



# MUSHROOMS AND HEALTH GLOBAL INITIATIVE BULLETIN

An ISMS Global Initiative to increase the worldwide consumption of mushrooms through the collection, evaluation and dissemination of scientifically validated information.

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### News from the initiative - Mary Jo Feeney

#### ► Mushrooms and Health website

The Initiative Team anticipates the launch of the Mushrooms and Health website early 2010. This website is a **direct benefit to Initiative investors and focuses on the nutrition and health benefits of mushrooms**. It will house *Mushrooms and Health 2008* and subsequent revisions. These reports provide a critical review of the science linking mushrooms and health and have been prepared by leading researchers at [CSIRO \(Commonwealth Scientific and Industrial Research Organization, Food Science Australia\)](#). Such information is a resource not only to the mushroom industry but to scientists, health professionals and health writers seeking summaries and abstracts of peer reviewed articles linking mushrooms and health.

#### ► How to add local interest to research

See John Collier's discussion of "Cordycepin inhibits protein synthesis and cell adhesion through effects on signal transduction" in News from the United Kingdom. John nicely explains the importance of the research, and also includes interview comments from the lead researcher who is at the School of Pharmacy in Nottingham. This is an example of how to add local/country interest to research that appears in international journals.

#### ► Correction to November Bulletin

We regret the omission of a section in the article "Vitamin D analysis in mushrooms" prepared by Glenn Cardwell in the November *Bulletin*. Here is the corrected full paragraph:

Since then, the Australian mushroom industry has collaborated with Warsash Scientific, distributors of the Xenon pulsed light machine, and the University of Western Sydney to test the effect of pulsed light on vitamin D levels in mushrooms post harvest. Tony Biggs presented the data generated so far. Punnets of mushrooms of two sizes (35 mm and 50 mm diameter) were placed on a conveyor belt and passed under pulsed light, resulting in vitamin D<sub>2</sub> levels at least 10 times greater than the 10 mcg (400 IU) recommended each day for

As a *Bulletin* reader, you will receive an e-mail alert when the website is launched.

adults under 70 years. Further studies will be conducted prior to Christmas to refine the process for commercial application.

## Mushroom research

### ► Maitake immunological effects in breast cancer patients

Deng, G., H. Lin, et al. (2009). "A phase I/II trial of a polysaccharide extract from *Grifola frondosa* (Maitake mushroom) in breast cancer patients: immunological effects." *J Cancer Res Clin Oncol* 135(9): 1215-21.

Oral administration of a polysaccharide extract from Maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood.

Cancer patients commonly use dietary supplements to "boost immune function". A polysaccharide extract from *Grifola frondosa* (Maitake extract) showed immunomodulatory effects in preclinical studies and therefore the potential for clinical use. Whether oral administration in humans produces measurable immunologic effects, however, is unknown.

In a phase I/II dose escalation trial, 34 postmenopausal breast cancer patients, free of disease after initial treatment, were enrolled sequentially in five cohorts. Maitake liquid extract was taken orally at 0.1, 0.5, 1.5, 3, or 5 mg/kg twice daily for three weeks. Peripheral blood was collected at days -7, 0 (prior to the first dosing), 7, 14, and 21 for *ex vivo* analyses. The primary endpoints were safety and tolerability.

No dose-limiting toxicity was encountered. Two patients withdrew prior to completion of the study due to Grade I possibly related side effects: nausea and joint swelling in one patient; rash and pruritus in the second. There was a statistically significant association between Maitake and immunologic function ( $p < 0.0005$ ). Increasing doses of Maitake increased some immunologic parameters and depressed others; the dose-response curves for many endpoints were non-monotonic with intermediate doses having either immune enhancing or immune suppressant effects compared with both high and low doses.

Oral administration of a polysaccharide extract from Maitake mushroom is associated with both immunologically stimulatory and inhibitory measurable effects in peripheral blood. Cancer patients should be made aware of the fact that botanical agents produce more complex effects than assumed, and may depress as well as enhance immune function.

### ► Systematic review on Maitake mushroom

Ulbricht, C., W. Weissner, et al. (2009). "Maitake mushroom (*Grifola frondosa*): systematic review by the natural standard research collaboration." *J Soc Integr Oncol* 7(2): 66-72.

