mushroom Ganoderma lucidum. J Agric Food Chem. 2004 Oct 20;52(21):6646-52.
- ⁴⁴ Wachtel-Galor S, Choi SW, Benzie IF. Effect of Ganoderma lucidum on human DNA is dose dependent and mediated by hydrogen peroxide. Redox Rep. 2005;10(3):145-9.
- ⁴⁵ Ajith TA, Sudheesh NP, Roshny D, Abishek G, Janardhanan KK. Effect of Ganoderma lucidum on the activities of mitochondrial dehydrogenases and complex I and II of electron transport chain in the brain of aged rats. Exp Gerontol. 2009 Mar;44(3): 219-23.
- ⁴⁶ Cherian E, Sudheesh NP, Janardhanan. Free-radical scavenging and mitochondrial activities of Reishi-Ganoderma lucidum (Curt: Fr) P. Karst and Arogyapacha-Trichopus zeylanicus Gaertn extracts. J Basic Clin Physiol Pharmacol. 2009;20(4):289-307.

- ⁴⁷ Sudheesh NP, Ajith TA, Janardhanan KK. *Ganoderma lucidum* (Fr.) P. Karst enhances activities of heart mitochondrial enzymes and respiratory chain complexes in the aged rat.
- ⁴⁸ Sudheesh NP, Ajith TA, Ramnath V, Janardhanan KK. Therapeutic potential of Ganoderma lucidum (Fr.) P. Karst. Against the declined antioxidant status in the mitochondria of post-mitotic tissues of aged mice. Clin Nutr. 2010 Jun;29(3):406-12.
- ⁴⁹ Lai KN, Chan LY, Tang SC, Leung JC. 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.
- ⁵⁰ Weng Y, Lu J, Xiang L, et al. Ganodermasides C and D, two new anti-aging ergosterols from spores of the medicinal mushroom Ganoderma lucidum. Biosci Biotechnol Biochem. 2011;75(4):800-3.
- ⁵¹ Weng Y, Xiang L, Matsuura A, Zhang Y, Huang Q, Qi J. Ganodermasides A and B, two novel anti-aging ergosterols from spores of a medicinal mushroom Ganoderma lucidum on yeast via UTH1 gene. Bioorg Med Chem. 2010 Feb;18(3):999-1002.
- ⁵²Yegenoglu H, Aslim B, Oke F. Comparison of antioxidant capacities of Ganoderma lucidum (Curtis) P. Karst and Funalia trogii (Berk.) Bondartsev & Singer by using different in vitro methods. J Med Food. 2011 May;14(5):512-6.
- ⁵³ Abdullah N, Ismail SM, Aminudin N, Shuib AS, Lau BF. Evaluation of selected culinary-medicinal mushrooms for antioxidant and ACE inhibitory activities. Evid Based Complement Alternat Med. 2012;2012:464238.
- ⁵⁴Wachtel-Galor S, Szeto YT, Tomlinson B, Benzie IF. Ganoderma lucidum ('Lingzhi'); acute and short-term biomarker response to supplementation. Int J Food Sci Nutr. 2004 Feb;55(1):75-83.
- ⁵⁵ Gao P, Hirano T, Chen Z, Yasuhara T, Nakata Y, Sugimoto A. Isolation and identification of C-19 fatty acids with anti-tumor activity from the spores of Ganoderma lucidum (reishi mushroom). Fitoterapia. 2012 Apr;83(3):490-9.
- ⁵⁶ Jin X, Ruiz Beguerie J, Sze DM, Chan GC. Ganoderma lucidum (Reishi mushroom) for cancer treatment. Cochrane Database Syst Rev. 2012;6:CD007731.
- ⁵⁷Wu QP, Xie YZ, Deng Z, et al. Ergosterol peroxide isolated from Ganoderma lucidum abolishes microRNA miR-378-mediated tumor cells on chemoresistance. PLoS One. 2012;7(8):e44579.
- ⁵⁸Yao X, Li G, Xu H, Lu C. Inhibition of the JAK-STAT3 signaling pathway by Ganoderic acid A enhances chemosensitivity of HepG2 Cells to cisplatin. Planta Med. 2012 Sep 7.
- ⁵⁹ Wu G, Qian Z, Guo J, et al. Ganoderma lucidum extract induces G1 cell cycle arrest, and apoptosis in human breast cancer cells. Am J Chin Med. 2012;40(3):631-42.
- ⁶⁰ Liu YJ, Shen J, Xia YM, Zhang J, Park HS. The polysaccharides from Ganoderma lucidum: Are they always inhibitors on human hepatocarcinoma cells? Carbohydr Polym. 2012 Oct 15;90(3):1210-5.
- 61 Martínez-Montemayor MM, Acevedo RR, Otero-Franqui E, Cubano LA, Dharmawardhane SF. Ganoderma lucidum (Reishi) inhibits cancer cell growth and expression of key molecules in inflammatory breast cancer. Nutr Cancer. 2011;63(7): 1085-94. Epub 2011 Sep 2.
