



INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

国际药用菌学会

International Society for Medicinal Mushrooms (ISMM) was founded in Vancouver, Canada. As a global non-profit organization, ISMM promotes the development of research, education, production, transportation, marketing and cultivation of medicinal mushrooms to have people to work towards common aspirations and goals. The integration will increase the impact of the international medicinal mushroom industry and benefit the health of people in the world.

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国际药用菌学会 (International Society for Medicinal Mushrooms), 简称ISMM, 在加拿大温哥华注册成立, 由从事药用菌产业的科研、教学、生产、流通、市场、文化及相关产业链的单位、团体和个人自愿组成的为实现共同意愿的非营利性国际组织。本学会致力于促进国际药用菌产业各个领域的融合与发展, 以提升药用菌行业在全球的影响力, 造福人类健康。

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News Reports

The 12th International Medicinal Mushrooms Conference (IMMC12) Held in Bari, Italy

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In September 2024, 230 delegates from 40 different countries (Fig. 1) gathered at The Nicolaus Hotel Bari - HO Collection (Bari, Italy), for the 12th International Medicinal Mushrooms Conference (IMMC12)— the second to be held in Italy after the Palermo Conference in 2017. The theme of the conference was “Medicinal mushrooms: the bet for the future of humanity” IMMC12 participants had the opportunity to discuss and share scientific innovations in the medicinal mushroom sector and to become aware of current research results.



Fig. 1. IMMC12 group photo.

IMMC12 was organized by Prof. Maria Letizia Gargano, associate professor of Environmental and Applied Botany at the

Department of Soil, Plant, and Food Sciences, University of Bari Aldo Moro, Bari, Italy and by Prof. Giuseppe Venturella as President of the Italian Society of Medicinal Mushrooms (SIFM) (Fig. 2).



Fig. 2. IMMC12 opening ceremony: from left to right: Prof. G. Venturella, Prof. F. Gentile, and Prof. M.L. Gargano

IMMC12 was sponsored by National Biodiversity Future Center (NBFC, LAND, SPOKE 3), National Center for Technology in Agriculture (AGRITECH), Italian Society of Medicinal Mushrooms (SIFM), Italian Botanical Society, Journal of Fungi (MDPI), pro Herbarium Mediterraneum International Foundation, Kääpä Biotech, Alkaest, Mycolife Roma, Mycolife, Hifas da Terra, Bona Furtuna, Italian Society of Formulators in Nutraceuticals (SIFNUT), Associazione Luca Coscioni, Italian Academy of Medical Residents (AIMS, Bari), Azienda Agricola Castelluccio, Natural I, MIRRI Italian Research Infrastructure for Sustainable Bioscience and Bioeconomy, Jangsu Alphay Biological Technology Co. Ltd, DXN Malaysia, Tyroler Glückspilze, Mycoverse, Funghi Energia e Salute, and Planta.

Attendees presented 4 keynote speeches and 94 oral presentations in 6 symposia and a round table, as well as 32 e-posters, during IMMC12.

On September 24, 2024, the keynote speeches were presented by A. Adili (Canada), "Psychedelic mushrooms as medicine: challenges and opportunities"; T. Páléníček (Czech Republic), "The phenomenology of psilocybin's experience mediates subsequent persistent psychological effects independently of sex, previous experience or setting"; L. Nagy (Hungary), "Basidiomycete fruiting body development: an exciting morphogenetic process and source of bioactive compounds" and M. Berovič (Slovenia), "Presence and The Future of Medicinal Mushroom Process Engineering".

Two parallel sessions were held in the afternoon: "Diversity, evolution and morphogenesis in medicinal mushrooms" and "Medicinal mushrooms culture collections, cultivation technology and circular economy in rural and marginal areas".

In the first session, chaired by G. Zervakis (Greece), 5 oral presentations were offered by Z.J. Bair (USA), "Mining 100 Agarikon genomes: an ongoing optimization of chemical constituents and bioefficacy", K. Kütt (Estonia), "Distribution of *Inonotus obliquus*, abundance of conks and peculiarities of basidiospore dispersal in Estonia", M. Zotti (Italy), "On

the ecological role of medicinal mushroom *Marasmius oreades*: a study case of fairy rings in the gardens of the Royal Palace of Caserta”, D. Lewinsohn (Israel), “The epidemiology of wild mushroom poisoning in Israel”, and A. Daba (Egypt/USA), “Remembering Tom Volk: A mycological Maestro in our hearts and minds”.