This study evaluated the scientific evidence including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology and dosing.

This study evaluated the scientific evidence on Maitake, including expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing. This review serves as a clinical support tool. Electronic searches were conducted in 10 databases, 20 additional journals (not indexed in common databases), and bibliographies from 50 selected secondary references. No restrictions were placed on the language or quality of the publications. All literature collected pertained to efficacy in humans, dosing, precautions, adverse effects, use in pregnancy and lactation, interactions, alteration of laboratory assays, and mechanisms of action. Standardized inclusion and exclusion criteria were used for selection.

Grades were assigned using an evidence-based grading rationale. There was a lack of systematic study on the safety and effectiveness of Maitake in humans. However, based on popular use and supportive scientific data, three indications are discussed in this review: cancer, diabetes, and immunostimulation. Despite the lack of scientific evidence, Maitake mushroom remains a popular agent in commercial products. Future randomized controlled trials are warranted.

#### ► Antioxidants and mushrooms

Ferreira, I. C., L. Barros, et al. (2009). "[Antioxidants in wild mushrooms.](#)" *Curr Med Chem* 16(12): 1543-60.

Maintenance of equilibrium between free radical production and antioxidant defences (enzymatic and non enzymatic) is an essential condition for normal organism functioning. When this equilibrium has a tendency for the production of free radicals the organism is said to be in oxidative stress. In this situation, excess free radicals may damage cellular lipids, proteins and DNA, affecting normal function and leading to various diseases. In aerobic organisms, the free radicals are constantly produced during the normal cellular metabolism, mainly in the form of Reactive Oxygen Species (ROS) and Reactive Nitrogen Species (RNS). Exposition of the organism to free radicals has led to the development of endogenous defence mechanisms to eliminate them. These defences were the response of evolution to the inevitability of ROS production in aerobic conditions. Natural products with antioxidant activity may help the endogenous defence system. In this perspective the antioxidants present in the diet assume a major importance as possible protector agents reducing oxidative damage. Particularly, the antioxidant properties of wild mushrooms have been extensively studied by our research group and by others, and many antioxidant compounds extracted from these sources have been identified, such as phenolic compounds, tocopherols, ascorbic acid, and carotenoids. We will review the compounds identified so far in mushrooms, as well as the mechanism of action involved in their antioxidant properties. Wild mushrooms might be used directly in diet and promote health, taking advantage of the additive and synergistic effects of all the bioactive compounds present.

Many antioxidant compounds extracted have been identified, such as phenolic compounds, tocopherols, ascorbic acid, and carotenoids.

Queiros, B., JC Barreira, et al. (2009). "[In search of synergistic effects in antioxidant capacity of combined edible mushrooms.](#)" *Int J Food Sci Nutr.* 2009 Sep 10: 1-13.

The antioxidant activity of different edible mushrooms was evaluated considering the different contribution of individual and combined extracts. The radical scavenging capacity was evaluated through hydrogen atom transfer and single electron transfer reaction-based assays: 1,1-diphenyl-2-picrylhydrazyl (DPPH) radical scavenging activity and reducing power, respectively. The inhibition of lipid peroxidation was studied in liposomes solutions by the beta-carotene-linoleate system. Three types of interactions (synergistic, additive and negative synergistic effects) were observed, synergism being the most abundant effect. *Marasmius oreades* is present in the mixtures with higher antioxidant properties and synergistic effects, while *Cantharellus cibarius* is present in the mixtures with lowest antioxidant properties and negative synergist effects. Two discriminant analyses were performed considering individual species in one case and mushroom mixtures in the other. The five mushroom species were clustered in five individual groups,

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but a similar result could not be obtained for the combined mushrooms, for which only the cases containing *C. cibarius* were separated in individual clusters.

► **Antitumor activities of Agaricus blazei**

Ziliotto, L., F. Pinheiro, et al. (2009). "Screening for *in vitro* and *in vivo* antitumor activities of the mushroom *Agaricus blazei*." Nutr Cancer 61(2): 245-50.