- ⁶² Lu H, Song J, Jia XB, Feng L. Antihepatoma activity of Lingzhi acids acid. Phytother Res. 2012 Jan 25.
- ⁶³ Available at: http://www.cdc.gov/VitalSigns/CancerScreening/#. Accessed October 23, 2012.
- ⁶⁴ Oka S,Tanaka S,Yoshida S, et al. A water-soluble extract from culture medium of Ganoderma lucidum mycelia suppresses the development of colorectal adenomas. Hiroshima J Med Sci. 2010 Mar;59(1):1-6.
- ⁶⁵ Kohda H, Tokumoto W, Sakamoto K, et al. The biologically active constituents of Ganoderma lucidum (Fr.) Karst. Histamine release-inhibitory triterpenes. Chem Pharm Bull (Tokyo). 1985 Apr;33(4):1367-74.
- ⁶⁶ Ko HH, Hung CF, Wang JP, Lin CN. Antiinflammatory triterpenoids and steroids from Ganoderma lucidum and G. Tsugae. Phytochemistry. 2008 Jan;69(1):234-9.
- ⁶⁷ 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.

- ⁶⁸ Lin CY, Chen YH, Hsu HY. Ganoderma lucidum polysaccharides attenuate endotoxin-induced intercellular cell adhesion molecule-1 expression in smooth muscle cells and in the neointima in mice. J Agric Food Chem. 2010 Sep 8;58(17):9563-71.
- ⁶⁹ Andoh T, Zhang Q, Yamamoto T, et al. Inhibitory effects of the methanol extract of Ganoderma lucidum on mosquito allergy-induced itch-associated responses in mice. J Pharmacol Sci. 2010;114(3):292-7.
- ⁷⁰ Zhang Q, Andoh T, Konno M, Lee JB, Hattori M, Kuraishi Y. Inhibitory effect of methanol extract of Ganoderma lucidum on acute itch-associated responses in mice. Biol Pharm Bull. 2010;33(5):909-11.
- ⁷¹ Zhou ZY, Tang YP, Xiang J, et al. Neuroprotective effects of water-soluble Ganoderma lucidum polysaccharides on cerebral ischemic injury in rats. J Ethnopharmacol. 2010 Aug 19;131(1):154-64.
- ⁷² Seto SW, Lam TY, Tam HL, et al. Novel hypoglycemic effects of Ganoderma lucidum water-extract in obese/diabetic (+db/ +db) mice. Phytomedicine. 2009 May; 16(5):426-36.
- ⁷³ Kino K, Mizumoto K, Sone T, et al. An immunomodulating protein, Ling Zhi-8 (LZ-8) prevents insulitis in non-obese diabetic mice. Diabetologia. 1990 Dec;33(12):713-8.
- ⁷⁴ Li F, Zhang Y, Zhong Z. Antihyperglycemic effect of Ganoderma lucidum polysaccharides on streptozotocin-induced diabetic mice. Int J Mol Sci. 2011;12(9):6135-45.
- ⁷⁵Teng BS, Wang CD, Yang HJ. A protein tyrosine phosphatase 1B activity inhibitor from Ganoderma lucidum (Fr.) Karst and its hypoglycemic potency on streptozotocin-induced type 2 diabetic mice. J Agric Food Chem. 2011 Jun 22;59(12):6492-500.
- ⁷⁶Teng BS, Wang CD, Zhang D, et al. Hypoglycemic effect and mechanism of a proteoglycan from Ganoderma lucidum on streptozotocin-induced type 2 diabetic rats. Eur Rev Med Pharmacol Sci. 2012 Feb;16(2):166-75.
- ⁷⁷ Fatmawati S, Shimizu K, Kondo R. Ganoderol B: a potent alpha-glucosidase inhibitor isolated from the fruiting body of Ganoderma lucidum. Phytomedicine. 2011 Sep. 15;18(12):1053-5.
- ⁷⁸ Mahomoodally MF, Subratty AH, Gurib-Fakim A, Choudhary MI, Nahar Khan S. Traditional medicinal herbs and food plants have the potential to inhibit key carbohydrate hydrolyzing enzymes in vitro and reduce postprandial blood glucose peaks in vivo. ScientificWorldJournal. 2012;2012:285284.
- ⁷⁹ Chen Y, Qiao J, Luo J, et al. Effects of Ganoderma lucidum polysaccharides on advanced glycation end products and receptor of aorta pectoralis in T2DM rats. Zhongguo Zhong Yao Za Zhi. 2011 Mar;36(5):624-7.
- ⁸⁰ He CY, Li WD, Guo SX, Lin SQ, Lin ZB. Effect of polysaccharides from Ganoderma lucidum on streptozotocin-induced diabetic nephropathy in mice. J Asian Nat Prod Res. 2006 Dec;8(8):705-11.
- ⁸¹ Tie L, Yang HQ, An Y, et al. Ganoderma lucidum polysaccharide accelerates refractory wound healing by inhibition of mitochondrial oxidative stress in type 1 diabetes. Cell Physiol Biochem. 2012;29(3-4):583-94.