The Clinical Journal of Mycology is dedicated to the dissemination of information on the clinical use of mushroom nutrition to health care practitioners.

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Comparative Differences in β-1,3-1,6 Glucan content between *Ganoderma lucidum* (Reishi) mushrooms (Biomass vs Extracted) in the Presence of Proteolytic Enzymes.

Prof. Amin Karmali – Chemical Engineering and Biotechnology Research Center and Department of Chemical Engineering of Instituto Superior de Engenharia de Lisboa (ISEL), Lisbon Polytechnic Institute , Portugal.

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Coriolus-MRL supplementation in patients infected with low-risk and high-risk HPV subtypes-Bulgarian experience.

Prof. Todor Chernev – University Hospital of Obstetrics and Gynecology, Sofia, Bulgaria

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*Coriolus versicolor* – Innovation in Prevention of Oncogynecological Diseases, especially HPV.

Dr. J. Bogdanova – Institute of Botany, Bulgarian Academy of Sciences, Sofia, Bulgaria

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Link between Herpes Simplex Virus and Alzheimer’s Disease: Potential Role of Mushroom Nutrition Supplementation in Prevention.

Prof. Tito Fernandes – Faculty of Health Sciences, Lurio University, Nampula, Mozambique.  
Prof. Vittorio Calabrese – Faculty of Medicine, University of Catania, Catania, Italy
INTRODUCTION
Some mushrooms have been known to exhibit several medicinal properties for thousands of years in Japanese and other Asian cultures. The Reishi mushroom, also known as *Ganoderma lucidum*, is well characterized (in Traditional Chinese Medicine) for the prevention and treatment of several disease states such as cancer, allergies and asthma.

In the West, *Reishi* is sold in an extracted form (extracted specifically for $\beta$-glucan content) or in a biomass form (mycelium and primordial (young fruit body)). The biomass form contains several substances of clinical interest such as enzymes, secondary metabolites and $\beta$-glucans. The specific quantification of $\beta$-glucans in mushrooms (extracted or biomass forms) with anti-tumour activity is of great clinical importance (1).

There are several types of $\beta$-glucans in mushroom species such as $\beta$-1,3 glucans and $\beta$-1,3-1,6 glucans(2). As far as anti-tumour immune enhancing and modulating activities, these three activities are attributed to $\beta$-1,3-1,6 glucans which exhibit a triple helix as their tertiary structure (3,4).

METHODS
Two samples (1g) of Reishi MRL and Reishi Myco were compared to detect and to quantify enzymes, $\beta$-glucans and secondary metabolites. These two samples are different since the former is a biomass that contains mycelia and primordia whereas the latter is a concentrated extract (20x) of fruiting bodies.

The $\beta$-1,3-1,6 glucan content was determined by a colorimetric method recently established in Germany (2). The enzyme and secondary metabolite contents were determined by methods commonly used.

In order to assess the impact of digestive enzymes on the constituents of each sample, both samples were compared in vitro; a) in the absence of proteolytic enzymes, b) in the presence of pepsin and c) in the presence of trypsin.

DISCUSSION
The data obtained reveal that, in the absence of proteolytic enzymes, both forms of Reishi contain significant levels of $\beta$-1,3-1,6 glucans with anti-tumour activity with Reishi Myco exhibiting higher values (hot water fraction and NaOH fraction). However, in the presence of pepsin and trypsin, Reishi-MRL (biomass form) exhibited higher $\beta$1,3-1,6 glucan values than Reishi Myco (extracted form) (See Table I and Fig. 7-11).

When comparing the enzyme values, in the absence of, and presence of, proteolytic enzymes, between the two forms of Reishi, (See Table II and Figures 1-6), there was an absence of important immune-enhancing enzyme activity, such as peroxidase, glucoamylase and protease activities in Reishi Myco (extracted form) when compared to Reishi-MRL (biomass form). The Reishi biomass form demonstrated a greater overall enzyme activity level over the extracted form of Reishi.

It has been known for over a century that some enzymes can be used in the prevention and even treatment of several clinical conditions. These enzymes are divided into the following activities:

- **Enzymes that prevent oxidative stress:**
  - Superoxide dismutase

- **Enzymes that prevent cellular growth:**
  - Protease
  - Glucoamylase

- **Enzymes that promote detoxification:**
  - Cytochrome P-450
  - Peroxidase
  - Glucose 2 oxidase

Reishi Myco exhibits low levels of secondary metabolites compared with the Reishi-MRL product.