Fig. 3. Keynote speakers: a) A. Adili (Canada), b) T. Páleníček (Czech Republic), c) L. Nagy (Hungary), and d) M. Berovič (Slovenia).

In the other parallel session, chaired by A.F. van Peer (The Netherlands) and C. Jaramillo López (Colombia), 15 oral presentations were offered. The “Effects of *A. bisporus* on the immune system, use of collections and can we improve by breeding?” was the topic of the oral presentation of A.F. van Peer (The Netherlands) followed by the C. Jaramillo López (Colombia) who presented an oral communication entitled “Advances in the biodegradability measurement of a hybrid material, product of the transformation of plastic and organic waste using macromycetes”. Other oral presentations were offered by M. Rollini (Italy), “Reclassification and biotechnological potential of mushrooms strains belonging to the collection of the Department of Food, Environmental and Nutritional Sciences (DeFENS) - University of Milan (Italy)”, D. Ferrero (Italy), “Fungi’s Midas touch: production of medicinal mushroom mycoprotein using agroindustrial by-products”, A. Turk (Korea), “Boosting cordycepin production in *Cordyceps militaris* via the influence of edible insects and medicinal plants”, J. Carrasco (Spain), “Micosylvicultural actions towards the conservation and sustainable cultivation of unique species (MicoAction)”, Anthea Desiderio (Italy), “Bio-recycling hazelnut shells to enrich *Lentinus tigrinus* with bioactive components”, I. Pereman (Israel), “Controlled cultivation of the medicinal mushroom *Hericium erinaceus* for the enrichment and extraction of functional health promoting metabolites, focusing on ergothioneine content, anti-oxidative potential and bioactivity in neuronal cells”, J. Kwon (USA), “Breeding and selection for high-temperature

tolerance in *Pleurotus ostreatus*", N. Holt (USA), "A novel high-temperature tolerant *Pleurotus* sp.: domestication, mating behaviour and interspecies compatibility", G. Koutotsios (Greece), "Impact of locally available lignocellulosic residues on the cultivation parameters and nutritional composition of the tropical milky white mushroom *Calocybe indica*", G. Balenzano (Italy), "Microwave-assisted extraction of *Pleurotus* mushrooms cultivated on wine pomace and antioxydant activity evaluation", M. Fang (China), "Transcriptome combined with enzyme activity analysis unveiled the key genes and pattern of lignocellulose degradation under the cultivation by corncob in *Auricularia heimuer*", M. Spagnuolo (Italy), "Innovative multifunctional production system in marginal areas", and G. Venturella (Italy), "Ex situ conservation, enhancement and sustainable use of *Pleurotus nebrodensis*, a rare species, endemic to Sicily (southern Italy)".

At the end of the sessions all participants were invited to take part in the Welcome Reception at the Cassiopea Hall of the Nicolaus Hotel. The organization offered a folk show at the opening, and all participants were able to dance the "Pizzica," a popular Italian folk dance, originally from the Salento peninsula in Apulia and later spreading throughout the rest of Apulia and the regions of Calabria and eastern Basilicata.

On Wednesday 25 September 2024, a session entitled "Biochemistry, biotechnology and pharmacology of medicinal mushrooms" and chaired by Marin Berovič (Slovenia) and Ángel Trigos (Mexico) took place in the venue of the Conference. In the morning session a plenary lecture was offered by U. Lindequist (Germany) who performed with a lecture by the title "Medicinal mushrooms as multicomponent mixtures (MOCS) - Demonstrated with the example *Lentinula edodes*". Other three members of the Scientific Committee offered lectures in this session, i.e. B. Jakopovic (Croatia), "Impact of medicinal mushroom extracts on ribosomal biogenesis, translation, and metabolic pathways in colorectal cancer: a proteomic study", A. Trigos (Mexico), "Ergosterol, a versatile metabolite of mushrooms", and A. Daba (Egypt/USA), "Medicinal marvels of mushrooms: unlocking their potential for health and wellness". An additional 6 oral communications completed the morning program, J. Feng (China), "Unveiling environmental influence on high molecular weight polysaccharides in *Ganoderma lucidum* submerged fermentation for industry", J. Zhang (China), "Study on active compounds of protecting nerve cells in *Ganoderma lucidum* based on spectrum-effect relationship method", E. Čapelja (Serbia), "Neuroprotective activity of polyamines and phenolic compounds derived from three *Fomes fomentarius* strains in the Balkan Region (Serbia, Croatia, Bosnia and Herzegovina)", S. Hýsek (Austria), "Mycelium of medicinal mushrooms for production of mycelium-based bio-composites and its physical and mechanical properties", V. Ferraro (Italy), "Hypoglycemic properties of *Leccinum scabrum* - An in vitro study on α -glucosidase and α -amylase inhibition activity", and C.-I. Jen (Taiwan), "Physicochemical characteristics and anti-breast cancer properties of medium molecular weight sulfated polysaccharides from *Laetiporus sulphureus*".

