

Status of *Ganoderma Lucidum* in United States: *Ganoderma Lucidum* as an Anti-inflammatory Agent

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The status of herbs has recently changed in the United States with the passage Dietary Supplement Health and Education Act of 1994(DSHEA). This law created a new category called "Dietary Supplements" which includes herbs. The act declares these substances are not food additives nor are they drugs. It allows manufacturers to publish more complete directions for use than previously allowed including warnings, contraindications, and side effects. The act also allows manufacturers to publish limited information regarding the benefits in the form of " Statements of Nutritional Support" as well as "Structure and Function Claims".

Alzheimer's Disease is primarily an old age disorder in which competent individuals become agitated, uncomprehending, with profound loss of cognitive function finally requiring continued, complete care. In the United States it is the leading cause of death. At present, the choice of therapeutic or preventive for use in Alzheimer's disease is limited and the best only slow the progress disease for about 40 weeks. Recent research has discovered evidence of inflammation in the brain of Alzheimer's patients and unless inflammation is present there is little evidence of neurodegeneration, even in patients with profuse amyloid B-peptide deposition and neurofibrillary tangles. Prospective and retrospectively collected data on men and women suggest that use of non steroidal anti-inflammatory drugs is associated with reduced risk of Alzheimer's disease. search heightens the importance of the ancient reports where Ganoderma was praised for its effect of increasing memory and preventing forgetfulness in old age reported in Shen Nong Ben Cao Jing vol 1 as early as 456-536 A.D. Research on mice using orally or topically administered Ganoderma provides evidence that Ganoderma lucidum has anti-inflammatory activity. This pharmacological activity may provide the basis for its activity on memory in although we do not know as yet that Ganoderma lucidum can enter the brain and exert anti-inflammatory activity. In cardiovascular research, it has been found that aspirin ingestion can reduce the incidence of cardiovascular disease. The possibility that it is anti-inflammatory activity of aspirin that can provide benefit in reducing the risk of cardiovascular disease is suggested by the finding that higher levels of C-reactive protein in the plasma which is an acute phasemarker for systemic inflammation is a predictor for increased risk of cardiovascular disease. These studies on inflammation provide important evidence that warrants further study of Ganoderma lucidum and its possible role in mitigating these two devastating diseases.

Another important event more specific for Ganoderma was the incorporation of the Ganoderma International Research Institute in New York in 1993 for the purpose of fostering international scientific and medicinal research on Ganoderma, setting standards of quality for related products and to promote popular awareness and appropriate use of Ganoderma.

Research on Ganoderma in the United States is not extensive. The major reason is the lack of research funds available. The interest of the public in herbal medicine is growing, the sales of herbal products is increasing yearly, with little effect on research funding.

Ecological studies along the Savannah river in South Carolina by Chen et al., (1993) identified Ganoderma as the first long-spore species in the genus to associate with oak. More recently Chen and Hu (1994) reported three successful strategies for obtaining monokaryons in Ganoderma species. To my knowledge the major

producer of fruiting body *Ganoderma lucidum* in the United States at present is Organotech of San Antonio.

In clinical studies Chang (1994) at Sloan-Kettering Cancer Center reported that applications of *Ganoderma* should be studied and considered for (1) chemoprophylaxis of cancer in individuals at high risk for developing cancer (2) adjuvant use in the prevention of metastasis or recurrence of cancer (3) palliation of cancer related cachexia and pain and (4) adjunctive use with concurrent chemotherapy to reduce side-effects, maintain leukocyte counts and allow a more optimal dosing of chemo or radiotherapeutics. In a very interesting report Chang (1993) addressed the question of proper dose of *Ganoderma* for therapy. Since studies of human dosage were traditional and empiric a dose range was calculated using this data and pharmacokinetic principals. The calculations suggested that a (1) *Ganoderma* dried fruit body dose of 0.5 to 1 g per day for health maintenance (2) 2 to 5 g per day if there is chronic fatigue, stress, autoimmune, or other chronic health problems (3) 5 to 10 g per day for serious illness.