CONCLUSIONS
The differences in $\beta$-1,3-1,6 glucan content between both samples may be due to differences in biological material in these samples since one contains mycelia and primordia whereas the other consists of concentrated (20x) extract of fruiting bodies. In fact, immunonutrients in mycelia and primordia (young fruiting bodies) in MRL product are more resistant to proteolytic enzymes (i.e simulation of digestive tract) since it is in a biomass form and not on cell extract. Therefore, the concentrated extract of the fruiting bodies is more exposed and available to the action of proteolytic enzymes (i.e simulation of digestive tract) since there are no physio-chemical barriers to prevent such exposure.

In addition to the importance of $\beta$-1,3-1,6 glucan content, one should assess the advantages of enzyme supplementation afforded by the biomass form of mushroom nutrition.
Comparative Differences in β-1,3-1,6 Glucan content between *Ganoderma lucidum* (Reishi) mushrooms (Biomass vs Extracted) in the Presence of Proteolytic Enzymes

Professor Amin Karmali
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Table I: Comparison of Impact of Proteolytic Enzymes on Beta 1,3-1,6 Glucan Activity between Reishi-MRL (biomass) and Reishi Myco (extract) (one gram of product in powder form)

<table>
<thead>
<tr>
<th></th>
<th>Reish A MRL</th>
<th>Reshi B Myco</th>
</tr>
</thead>
<tbody>
<tr>
<td>In absence of Proteolytic Enzymes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1 Water soluble fraction</td>
<td>24.0µg</td>
<td>117.0µg</td>
</tr>
<tr>
<td>2.2 Hot water fraction</td>
<td>29.0µg</td>
<td>750.0µg</td>
</tr>
<tr>
<td>2.3 NaOH fraction</td>
<td>976.0µg</td>
<td>2193.0µg</td>
</tr>
<tr>
<td>2.4 KOH fraction</td>
<td>2213.0µg</td>
<td>246.0µg</td>
</tr>
<tr>
<td>2.5 HCl fraction</td>
<td>642.0µg</td>
<td>378.0µg</td>
</tr>
</tbody>
</table>

II IN THE PRESENCE OF PEPsin (per gram of product)

<table>
<thead>
<tr>
<th></th>
<th>Reish A</th>
<th>Reshi B</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Water soluble fraction</td>
<td>21.0µg</td>
<td>11.5µg</td>
</tr>
<tr>
<td>2.2 Hot water fraction</td>
<td>22.0µg</td>
<td>5.0µg</td>
</tr>
<tr>
<td>2.3 NaOH fraction</td>
<td>956.0µg</td>
<td>21.9µg</td>
</tr>
<tr>
<td>2.4 KOH fraction</td>
<td>2103.0µg</td>
<td>26.0µg</td>
</tr>
<tr>
<td>2.5 HCl fraction</td>
<td>632.0mg</td>
<td>33.0mg</td>
</tr>
</tbody>
</table>

III IN THE PRESENCE OF TRYPSIN (per gram of product)

<table>
<thead>
<tr>
<th></th>
<th>Reish A</th>
<th>Reshi B</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1 Water soluble fraction</td>
<td>21.0µg</td>
<td>11.2µg</td>
</tr>
<tr>
<td>2.2 Hot water fraction</td>
<td>25.0µg</td>
<td>7.1µg</td>
</tr>
<tr>
<td>2.3 NaOH fraction</td>
<td>962.0µg</td>
<td>21.93µg</td>
</tr>
<tr>
<td>2.4 KOH fraction</td>
<td>2113.0µg</td>
<td>24.7µg</td>
</tr>
<tr>
<td>2.5 HCl fraction</td>
<td>630.0µg</td>
<td>32.0µg</td>
</tr>
</tbody>
</table>
Comparative Differences in β-1,3-1,6 Glucan content between *Ganoderma lucidum* (Reishi) mushrooms (Biomass vs Extracted) in the Presence of Proteolytic Enzymes

Professor Amin Karmali
akarmali@ideq.isel.ipl.pt

Table II: Comparison of Impact of Proteolytic Enzymes on Beta 1,3-1,6 Glucan, Enzyme and Secondary Metabolite Activity between Reishi-MRL (biomass) and Reishi Myco (extract) in one gram of powder.