The study investigated the *in vitro* antitumor activity of the mushroom *Agaricus blazei* Murill on human cancer cell lines as well as its potential anticancer activity in a model of rat colon carcinogenesis. The *in vitro* anticancer analysis was performed using nine human cancer cell lines incubated with organic and aqueous extracts of *A. blazei*. Antitumor activity was observed with the dichloromethane/methanol and hexanic extracts of *A. blazei* at 250 µg/ml for all cancer cell lines tested. No antiproliferative/cytotoxic activities were detected for the aqueous, methanol, ethyl acetate, or n-butanolic extracts. In the *in vivo* analysis, crude *A. blazei* was given orally after carcinogen treatment in a rat medium-term study (20 weeks) of colon carcinogenesis using aberrant crypt foci (ACF) as biomarker. Male Wistar rats were given dimethylhydrazine (DMH) and then were fed *A. blazei* at 5% in the diet until Week 20. ACF were scored for number and crypt multiplicity. *A. blazei* intake did not suppress ACF development or crypt multiplicity induced by DMH. No differences in tumor incidence in the colon were observed among the DMH-treated groups. Our results indicate that employing *A. blazei* in the diet does not have a suppressive effect on colon carcinogenesis.

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**News from the Netherlands - Raymond Van Buuren**

► **New websites launched**

Raymond van Buuren, Programme Director, Mushroom Promotion Foundation and member of the Initiative's Strategic Communications Group, invites everyone to visit newly launched websites on mushrooms: <http://www.champignonidee.de/> and <http://www.champignonidee.nl/>. According to Raymond: "Please have a look, even without a clue about the German and Dutch language it does give you a feel about the style applied - light, fun and accessible, very consumer oriented. We are finishing uploading and testing for the launch of the United Kingdom and French version and will discuss with Spanish colleagues about a possible translation into Spanish and loading of Spanish recipes. Have fun!"

Visit <http://www.champignonidee.de/> and <http://www.champignonidee.nl/>





► **From a caterpillar develops a new cancer drug from mushrooms**

In research to be published in the *Journal of Biological Chemistry*, Dr Cornelia de Moor of The University of Nottingham, UK and her team have investigated a drug called cordycepin, which was originally extracted from a rare kind of wild mushroom called *Cordyceps* and is now prepared from a cultivated form.

*Cordyceps* is a strange parasitic mushroom that grows on caterpillars. Properties attributed to *Cordyceps* mushroom in Chinese medicine made it interesting to investigate and it has been studied for some time. In fact, the first scientific publication on cordycepin was in 1950. The problem was that although cordycepin was a promising drug, it was quickly degraded in the body. It can now be given with another drug to help combat this, but the side effects of the second drug are a limit to its potential use.

► **So what is this research all about?**

Messenger RNA is a transcript from the DNA that contains the code for a specific protein. During protein synthesis, the code from the messenger RNA is used to assemble the protein. The efficiency at which this happens is affected by the polyadenosine tail that is added to each messenger RNA and shortened during its lifetime. As expected from its structure, cordycepin affects the length of the polyadenosine tail of specific mRNAs. When the researchers checked what effect cordycepin had on total protein synthesis, they were surprised to see that it nearly completely blocked protein synthesis at the maximum concentration, a far greater effect than expected from the observed effects on individual messenger RNAs. It was determined that this effect was due to an inhibition of a regulatory pathway in the cell that promotes cell proliferation, the mTOR pathway and activation of a pathway linked to energy conservation, the AMPK pathway.

► **What is the significance of this research?**

The mTOR pathway is critical for cell proliferation and survival and overactivation of this pathway is common in many cancers. The AMPK pathway is normally activated by a lack of energy in the cell. In recent years it has become clear that it also is an antagonist of the mTOR pathway in the regulation of cell proliferation. Many current cancer drug discovery programs are targeting inhibition of the mTOR pathway or activation of the AMPK pathway.

Cordycepin has been under investigation as a potential cancer drug for a long time, and indeed is now in phase I/II clinical trials in the US. This paper explains how the drug acts at the molecular level and opens up the possibility of developing combination therapies with other cancer drugs on a rational basis. It also indicates that cordycepin might be a drug for type 2 diabetes. Intriguingly, the type 2 diabetes drug metformin has very similar cellular effects to cordycepin, and it might be worth testing cordycepin for that disease. From a mushroom industry point of view, this research is important because it shows a definite effect of a mushroom based drug on cancer cell proliferation and is critical for verifying that fungi have huge potential as health-related products. This type of research is not done often with mushroom-based drugs and will hopefully lead to a greater interest in industry for developing drugs from fungi and finally validating the importance of fungi in both our health and nutrition.