The session continued in the afternoon under the coordination of A. Daba (Egypt/USA) and B. Jakopovic (Croatia). 8 oral communications were offered by F. Medri (Italy), "Chemical and functional characterization of *Leccinum scabrum* and *Leccinum versipelle*", V. Šolaja (Serbia), "Mycochemical profile and antioxidant activity of two cultivated *Pleurotus* species: *P. ostreatus* (Jacq.) P. Kumm. 1871 and *P. eryngii* (DC.) Quél. 1872", F. Polito (Italy), "Composition and antimicrobial activity of hydroalcoholic extracts of *Pleurotus eryngii* var. *ferulae* and *P. eryngii* var. *elaeoselini*", M. Karaman (Serbia), "Potential of submerged exo- and intra-polysaccharides from two *Schizophyllum commune* Fr. 1815 strains in biopriming of pea (*Pisum sativum* L.) seed", S. H. Kim (South Korea), "Pharmacological activities and standard compounds of *Cordyceps pruinosa* mycelial extracts", O. Isikhuemhen (USA/Nigeria), "Advances in the use of medicinal

mushrooms in animal production", O. Seniuk (Ukraine), "Means from *Fomes fomentarius* for adding to the feed of domestic animals in order to improve the quality of milk and meat products", and E. Zapora (Poland), "*Pleurotus ostreatus* as a new antimicrobial agent against bovine mastitis".

On Thursday 26 September 2024, the Symposium, "Medicinal mushrooms in human studies: from healthy aging to different diseases" chaired by P. Rossi (Italy) and L. Kalitukha (Germany) began with a plenary lecture by C. Kessler (Germany) entitled "Clinical experiences from the use of medicinal mushrooms in outpatient hospital settings in Germany". L. Kalitukha (Germany) offered a oral presentation by the title "Benefits of *Fomes fomentarius* fibres (Good Feeling Power®) in the treatment of Addison's disease. Case study" followed by C. Fernandez de Ana Portela (Spain), "Nanoemulsified fungal compounds emerge as natural immunoadjuvants for cancer prevention and treatment in ongoing clinical trials", N. Kurochko (Ukraine) "Chitin-glucan-melanin complex from *Fomes fomentarius* as a means to stop bleeding and treat lacerations and burns in combat conditions", F. Brandalise (Italy), "Electrophysiological Insights into *Hericium erinaceus*: Unveiling its Neuroprotective Potential", S. Masaphy (Israel), "Mushroom versus rare diseases: activity against the Leishmania parasite", V. Parisi (Italy), "*Pisolithus arhizus*: a bio-factory of terpenoids and pigments with health-promoting activity", M. Karaman (Serbia), *Ganoderma pfeifferi* Bres. 1889 and *G. resinaceum* Boud. 1889 as potential therapeutic agents: A comparative study on antioxidant, antiproliferative and lipid-lowering properties in alloxaninduced diabetic rats", I. Hininger-Favier (France), "Extracts from King Oyster mushrooms (*Pleurotus eryngii*), and their major bioactive compounds, reduce inflammatory stress signals in HAPI microglia cells", E. Eno-Edobor (Nigeria), "Administration of *Coriolus mrl* resulted in a significant reduction in PSA levels among prostate cancer patients", J. Zhang (Japan), "Biological role of ricin B-type lectins from the entomopathogenic fungi, *Cordyceps militaris*", Y. Park (Korea), "The improved effect of bone health in animal models of osteoporosis administered ethanolic extracts of *Wolfiporia hoelen*", N. Watanabe (Japan), "Genome and transcriptomic analysis of biologically active angel-wing mushroom *Pleurocybella porrigens* that cause acute encephalopathy", Y. Yang (China), "Function evaluation and mechanism study of Sanghuangporus vaninii in inhibiting cervical cancer and lowering uric acid", and C. Fields (USA), "Acute effects of naturally occurring nordic Lions Mane extracts on cognitive performance".