<table>
<thead>
<tr>
<th>Enzymes, polysacharides and secondary metabolites per gram of product</th>
<th>In absence of Proteolytic Enzymes</th>
<th>In presence of Pepsin</th>
<th>In presence of Trypsin</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Reish A MRL</td>
<td>Reshi B Myco</td>
<td>Reish A MRL</td>
</tr>
<tr>
<td>1 Protein content</td>
<td>44.8mg</td>
<td>40.5 mg</td>
<td>35.9 mg</td>
</tr>
<tr>
<td>2 β-1,3-1,6-glucans with anti-tumour activity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.1 Water soluble fraction</td>
<td>24.0mg</td>
<td>117.0mg</td>
<td>21.0mg</td>
</tr>
<tr>
<td>2.2 Hot water fraction</td>
<td>29.0mg</td>
<td>750.0mg</td>
<td>22.0mg</td>
</tr>
<tr>
<td>2.3 NaOH fraction</td>
<td>976.0mg</td>
<td>2193.0mg</td>
<td>956.0mg</td>
</tr>
<tr>
<td>2.4 KOH fraction</td>
<td>2213.0mg</td>
<td>246.0mg</td>
<td>2103.0 mg</td>
</tr>
<tr>
<td>2.5 HCl fraction</td>
<td>642.0mg</td>
<td>378.0mg</td>
<td>632.0mg</td>
</tr>
<tr>
<td>3 Peroxidase activity</td>
<td>20.9mU</td>
<td>0.0mU</td>
<td>18.3mU</td>
</tr>
<tr>
<td>4 Glucoamylase/Beta-glucanasase activity</td>
<td>5.3 U</td>
<td>0.0 U</td>
<td>4.8 U</td>
</tr>
<tr>
<td>5 Protease activity</td>
<td>9.1mU</td>
<td>1.1mU</td>
<td>8.4mU</td>
</tr>
<tr>
<td>6 Glucose 2-oxidase activity</td>
<td>14.3mU</td>
<td>10.1mU</td>
<td>12.1mU</td>
</tr>
<tr>
<td>7 Superoxide dismutase (SOD) activity</td>
<td>98.4mU</td>
<td>99.8mU</td>
<td>82.3mU</td>
</tr>
<tr>
<td>8 Cytochrome &quot;P-450&quot; (nmoles)</td>
<td>1.4 nmoles</td>
<td>1.5nmoles</td>
<td>1.3nmoles</td>
</tr>
<tr>
<td>9 Cytochrome P 450 reductase</td>
<td>15.5mU</td>
<td>12.5mU</td>
<td>12.6mU</td>
</tr>
<tr>
<td>10 Secondary metabolites (Thrombin inhibitors)</td>
<td>4.9%</td>
<td>1.1%</td>
<td>4.6%</td>
</tr>
</tbody>
</table>

References

1. Production, purification and characterization of polysaccharides from *Pleurotus ostreatus* with antitumour activity

2. A new colorimetric method to quantify β-1,3-1,6-glucans in comparison with total β-1,3-glucans and a method to quantify chitin in edible mushrooms

3. The structure and conformation of a water-insoluble (1→3)-, (1→6)-beta-d-glucan from the fruiting bodies of *Pleurotus florida*


Note: One enzyme unit (U) is defined as the amount of enzyme required to convert one micromole of substrate to product per minute under certain experimental conditions. One milli-enzyme unit (mU) is defined as the amount of enzyme required to convert one nanomole of substrate to product per minute under certain experimental conditions

*Centro de investigação de Engenharia Química e Biotecnologia - ISEL*
Introduction:
Coriolus-MRL is a food supplement which contains biomass of the fungus *Coriolus versicolor*. Recent studies showed a positive effect of this non-specific immunomodulator in HPV patients. The specialists in Bulgaria have a five-year experience with the use of Coriolus-MRL and the results show high effectiveness in HPV carrying patients.

