The use of *Ganoderma lucidum* (Reishi) in the management of histamine-mediated allergic responses

Martin Powell (BSc.(Hons), Dip.Ac, Dip.CHM, MRCHM), reveals the benefit of the Gandoderma lucidum mushroom for the treatment of TH2 conditions.

Allergies and asthma are two examples of histamine-mediated allergic responses. Both conditions are increasing in frequency and are difficult to target with modern medicine. The modern approach to drug research is target-specific and does not consider the natural defence mechanisms of the body or the causative factors (the shift to a predominantly TH2 cytokine profile) underlying histamine-mediated allergic responses. Ganoderma lucidum *(Reishi) as immunonutrition, with its unique array of compounds working in concert, could play a major role in treatment of histamine-mediated allergic responses.*

What is Immunonutrition ?

The potential to modulate the activity of the immune system by intervention with specific nutrients is termed immunonutrition. This concept may be applied to any situation in which an altered supply of nutrients is used to modify inflammatory or immune responses. However, immunonutrition has become associated most closely with attempts to improve the clinical course of clinically ill and surgical patients, who often require an exogenous supply of nutrients.[1]

Major surgery is followed by a period of immune suppression that increases the risk of morbidity and mortality due to infection. Improving immune function during this period may reduce complications due to infection. Critically ill patients are at a greater risk of adverse outcomes than surgery patients. In these patients complex variable immune and inflammatory changes occur that are only now being well defined. A biphasic response with an early hyper-inflammatory response followed by an excessive compensatory response associated with immune suppression is seen in many such patients.[2] Here, early treatment is aimed at decreasing the inflammatory response (reversing a TH1 to TH2 shift) rather than enhancing it, in order to stop the hyper-inflammation and prevent the following compensatory immune suppression.[3]

In histamine-mediated allergic responses, treatment should be aimed at decreasing the inflammatory response (reversing a TH1 to TH2 shift).

Historical use of *Ganoderma lucidum* (Reishi)

The numerous legends surrounding reishi mushroom provide an historical record that spans 2000 years. Traditionally, it was used in China by Taoist monks to promote a centred calmness, improve meditative practices and attain a long and healthy life.[4]

Chinese royalty, seeking longevity, held reishi mushroom in high esteem and it became immortalized throughout Chinese culture in paintings, statues, silk tapestries and as designs on the robes of emperors. Reishi mushroom has also been revered in Japanese culture where it is considered the most important of all Japanese medical polypores (Matsumoto 1979).[5]

Variously known as the "mushroom of immortality", "ten-thousand-year mushroom", and "mushroom of spiritual potency", *Ganoderma lucidum* (Reishi) has been used for many centuries in the traditional herbal medicine of China and Japan for its immuno-modulatory and adaptogenic properties.[6]

In the most comprehensive Chinese *materia medica*, the '*Ben Cao Gang Mu*', published in 1578AD, reishi was

listed as the most respected herb out of 120 superior herbs (shang pin) (Masumoto 1979, Unsehuld 1986). Superior herbs were classified as the highest category of medicines since they were considered to prolong life, prevent aging, boost energy (*qi*), and make the body light and limber.[7]

Modern research has shown *Ganoderma lucidum* (reishi) to have anti-allergic, anti-oxidant, anti-tumour, anti-viral, cardiotonic and liver-protective properties. Reishi mushroom has a long history of use in Traditional Chinese Medicine (TCM) for treatment of chronic bronchitis (Tasaka and others 1988).

In one small uncontrolled study of 20 patients with chronic bronchitis, reishi mushroom was administered for 4 months. According to the review, in all but 2 patients there was a significant decline in blood cholinesterase activity, suggesting a reduction in the excitability of the parasympathetic nerves (Chang and But 1986).[8]

Ganoderma lucidum (Reishi) – anti-inflammatory properties

Animal Studies

Water extracts of reishi mushroom were found to possess significant activity against carrageenin*–induced paw oedema when administered subcutaneously (sc) to rats. In one controlled study, groups of animals received either saline as a placebo control, indomethacin as a positive control (10 mg/kg sc), or a test article, one of which was a reishi mushroom water extract (2 g/kg).