In the same day a parallel session entitled "Medicinal mushrooms as a source of novel functional food and health benefits" was chaired by L. Barros (Portugal) and A. Colletti (Italy). 17 oral communication were included in this session performed by the following authors: M. Pellizzato (Italy), "Full spectrum mycoproducts explained", A. Colletti (Italy), "Safety and efficacy of medicinal mushroom supplements: is a "significant history of consumption" enough", V. Citi (Italy), "Medicinal mushrooms: not only β -glucans for clinical practice", S. Badalyan (Armenia), "Recent Advances in Biotechnological and Biomedical Research of Macrofungi", Y. Liu (China), "Degradation of β -D-glucan from *Ganoderma lucidum* to produce oligosaccharides and the separation, structural and immunoregulatory property investigation", D. Casulli (Italy), "Completeness of Spagyric multiextraction from medicinal mushrooms and their relative structures of crystallizations", M. K. Lee (Korea), "Production of new bioactive metabolites from *Hericium erinaceus* by the regulation of cultivation conditions", J. Daoust (USA), "*Hericium erinaceus* supplementation as a prebiotic fibre impacting microbiome composition and neuroactive targeted metabolomics", I. Sofrenić (Serbia), "Application of design of experiment and multivariate analysis in the process of *Ganoderma lucidum* basidiocarps extraction", B. Anđelković (Serbia), "Application of FTIR spectroscopy in monitoring of *Fomitopsis betulina* fruiting bodies chemical composition", L. Goppa (Italy), "Integrative Omics analysis of *Hericium erinaceus*: comparative insights from proteomics and NMR metabolomics", P. García-Ponsoda (Spain), "Extraction of antioxidant and anti-inflammatory fractions from *Sparassis*

crispa using dpressurized fluids”, W. Goss (USA), “Industrial cultivation of medicinal mushrooms: unlocking functional food potential”, K. Kiss (Italy), “Mycolife liquid extracts, the new generation of medicinal mushroom preparations. Innovative know-how procedure and what is behind it”, E. Pereira (Portugal), “Mushroom bio-residues as a source of dietary fibre”, O. Seniuk (Ukraine), “Biopreparation Mikosan from *F. fomentarius* for plant protection” and, R. Guarcello (Italy), “Implementation of the MIRRI-SAAF catalogue of culture collections: an example of data v management and resources sharing”.

In the afternoon a visit to the city of Altamura (Bari) was organized for all IMMC12 participants. The participants made atour of Altamura's main landmark, i.e. the Romanesque cathedral, begun in 1232 by Federico II. Also organized was a tasting of Altamura bread, baked in traditional wood and stone ovens, and known for its fragrance, flavor and aroma.

Following this, participants took part in a social dinner at the The Relais "I Luoghi di Pitti", built in the 16th century as a rural home, is a wonder offered by the ancient city of Altamura (province of Bari, Puglia), set in one of the most majestic structures of Italy's first Rural Park.

On Friday 26 September 2024, a session entitled “Therapeutic potential of psychedelic mushrooms”, chaired by T. Re (Italy) and O.S. Isikhuemhen (USA), featured the expected participation of Paul Stamets (USA) who offered a plenary lecture titled “Psilocybin mushrooms: history, use and identification”. It was followed by the lectures of D. Zullino (Italy), “Psychedelic-assisted psychotherapy - How to catalyze the mechanisms of psychotherapeutic action”, W. Goss (USA), “Ethnomycology and the therapeutic potential of psychedelic mushrooms: Policy and advocacy perspectives”, T. Re (Italy), “End of life: a new training approach”, A. Metastasio (Italy), “The use of phenomenology to understand the psychedelic experience induced by psilocybin. New potential applications in research and clinical practice”, F. Bosco (Italy), “Neurophenomenology in Tibetan mediation and in psychedelics”, A. Chiolerio (Italy), “Correlation and complexity of fungal electrome”, L. Pawlik (Austria), “Heavenly prospects: Psilocybin-induced death and god encounters compared”. The morning program was complemented by two oral communications with remote connection to Canada by E.C. Lewis (Canada), “Exploring the therapeutic potential of psilocybin in neurology” and H. Farzin (Canada), “De novo implementation of publicly-funded Psilocybin-Assisted Therapy for cancer patients in a palliative care outpatient practice: A Montreal story”.