Study 1 (2009-2010)
Materials and methods:
100 women aged 16-50, infected with low-risk and high-risk HPV subtypes; Period of treatment: 6 months,
Conservative treatment: Coriolus-MRL 2 x 3 tablets;
Combined treatment: Surgical intervention + Coriolus-MRL 2x3 tablets;

Results:
The results showed that 64 (88%) out of 73 patients on conservative treatment and 25 (93%) out of 27 patients on combined treatment were HPV-negative.

Table 1. Results of a 6-month study: number of the patients and the PAP smears in the respective groups.

<table>
<thead>
<tr>
<th>1ST MONTH</th>
<th>6TH MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>PAP I</td>
<td>PAP II</td>
</tr>
<tr>
<td>47</td>
<td>47</td>
</tr>
<tr>
<td>PAP III a</td>
<td>29</td>
</tr>
<tr>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>PAP III b</td>
<td>3</td>
</tr>
<tr>
<td>15</td>
<td>6</td>
</tr>
<tr>
<td>PAP III d</td>
<td>6</td>
</tr>
<tr>
<td>100</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Results of a 6-month study: patients who were found to carry high-risk or low-risk HPV subtypes.

<table>
<thead>
<tr>
<th>1ST MONTH</th>
<th>6TH MONTH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low-risk HPV subtypes</td>
<td>4</td>
</tr>
<tr>
<td>High-risk HPV subtypes</td>
<td>96</td>
</tr>
</tbody>
</table>

Study 2 (2010-2012)
Materials and methods: 200 patients;
Period of treatment: 6 months; Treatment: Coriolus-MRL 2 x 3 tablets.

Results:
95% of the patients reverted to HPV-negative status. HPV subtype 16 was again most resistant. HPV-positive patients without histological changes reverted to HPV-negative status in 3 months. In patients with mild dysplasia (CIN I) Coriolus-MRL supplementation can help the body clear the infection. In cases with severe dysplasia (CIN II and CIN III) Coriolus-MRL supplementation can strengthen the immune system and reduce the risk of relapse.

Conclusions:
Coriolus-MRL has no adverse reactions and drug interactions with the main drugs used for the treatment and it could be taken during pregnancy. It is an addition to the methods for prevention and treatment (both combined and conservative) of HPV infection.

References
1. The importance of the immunity in the treatment of HPV infections. Tcholakova A. MEDINFO 2012 (2), 28-29. e-mail: atcholakova@abv.bg
2. Assessment of the effect on patients infected with low and high-risk types of HPV. Borisov S. 2012. Coriolus-MRL Clinical Journal of Mycology, Vol.3, Ed.2, 2-3. e-mail: sborissov@mail.bg
Coriolus versicolor – Innovation in Prevention of Oncogynecological Diseases, especially HPV.

Yuliya Bogdanova, PhD  Email: bogdanova@mail.bg
Institute: Institute of Botany, Bulgarian Academy of Sciences, 2 Chernorizec Hrabar Str., app.11, 1164 Sofia, Bulgaria Tel/Fax +359 2 963 1441

ABSTRACT
Coriolus-MRL is a nutrient adjuvant, which contains biomass of the fungus Coriolus versicolor and is studied to reverse early stages of cervical cancer and to reduce risk factors of reoccurring HPV virus. (PMID:19449722 / Akush Ginekol (Sofia). 2008; 47 Suppl 3:51-3. [PubMed – indexed for MEDLINE [Original Article in Bulgarian; the following an English Translation approved by author.]

SUMMARY
Coriolus-MRL is a nutrient adjuvant, which contains biomass of the fungus Coriolus versicolor with immune-modulating components – β-glucans and proteoglucans. Research has been carried out in recent years, establishing the effects of the mushroom biomass in the prevention of HPV patients from developing cervical cancer as well as the prevention against other cancer-causing viruses.

Immuno-modulating nutrition is a new concept, representing the potential for modulating the activities of the immune system through intake of specific nutrients and strengthening the capability of the organism for self-defense and prevention.

Fungotherapy (treatment with medicinal mushrooms) is an important part of immune-modulating nutrition. The biological activity of the fungi is connected with improvement in cardiac activity, strengthening of the immune system, alleviation of allergic symptoms, normalization of sugar blood levels and detoxification of the organism. One of the most important effects is the prevention from cancer-inducing viruses. Such viruses are the Human Herpes virus type 8 (HHV-8), Human papillomavirus (HPV), Epstein-Barr virus (EBV) and hepatitis B virus (HBV)7.