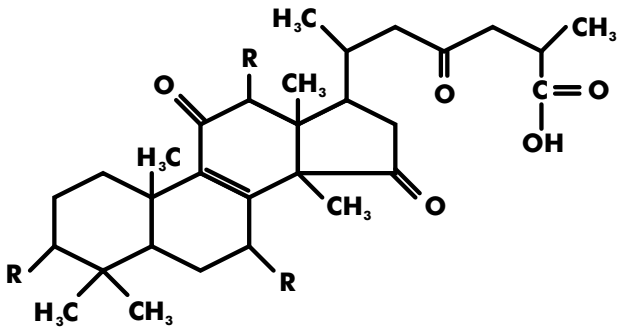
Both indomethacin and reishi mushroom showed significant anti-inflammatory effect (P<0.01) against carrageenin-induced oedema at all time intervals from 1-6 hours (Lin and others 1993)[9]

*carrageenan (= carrageenin): Sulphated cell-wall polysaccharide found in certain red algae. Contains repeating sulphated disaccharides of galactose and (sometimes) anhydrogalactose. It is used commercially as an emulsifier and thickener in foods, and is also used to induce an inflammatory lesion when injected into experimental animals (probably activates complement). http://www.mblab.gla.ac.uk/~julian/dict2.cgi?1090

Chemical Identification and *in vitro* Studies

More than 100 different highly oxygenated lanostanoid triterpenes have been identified in reishi mushrooms. The predominant triterpenes are ganoderic acids A-Z.[10]

As well as its general health-enhancing action, *Ganoderma lucidum* has been shown to have specific anti-inflammatory properties and this traditional usage has been linked to the presence of these ganoderic acids that exhibit anti-inflammatory properties:[11]



The above illustrated compound Ganoderic Acid C, isolated by careful fractionation of a non-polar solvent extract of *Ganoderma lucidum*, was found to account for most of the anti-inflammatory activity from the herb as determined by in vitro tests, such as histamine release from mast cells.[12]

An ethyl acetate extract rich in ganoderic acids was later found, by another group of researchers, to exhibit both systemic and topical anti-inflammatory activity in standard animal models, such as the croton oil-induced mouse ear inflammation test.[13]

Ganoderma lucidum (Reishi)-immunomodulating properties

Chemical and biological properties

In 2003, the Portuguese Instituto Superior de Engenheria de Lisboa (Biotechnology Section), led by Professor Amin Karmali, conducted an analysis of the enzyme properties of 500mg of *Ganoderma lucidum* (reishi) biomass (mycelium and primordia [young fruitbody]) with the results shown in the table on page 28.

Ganoderma lucidum (Reishi) biomass Analysis of Enzymes, Proteins and Sugar in presence of trypsin (*in vitro*)	Content per 500 mg
1 Protein-bound polysaccharide	65.2 mg
2 Peroxidase activity	10.6 μU
3 Laccase activity	461.3 μm
4 Glucoamylase / Beta-glucanases activity	2.5 U
5 Protease activity	3.7 μU
6 Glucose 2-oxidase activity	8,4 U
7 Superoxidase dismutase (SOD) activity	51.4U
8 Cytochrome P-450	0.63 nmoles
9 Cytochrome P-450 reductase	6.98mU

Professor Karmali concluded that the immunotherapeutic properties in mushroom nutrition are due to the delivery of:

i) Protein-bound polysaccharide complexes responsible for immune enhancement.
ii) Enzymes that both prevent oxidative stress (laccase activity and SOD activity) and inhibit cell growth (protease activity).
iii) enzymes involved in detoxification process (cytochrome P-450).[14,15]

In summarizing the immune-modulating effects of reishi mushroom polysaccharides, researchers Lin and Lei (1994) state that reishi mushroom polysaccharides significantly promote mixed lymphocyte response, antagonise the inhibitory effects of immunosuppressive and anti-tumour drugs, display a biphasic effect on interleukin (IL)-2 activity, increase both L3T4+ and Lyt 2+ cell subpopulations (L3T4 and Lyt 2+ cells are thymocytes that are responsible for producing significant quantities of interleukin 2 (IL-2) following mitogen stimulation), enhance cytotoxic activity of T lymphocytes, and promote the secretion of IL-1 in peritoneal exudate cells. Chang (1994a) concluded that the polysaccharide fraction, with ß-glucans, has stimulatory effects on these white blood cell lines: leukocytes, monocytes, macrophages, natural killer (NK) cells, lymphokine-activated killer (LAK) cells, tumour-infiltrating lymphocytes (TIL), and other lymphocytes.