Of great interest has been the recent reports from the United States indicating a possible central role for inflammation in the development of such diverse diseases as Alzheimer's Disease and Cardiovascular disease. This research has the possibility of linking some of the historical uses of *Ganoderma* in promoting longevity with contemporary Western scientific theory. The provocative connections are: (1) *Ganoderma* was used to prevent memory loss in old age (2) *Ganoderma* is anti-inflammatory, (3) inflammation is involved in the development of Alzheimer's disease (4) Alzheimer's disease appears to be ameliorated by chronic anti-inflammatory use.

(1) *Ganoderma* and old age: The ancient Chinese text *Shen Nong Ben Jing* volume 1 from about the year 500 states that *Ganoderma lucidum* is useful for enhancing vital energy, increasing thinking faculty and preventing forgetfulness. It can refresh the body and mind, delay aging and enable one to live long. It stabilizes one's mental condition (Mizuno 1996). The importance of retaining memory into old age probably lies in the Taoist belief that sickness was caused by past transgressions and that the patient had to remember the transgressions, record them and then destroy the record. This belief placed a strong emphasis on memory in the maintenance of health and longevity.

(2) Anti-inflammatory : In research in mice Stavinoha et al. (1991, 1996) found *Ganoderma lucidum* to be potent anti-inflammatory agent. The water extract of the fruiting body was active orally against both carrageenan induced inflammation and croton oil induced inflammation. The ethyl acetate extract was active as an anti-inflammatory agent both orally and topically. The active compound was isolated and identified. This compound is equivalent in anti-inflammatory activity to hydrocortisone. It does not show the typical side effects of steroids such as thymic involution nor appear to cause gastropathy which is the major side effect of the non-steroidal anti-inflammatory drugs such as aspirin.

(3) Inflammation and Alzheimer's disease: A number of indicators of active inflammation have been found in the Alzheimer's diseased brain. Unless inflammation is present there is no notable neurodegeneration or Alzheimer's signs and symptoms even in the presence of extensive neurofibrillary tangles and Amyloid B-peptide plaque deposition (Rogers 1995).

(4) Nonsteroidal anti-inflammatory drugs in Alzheimer's disease: Researchers in the United States and Canada have found that ingestion of non steroidal anti-inflammatory drugs can slow the progress of the disease (McGeer and Rogers 1992). In a report by Corrida et al. (1996) reported on findings on 1417 men and 648 women from the Baltimore Longitudinal Study of aging which is a 37 year multidisciplinary study of normal aging. The preliminary results suggest that use of nonsteroidal anti-inflammatory drugs is associated with a decreased incidence of Alzheimer's disease.

In studying incidence of cardiovascular disease, Ridker et al. (1997) measured C-reactive protein, an acute phase reactant used as a marker for systemic inflammation, in plasma. They found that baseline plasma concentration of C-reactive protein predicts the risk of future myocardial infarction and stroke. The reduction

of risk associated with aspirin appears to be directly related to the level C-reactive protein, suggesting that anti-inflammatory agents may have benefits preventing cardiovascular disease. The increase risk was independent of lipid related and non-lipid related cardiovascular factors. Masari (1997) felt that he has come to re-examine that pathogenetic components of these disease to identify patients who would benefit from particular therapies. Considering these recent findings, research on *Ganoderma* as a potential useful anti-inflammatory for long term use as a prevention of disease appears warranted.

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1988 Chairman, Scientific Committee Academic/Industry Joint Conference, Japan, March 13-16. San Antonio, Texas

1990 Session Chairman and on Scientific Committee, The Third Acadimic/Industry Joint Conference, August 18-20, 1990, Sapporo, Japan

1991 Third International Symposium on Ganoderma, Seoul, Korea.. The First WHO Symposium on Plants and Health for All: Scientific Advancement, Kobe, Japan

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We conceived, designed and built two instruments for rapid inactivation of brain enzymes to facilitate the study of rapidly metabolized substrates in the brain. One is now commercially available, but our large 915 MHz instrument is still the only one extant. We continue the work and aid other national and international scientists who wish to work n this area by making appropriate design modifications on our instruments and helping in the operation of our instruments.



Reishi