The relation between HPV and the development of cervical cancer has been proved. It has been established that 80% of all women get infected with HPV within 4 years after they start their sexual life, and that 90% of all cases of cervical cancer are caused by HPV. Thirteen out of 100 subtypes of HPV are considered high-risk for the development of cervical cancer. Studies by many authors point out a relation between HPV and prostate cancer 7; some esophagus cancer cases may be also resulting from same virus both in man and women, possibly through oral sex.

The anti-HPV vaccines introduced in the 1990s are effective against 2 to 4 of the high-risk subtypes HPV and are effective only in HPV-uninfected women. Surgical treatment of HPV lesions is not possible in the early stages and in many cases there is a risk of recurrence of the process. Coriolus versicolor is a fungus whose biomass acts as a non-specific immunomodulator and is a suitable adjuvant in cancer patients for the strengthening of the immune system, especially after chemotherapy and radiotherapy 11.

This medicinal mushroom is widely distributed in the woodlands of North America, Asia and Europe. It is parasitic on deciduous and coniferous tree species or saprophytic on tree stumps. It consists of mycelium (made up of hyphae) and fruit bodies, where spores for reproduction are formed.

The immunostimulating effect of Coriolus versicolor is due to the β-glucans and proteoglucans it contains. β-glucans are polysaccharides, consisting only of glucose residues, and proteoglucans are proteins connected with polysaccharide chains. They have the selective ability to cause apoptosis (programmed cell death) in cancer cells without damaging the healthy ones 14.

Fig.1  Selective ability of the β-glucans to cause apoptosis in cancer cells
Diseases, especially HPV.

Coriolus versicolor – Innovation in Prevention of Oncogynecological

IgG or IgM to a range of viruses. Patients took Coriolus-MRL – 6 tablets of 500mg for 15 days, and 3 tablets of 500mg for 45 days. At the end of the study a doubling of the levels of natural killer cells and decreases in viral loads was established. On the basis of these results and previous studies on the influence of folic acid in HPV control, Dr. Monro recommends a scheme of intake of Coriolus-MRL and folic acid for 8 weeks with the aim of preventing HPV patients from developing cervical cancer and reversing the process of dysplasia. During the treatment period patients are given 3g Coriolus-MRL daily as well as 300mg folic acid daily for 1 week and 10mg folic acid daily for 7 weeks. Control of microbiological and immune markers is recommended in order to evaluate the synergistic effect of Coriolus-MRL and folic acid.

Dr. L. J. Standish from the School of Naturopathic Medicine at Bastyr University has received funding from the Cancer Treatment Research Foundation (CTRF) to perform a placebo-controlled clinical trial looking at the effects of Coriolus versicolor supplementation on the immune system, quality of life and fatigue of women with breast cancer after completing radiation therapy.

Coriolus-MRL is appropriate as a dietary supplement for patients with immune deficit after illness and after surgical intervention, for prevention of cancer-causing viruses and as adjuvant therapy in patients with cervical cancer, breast cancer and prostate cancer.

References:

Additional Bulgarian Pub Med References to Coriolus-MRL:
Herpes exists in two common forms. The majority of the population acquires Herpes Simplex Virus (HSV-1), which causes cold sores, during childhood from non-sexual contact. Herpes Simplex Virus 2 (HSV-2), also known as genital herpes, is transmitted by sexual contact.

In 2000, researchers led by Dr. Frank M. LaFerla at the department of Neurobiology and Behaviour at the University of California Irvine, Irvine, USA, demonstrated that a synthetic protein that resembles the Herpes Simplex Virus (HSV-1) mimics the structure and function of a protein called β-amyloid, a toxic agent that accumulates in the brains of Alzheimer patients. (1)

Genetic sequencing revealed that two-thirds of the viral protein is identical to the β-amyloid protein. The researchers showed that, like β-amyloid, it could destroy brain neurons, a key feature in the development of Alzheimer’s. Moreover, in laboratory experiments, the viral protein formed abnormal twisted fibres (neurofibrillary tangles, called ‘tau’), like those found in the brains of Alzheimer’s patients—the definitive hallmark of the disease. (2)