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### ► About Cornelia de Moor

Cornelia de Moor, originally from the Netherlands, studied for an undergraduate degree in Biology and a graduate degree in Developmental Biology from Utrecht University, the Netherlands. The subject of her thesis was the regulation of protein synthesis of a growth factor in human cells. She has postdoctoral research experience in Massachusetts at the former Worcester Foundation and the University of Massachusetts, on the regulation of protein synthesis in frog eggs. In 2000 she got a position as Lecturer in Molecular Biology at the School of Biomedical Sciences in Nottingham and in 2005 moved to the School of Pharmacy in Nottingham as a lecturer in RNA biology. The study of the regulation of protein synthesis in frog eggs and mammalian cells is still on her research agenda, but Cornelia has been interested in mushrooms since childhood, "as my father's family had a tradition of collecting chanterelles in 'secret' locations in the central Netherlands." Based on her long experience with DNA techniques Cornelia would like to develop a sensitive and practical detection system for chanterelle DNA in soil samples and use it to look at the distribution of the mycelia in nature.

The work that was published recently started with a simple interest in the properties of the pure compound, 3' deoxadenosine, which is known as cordycepin and for sale from regular laboratory suppliers. The chemical structure predicted it would affect the maturation of messenger RNA by a process called polyadenylation. "We were able to show that this indeed happened, but we also found that the compound had profound effects on cell adhesion and total protein synthesis that were unexpected. Whenever I ordered cordycepin, I saw in the catalogue '*purified from Cordyceps militaris*'. One day the dormant biologist in me kicked in and I started researching what sort of organism this was. I then found out that there was a vast literature on the curative properties of *Cordyceps*, even dating back to the 15th century in Tibet." This prompted her to look in more detail at the mechanism by which cordycepin affects protein synthesis and found that it works through cell regulatory systems that are very important in cancer. "So far we haven't worked with the fungus yet, but we'd like to compare the activity of the pure compound with crude extracts, to see if cordycepin is really the main active ingredient" said Cornelia.

This research is a prime example of the diversity of mushrooms and why they are most fascinating and interesting to work with. There are research opportunities for mushrooms everywhere even if the mushroom aspect was accidental. This research was funded through the BBSRC (a governmental funding body), through which traditionally mushroom scientists have a low rate of success in achieving funding. This research though will hopefully result in more collaboration between life or health science researchers and mycology researchers and a greater interest and understanding of the importance of fungi amongst the funding bodies.

The research article is available at:

<http://www.jbc.org/cgi/doi/10.1074/jbc.M109.071159>



## News from Australia - Glenn Cardwell

### ► AMGA talks to the health world

The Australian Mushroom Growers Association has made 2010 the year to spread the word to health professionals and key members of the public. Kicking in off in April will be a promotion at the three day Healthy Food Show in Melbourne with cooking demonstrations and advice to the public, who will be encouraged to join the Mushroom Lovers Club.

Later that month, Glenn Cardwell, Accredited Practising Dietitian, will present the University of Western Sydney (UWS) research to the Public Health Association of Australia conference. The theme of the conference is Food Futures: an Australian approach. The UWS work on both the bio-available vitamin B12 in mushrooms and the trials on increasing the vitamin D2 levels to 15 mcg (600IU) and beyond in a serve of mushrooms, can have a significant influence on public health. At the moment, 15 mcg of vitamin D is considered the Adequate Intake level for older adults.

### ► Dietitians get a second dose

In May we return to the Dietitians Association of Australia (DAA) annual conference to provide a mushroom breakfast, along with a cooking demonstration from celebrity chef, Fast Ed, presentations from the CSIRO, who did the *Mushrooms and Health 2008* Report, and Glenn Cardwell. This was a big success last year and really got dietitians thinking about mushrooms being different to vegetables from a health perspective.