In the afternoon a Round Table by the title “Psychedelics between the right to science and national laws” was co-organized with “Associazione Luca Coscioni”, association for the freedom of scientific research founded on 2002, by Luca Coscioni, who had amyotrophic lateral sclerosis and was a member of the Italian Radical Party who promoted the campaign for the freedom of scientific research on embryonic stem cells. The Round Table was attended by P. Cipriano (Italy), “Psilocybin fungi: bridge between life and death”, G. Perrone (Italy), “The right to science and substances under international control”, M. D’Alonzo (Italy), “The clinical experiences that do not exist”, C. Moretti (Italy), “Compassionate therapies at the end of life”, M. Barocchi (Italy), “MAPS in Italy – First Italian conference on psychedelics”, and A. Faggioli (Italy), “Great treatment with psilocybin and Ayahuasca: preliminary results”.

The conclusions were entrusted to Marco Cappato (Italy), an Italian nonviolent activist for fundamental rights and liberties and politician.



Fig. 4. G. Venturella introduce the round table with the participation of Marco Cappato.

The 32 e-posters provides immediate visualization of content and allows participants the opportunity to download the posters to a mobile device, thereby contributing to the environment in terms of reducing paper use.

During the closing ceremony, P. Stamets (USA) submitted the candidacy of Seattle (USA) as the venue for the next IMMC13. Then M. L. Gargano and G. Venturella declared IMMC12 closed.

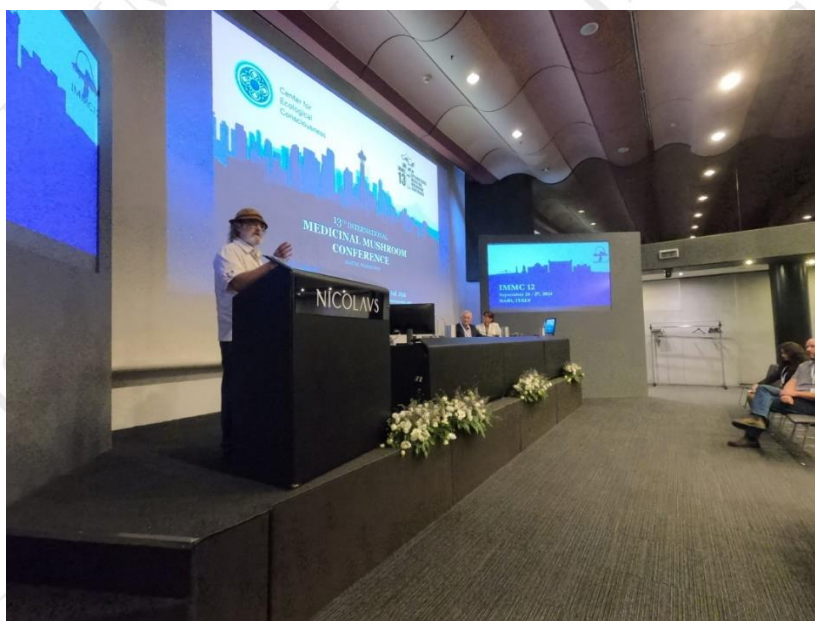


Fig. 5: P. Stamets, the organizer of IMMC13 in Seattle, USA.

Prize money, offered by the sponsor “Funghi Energia e Salute”, was awarded to 3 young participants whose oral presentations were guided by highly scientific content.

C. I. Jen (Taiwan) received a prize of euro 1000,00 for her oral presentation titled “Physicochemical characteristics and anti-breast cancer properties of medium molecular weight sulfated polysaccharides from *Laetiporus sulphureus*”, I. Sofrenić (Serbia), received a prize of euro 500,00 for her oral presentation titled “Application of design of experiment and multivariate

analysis in the process of *Ganoderma lucidum* basidiocarps extraction”, and A. Desiderio (Italy,), received a prize of euro 500,00 for her oral presentation titled “Bio-recycling hazelnut shells to enrich *Lentinus tigrinus* with bioactive components”.

In the end, the Italian Medicinal Mushroom Society (SIFM) had the pleasure and honor to welcome as an Honorary Member Paul Stamets, and award him a plate for his important and valuable cultural activities and as a staunch supporter of mycotherapy.

The FDA Restricts a Psychoactive Mushroom Used in Some Edibles

By Will Stone



*Federal regulators have cracked down on mushroom edibles containing *Amanita muscaria* — also known as fly agaric — after mounting safety concerns. Karl-Josef Hildenbrand/DPA/AFP via Getty Images*

Federal regulators are taking aim at a popular category of psychoactive edibles that contain an iconic red-capped mushroom in the wake of a rash of illnesses and even a few suspected deaths.