According to Dr. LaFerla “Most people are exposed to HSV-1, but do not develop Alzheimer’s. However, recent studies show that people genetically predisposed to Alzheimer’s are more likely to develop the disease if they are exposed to herpes”. (3)

In support of Dr. LaFerla’s hypothesis, in December 2008, Professor Ruth Itzhaki and her team in the United Kingdom, at the Manchester University’s Faculty of Life Sciences published in the Journal of Pathology that the HSV-1 DNA is located very specifically in amyloid plaques: 90% of plaques in Alzheimer’s disease sufferers’ brains contain HSV-1 DNA, and most of the viral DNA is located within amyloid plaques. (4,5)

The team had previously shown that HSV-1 infection of nerve-type cells induces deposition of the main component, β-amyloid, of amyloid plaques. Together these findings strongly implicate HSV-1 as a major factor in the formation of amyloid deposits and plaques, abnormalities thought by many in the field to be major contributors of Alzheimer’s disease.

The University of Manchester’s data strongly suggest that HSV-1 has a major role in Alzheimer’s disease and point to the usage of antiviral agents for treating the disease, in fact in preliminary experiments they have shown that acyclovir reduces the amyloid disposition and also reduces certain other features of the disease which they have found are caused by HSV-1 infection. Further research has been conducted on the potential use of acyclovir, penciclovir and foscarnet as therapeutic agents for the treatment of Alzheimer’s disease. (6,7,8)

In addition to the use of anti-HSV1 antiviral agents to disrupt the HSV1 virus, researchers at the Medical University of South Carolina have suggested the use of immunoglobulin (IG) GM genes based on their putative role as the modulators of host immune response. In some studies, the intravenous use of immunoglobulin acts synergistically with the antiviral, acyclovir. (9,10)

More recently, in May of 2013, Dr. LaFerla and his associates at the Institute of Memory Impairments and Neurological Disorders at the University of California, Irvine, Irvine California published in the American Journal of Pathology, that there could be another method to reduce Alzheimer’s disease (AD).

The researchers demonstrated that aspirin–triggered Lipoxin A4 (LXA4) (15 μg/kg) s c, twice a day, reduced NF-kB activation and levels of pro-inflammatory cytokines and chemokines, as well as increased levels of anti-inflammatory IL-10 and transforming growth factor B (beta). Such changes in the cerebral milieu resulted in recruitments of microglia in an alternative phenotype as characterized by the up-regulation of YM1 and arginase-1 and the down-regulation of inducible nitric oxide synthase expression. (11,12) In effect the researchers contend that activating LXA4 signaling may represent a novel therapeutic approach for AD. (13)

Given the potential gastrointestinal discomfort associated with aspirin intake, is there another manner to achieve to trigger LXA4 as well as provide both anti-viral protection and anti-oxidant protection in the form of SOD (Super-oxide dismutase) supplementation?

Why Mushroom Nutrition?

In the past ten years, the clinical development of mushroom nutrition has determined that Coriolus versicolor (biomass) has virus protective properties, while Hericium erinaceus (biomass) is extremely high in SOD content. Given this information, there are four reasons to consider the use of mushroom nutrition in the preventative use for patients with Alzheimer’s disease if HSV-1 induced:

Coriolus versicolor has a clinically verified use in the reduction of viruses (EBV, CMV and HHV-6) related to the Chronic Fatigue Syndrome condition. (14)

Coriolus versicolor has been used to increase the regression rate of LSIL lesions in HPV patients and to reduce the viral load in HPV patients. (15)

Hericium erinaceus has an extremely high SOD content, which in the presence of proteolytic enzymes per 500 mg tablet has a SOD content of 19.430x10^4 U. (16) This high SOD content is important given that herpes simplex virus infection, apoE4 intensifies virus latency and is associated with the increased oxidative damage of the central nervous system, and there is some evidence that herpes simplex virus infection in combination with the apoE4 genotype may be associated with increased risk of Alzheimer’s disease (AD). (17)

For those patients not able to both tolerate the side effects of anti-HSV1 viral and/or afford intravenous immunoglobulin IG therapy, having an alternative.