He considers these actions to be responsible for the anti-viral, anti-tumour, anti-inflammatory, granulopoietic, and bactericidal effects that have been reported for reishi mushroom in laboratory animal studies.[16]

Histamine-mediated allergic response is a Cytokine TH1 to Cytokine TH2 shift

The body is considered to be in a "balanced" immune state when there is a constant movement between TH1 and TH2 immune states in a 24-hour period.

Cytokine TH1 vs. Cytokine TH2 Immune Responses	
TH1	**TH2**
8:00 to 20:00	20:00 to 8:00
Cytokine TH1 Immune State	Cytokine TH2 Immune State
Cellular Immune System	Humoral Immune System
Anti-Viral Activity	Pro-inflammatory
Anti-Bacterial Activity	(Histamine-mediated allergic response)
Anti-Parasitic Activity	
Interleukin 2 (IL-2)	Interleukin 4 (IL-4)
Interleukin -12 (IL-12)	Interleukin-6 (IL-6)
Gamma Interferon (γIFN)	Interleukin-10 (IL-10

These two arms of the immune system are mutually inhibitory and in a balanced state: the body spends twelve (12) hours in a TH1 state (anti-viral, anti-bacterial and anti-parasitic activities) and then twelve (12) hours in a TH2 state (pro-inflammatory activity).

Factors such as stress and chemical exposure weaken our body's ability to defend itself, not through impairing the cellular immune response (TH1 - the ability of the body to recognize and destroy foreign bodies) *per se* but through leading to a chronic elevation of the humoral immune response (TH2), a pro-inflammatory state, which normally predominates in cases of local wound healing or histamine-mediated allergic response.

When a chronic elevation of the humoral immune response is prolonged, this is known as a "TH1 to TH2 Shift". In a TH1 to TH2 Shift, the pattern of cytokines has moved from an anti-viral, anti-bacterial and anti-parasitic pattern (TH1) to an inflammatory repairing pattern (TH2) but **does not return** to a TH1 state within 12 hours as usual. This chronically elevated pro-inflammatory immune response is termed a TH2 immune state. Histamine-mediated allergic responses are prolonged TH1 to TH2 shifts. For this reason, allergies and asthma are considered "TH2 conditions". As long as the shift continues, there is little relief from symptoms caused by such "TH2 conditions".

Recent clinical studies have established that mushroom nutrition (using the mushroom *Coriolus versicolor*) is able to rebalance the TH1 and TH2 immune states, thereby reversing a "TH1 to TH2 shift".[17,18]

In addition, studies have supported the ability of reishi mushroom polysaccharides to restore the level of IL-2 production that has been inhibited by aging. In three studies this was demonstrated in aged mouse splenocytes (spleen cells) (Lei and Lin 1991, 1993: Zhang and others 1993). An additional study in mice showed that reishi mushroom can promote cell proliferation in murine splenocytes (Xiao and others 1994).[19]

Existing treatment modalities for histamine-mediated allergic responses

The currently used topical and systemic anti-inflammatory drugs have serious drawbacks; for example corticosteroids can suppress pituitary-adrenal function, dangerously unbalance fluids/electrolytes and cause undesirable changes in skin texture,[20] whilst the salicylic acid-derived prostaglandin inhibitors can result in severe gastric irritation.[21] Consequently, the potential use of *Ganoderma lucidum* (reishi) supplementation could offer a safe and effective alternative for the reduction of histamine-mediated immune responses.

Case studies: hayfever patients

These were carried out to assess the efficacy of non-fractionalised *Ganoderma lucidum* supplementation in two hay fever patients. The principal parameters used were symptom elevation.