### ► Doctors around Australia to get the mushroom message

Just prior to the DAA conference will be the General Practitioners Conference and Exhibition (GPCE), a medical doctors' conference run over three days in Sydney. Here we shall be offering three workshops and a seminar, using experts such as Professor Rebecca Mason, Professor of Physiology at the University of Sydney. This is a great opportunity to get doctors to think of mushrooms whenever giving dietary advice, especially to reduce the risk of long-term disease.

The GPCE in Sydney will be the first of five GPCE doctors' conferences throughout Australia where we shall be promoting mushrooms and health, the final one being in Melbourne in November 2010. The AMGA was thrilled by the response from the GPCE event we attended in 2009, where we were able to get a quarter of all delegates to sign up to receive regular information on mushrooms.

Many Australians have insufficient vitamin D, with dermatologists heading the list, probably due to avoidance of the sun. Mushrooms exposed to light can offer a very simple and tasty solution to all those people who get inadequate sunlight due to long hours inside or fear of getting skin cancer. We shall be telling the world that mushrooms offer so much more than you will get from a vitamin D pill alone.

In 2010, the AMGA shall be spreading the mushrooms and health message directly to doctors, dietitians, public health advocates and the informed public.



## News from the United States - Heidi Gengler

### ► Partnering with nutrition experts to highlight the benefits of mushrooms

With increasing consumer and media interest vested in the value of superfoods, the U.S. Mushroom Council kicked off 2010 with a media strategy intended to communicate mushrooms' superfood status. Foremost in the Council's plan was identifying a spokesperson whose expertise and approach aligned with the Council's focus; Keri Glassman, M.S., R.D., C.D.N., fit the bill precisely. In addition to running a successful nutrition practice in New York City, Keri is a regular contributor to top U.S. broadcast, print and online media outlets. In her most recent book, **The O2 Diet**, released at the end of December, Glassman recognizes the mushroom as a 'nutritional powerhouse,' rich in nutrients and antioxidants. Leveraging her new book, the Council enlisted Glassman to appear in interviews for national television segments, national and local radio outlets, daily newspapers and relevant health and nutrition Web sites.

The Council developed a series of media angles positioning mushrooms as a hero to take on post-holiday diet slumps as a satiating replacement for higher-calorie meats, maintaining New Year's resolutions as a nutrient-rich superfood, and beating the winter blues given mushrooms are the only fruit or vegetable to contain natural vitamin D. Glassman's role as the nutrition expert is to provide authoritative tips for healthful eating, including ways to incorporate superfoods – like mushrooms – into a healthy diet. Media outreach kicked off with a press release which has been picked up in more than 200 outlets to date and generated placements in consumer, retail and trade publications. The Council is also planning a national radio media tour with Glassman that will focus on National Nutrition Month (March), and a series of integrated social media applications through the Mushroom Channel blog, Twitter and Facebook to highlight mushroom tips, nutrition and recipes for consumers.

### ► Initiative project team

- Greg Seymour, President, ISMS General Manager AMGA, Australia; Manager, Mushrooms and Health Global Initiative
- Bart Minor, President, Mushroom Council, United States
- John Collier, Group Research and Development Manager, Monaghan Mushrooms Ltd, Republic of Ireland
- Mary Jo Feeney, Mushrooms and Health Global Initiative Operations Manager, Bulletin Editor, United States
- Glenn Cardwell, Accredited Practising Dietitian, Nutrition Impact P/L, Australia
- Chris Rowley, Communications Consultant, Australia
- Heidi Gengler, Vice President, Edelman Public Relations, United States

### ► Strategic communications group

Members of the Strategic Communications Group strengthen the Initiative's communication capability and develop a local public relations presence in each country whose industry is contributing financially to the project. Members of this group help facilitate stories about mushrooms and health appearing in their local media, monitor mushroom nutrition and health research, liaison with scientists, media and other influencers, and provide feedback to the Initiative. They include

- Franz Schmaus - Germany
- Francois Marche - France
- Ignace Deroo, Evy Detroch - Belgium
- Jose Antonio Jimenez Hernandez - Spain
- Kent Stenvang - Denmark
- Raymond van Buuren - Netherlands
- Elizabeth O'Neil - Canada