The following is a proposed two part study to determine if biomass form of both Coriolus versicolor and Hericium erinaceus are able to trigger LXA4 stimulation of microglia and indirectly reduces Alzheimer disease symptoms in early stage patients. Working with the University of Catania, the protocol structure is the following:

Protocol to determine if Coriolus versicolor and Hericium erinaceus stimulates Lipoxin A4 (LXA4) activation in peripheral blood and in the CNS of rats treated with an equivalent human dose of 3 g per day MRLs given, orally, separately or in combination, morning and evening, for 1 and, respectively, 3 months. At the end of experimental period animals will be sacrificed and the activity of LXA4 will be determined in serum, lymphocytes and in different brain regions (cortex, striatum, substantia nigra, hippocampus and cerebellum) and compared with LXA4 of untreated animals, as control.
20 control subjects and 20 patients with early stage AD diagnosis will be treated with MRLs (**Coriolus versicolor** and **Hericium erinaceus**) for a period of 180 days (See section III). For each mushroom (**Coriolus versicolor** and **Hericium erinaceus**) the supplementation schedule should be six tablets (500 mg) per day or 3 g per day (3 tablets in mornings before breakfast and 3 tablets in evening before dinner). Supplementation period: 180 days. After the treatment period blood samples will be taken and LXA4 activity will be determined in serum and lymphocytes together with heme oxygenase-1 expression as marker of anti-inflammatory and antioxidant potential.

Upon determination of the potential for mushroom nutrition to trigger LXA4 activity, the next step will be to clinically test the hypothesis in early stage Alzheimer’s patients.

Protocol Outline for use of Mushroom Nutrition in Early Stage Alzheimer Patients.

**Table I**: Proposed Human Trial Protocol and Corresponding Cost per Day for Use of Mushroom Nutrition in AD.

<table>
<thead>
<tr>
<th></th>
<th><strong>Coriolus versicolor</strong></th>
<th><strong>Hericium erinaceus</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>500mg tablets</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 tablets/day = 3g</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MONTH 1</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td>MONTH 2</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td>MONTH 3</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td>MONTH 4</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td>MONTH 5</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td>MONTH 6</td>
<td>180 TABLETS</td>
<td>180 TABLETS</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>1080 TABLETS</td>
<td>1080 TABLETS</td>
</tr>
<tr>
<td>Bottle of 90 Tablets</td>
<td>12</td>
<td>12</td>
</tr>
<tr>
<td>Assumed cost per bottle 26.00</td>
<td>318</td>
<td>318.00</td>
</tr>
<tr>
<td><strong>cost per day (€)</strong></td>
<td>1.77</td>
<td>1.77</td>
</tr>
</tbody>
</table>

*If due to untreated Lyme disease, then one has to understand that the *Borrelia burgdorferi* bacterium is not the only potential cause of the neurological disorder as the disorder is multi-factorial due to potential of co-infections caused by the initially weakened immune state of the individual. In Lyme disease, one has to diagnose the bacterium and then address the immune state of the patients with specific supplementation and diet change [16].
D. Potential Daily Cost per day of Mushroom Supplementation to Patient

Supplementation at the price of a full treatment for six months would be equal to two “Big Macs” and soft drinks per day.

Concluding Remarks:

In sum, given the fact that there may be a viral trigger for the onset of Alzheimer’s disease and given the recently confirmed profile of mushroom nutrition supplying both immune modulation and SOD supplementation, it seems with worth the effort to

a) determine if mushroom nutrition does trigger lipoxin A4 activity in the microglia; and if so:

b) conduct a clinical trial in early stage patients with an established (and recognized) parameters for success. Such parameters could be a) decrease in onset of AD and b) decrease in rate of increase “tau” production.

Conclusion

Given the expanding number of patients with Alzheimer’s disease and the increasing cost of care for Alzheimer patients, government healthcare services require safe, clinically reliable and cost effective protocols that treat the symptoms of Alzheimer’s disease; the aforementioned two part protocol may offer a cost effective tool for the management of this condition in developing and developed countries.

References


3 MA Wozniak, AP Mee and RF Itzhaki. Herpes simplex virus type I DNA is located within Alzheimer’s disease amyloid plaques. The Journal of Pathology, Volume 217, Issue 1, Pages131 - 138  2009 DOI: 10.1002/path.2449