Study design

Open label study in United Kingdom in (2) patients.
Patients were interviewed during the *Ganoderma* supplementation period, in order to assess changes in perceived quality of life, with reference to general hay fever symptoms.

Supplementation scheduling

For the first patient supplementation commenced at 3 grams (6 tablets x 500 mg) per day and was maintained at this level until the symptoms abated at which point it was reduced to a maintenance dose of 1.5 grams (3 tablets x 500 mg) per day until the end of the hay fever season. For the second patient supplementation commenced at 2 tablets per day and was maintained at this level through the season.

Results

Patient 1

39 year old male. Chronic hay fever sufferer since childhood with little relief from conventional herbal medication. After 3-4 days supplementation at 3.0 grams (6 tablets x 500 mg) per day of *Ganoderma lucidum* there was a marked decrease in drowsiness, itchiness and sneezing. After 10 days the patient was able to mow the grass without significant discomfort. Continued alleviation throughout the season. Repeated benefit the following year.

Patient 2

5 year old male. Developed hay fever age 4. Unable to go outside for much of early summer. Supplementation started at 2 tablets x 500 mg a day, 1 a.m. and 1 p.m. After 1 week 90% reduction in symptoms. No red/sore eyes or sore throat. Only occasional sneezing. Able to play football outside again. Dosage maintained at 2 tablets a day until the end of the season.

Discussion

In both cases there was a rapid and significant alleviation of symptoms on commencement of supplementation with *Ganoderma lucidum*, indicating that *Ganoderma* supplementation may have a role to play in the management of histamine-mediated immune responses.

Adult – Chronic Hay fever		
Week	Tablets/day	Total tablets
		Per week[1]
1	6	42
2	6	42
3	3	21
4	3	21
5	3	21
6	3	21
7	3	21
8	3	21

[1]Three tablets in a.m. and three tablets p.m. before meals.

Child (5 years) – Chronic Hay fever		
Week	**Tablets/day**	**Total tablets**
		Per week[2]
1	2	14
2	2	14
3	2	14
4	2	14
5	2	14
6	2	14
7	2	14
8	2	14

[2]1 tablet p.m. and 1 tablet a.m.

Conclusion

Histamine-mediated allergic responses are provoked by chronically elevated pro-inflammatory immune responses. For this reason, allergies and asthma are considered "TH2 conditions". As long as the cytokine TH1 to cytokine TH2 shift continues, there is no relief from symptoms caused by either asthma or allergies.

To date, medical tools have focused on treating the symptoms of asthma and allergies, but not the prolonged TH2 condition. Modern approach to drug research is target-specific and does not consider the natural defence mechanisms of the body or the causative factors (cytokine TH1 to cytokine TH2 shift) underlying histamine-mediated allergic response.

Ganoderma lucidum (reishi) as immunonutrition, with its unique array of compounds working in concert, could play a major role in current treatment practices for histamine-mediated allergic response. *Ganoderma lucidum* (reishi) is an effective agent to restore the normal balance between the TH1 and TH2 immune states in patients with histamine-mediated immune response. Such an approach treats the underlying cause for the TH2 condition.

Given that adult *Ganoderma lucidum* (reishi) supplementation costs between £14.00 and £28.00 per month, the daily cost of the immunonutrition would be £0.50 to £1.00 per day. *Ganoderma lucidum* (reishi) supplementation as immunonutrition in patients with histamine-mediated allergic responses offers the clinician a cost-effective option for such clinical cases.

About the author

Martin Powell is a traditional Chinese medicine (TCM) practitioner and lecturer who has been involved in the clinical use of mushroom nutrition for over 10 years. After graduating in Biochemistry from the University of Birmingham, he went on to study acupuncture, Chinese herbal medicine and Chinese massage (Tui Na), initially at the London School of Acupuncture and Traditional Chinese Medicine, and then in Taipei and Shanghai. As well as running a practice in Luton, he co-edits Mycology News and lectures on TCM and on mushroom nutrition at the University of Westminster and abroad.

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Notes

1) For more information on *Ganoderma lucidum* (Reishi), please access the following website: www.mycologyresearch.com
2) For more information on extracted Ganoderic C compounds, please contact Essential Nutrition Ltd on +44 (0) 1482 667634