This week, the Food and Drug Administration warned food manufacturers that *Amanita muscaria* and the compounds in that mushroom are not authorized for use in food, citing a review of the scientific evidence that found these ingredients do not meet "safety standards."

There's considerable folklore surrounding the white-spotted fungus, also known as "fly agaric," which still permeates popular culture, even appearing in the Mario video game franchise and as emojis. Unlike psilocybin, the active ingredient in magic mushrooms, *Amanita muscaria* isn't listed as a controlled substance. It's advertised as an ingredient in some edibles, which are touted as having cognitive-enhancing "nootropic" or "microdosing" blends. Many are sold in trippy-looking packaging at convenience stores, smoke and vape shops, and online.

In its warning letter to food manufacturers, the FDA notes these are sometimes marketed as "psychedelic edibles" or "legal psychedelics," and that "adverse event reports" prompted the agency to assess the mushroom's safety profile.

"I feel it's the right call," says Eric Leas, an epidemiologist at the University of California, San Diego who has documented public health concerns around the mushroom. "It could potentially have very large implications for this market." Christian Rasmussen, who runs an online retailer of *Amanita muscaria*, said his lawyers are still figuring out the implications, but called it a "huge obstacle" for his business, the industry and individuals who've been using the mushroom. "A lot of this seems to be brought on by the actual adulterated products that have hit the market in recent years, containing various synthetic drugs and being marketed as Amanita," Rasmussen, who runs MN Nice Botanicals,

said in an email. NPR contacted several other major companies that sell these mushroom edibles and did not receive a response.

Hospitalizations led to edible recall

These products drew considerable attention earlier this year as poison centers across the country received reports of people being hospitalized after consuming chocolates and gummies marketed under the brand name Diamond Shroomz, which were made by a California-based company known as Prophet Premium Blends. The company recalled the products.

Subsequent testing revealed some of those edibles contained "muscimol," one of the active ingredients in *Amanita muscaria*. However, there was also a mixture of other substances, including a synthetic version of psilocybin, the prescription anticonvulsant drug pregabalin and the supplement kava. Others who've tested mushroom edible products have also documented a variety of undisclosed substances, as NPR reported earlier this year.

The FDA investigation concluded that muscimol "couldn't explain all the symptoms reported by ill people who consumed the Diamond Shroomz-brand products."

The agency is now prohibiting the use of three compounds in the mushroom — muscimol, ibotenic acid and muscarine — given safety concerns identified in its review of the evidence. Exactly how the FDA will decide to enforce its decision remains to be seen.

The market for these psychoactive edibles has grown substantially in just the last few years.

"There are hundreds of brands sold online," says UCSD's Leas, "This threatens the legal status of manufacturers so it could put a stop to that trend."

And Dr. Mason Marks, a law professor and senior fellow with the Project on Psychedelics Law and Regulation at Harvard Law School's Petrie-Flom Center, says inaccurately labeling food products is "quite concerning" and against federal regulations, regardless of whether or not they contain *Amanita muscaria*.

"The problem with these products is we just don't know what's in them," says Marks. "It's a little bit difficult to predict what comes next."

It's unclear how the FDA will enforce mushroom prohibition

The FDA has a variety of options at its disposal — it can work with companies to initiate a recall, as it already did with Diamond Shroomz, seize products on store shelves, get a court order or an injunction to prevent sales.

In theory, the agency could even push the Drug Enforcement Administration to designate the mushroom or its active ingredients a controlled substance, although that would depend on how the incoming Trump administration wants to handle the matter, says Marks.

"The FDA issues a lot of these warning letters," he says. "There's a possibility that nothing will happen."

The situation has parallels to what's happening with certain hemp-derived products like Delta-9 THC and CBD, or cannabidiol.

Those populate stores even though they're "not considered legal ingredients by the FDA," says Shawn Hauser, a partner at the Colorado-based law firm Vicente, which focuses on psychedelics, cannabis and novel natural ingredients like mushrooms.

"There have been warning letters around that, but they generally haven't been enforced unless there's unlawful drug claims, marketing to children or other public safety issues," she says.

A spokesperson for the National Association of Convenience Stores said they were alerting their members so that they "can take appropriate action" in response to the warning letter.

Marks says the FDA ruling doesn't prohibit people from growing or picking this kind of mushroom, which has a relatively small following compared to other psychedelics.

Amanita muscaria targets GABA receptors (unlike psilocybin that primarily acts on serotonin receptors) and can lead to a dissociative state that some describe as quite unpleasant and even disturbing in high doses.

"There are people that are interested in having heavy psychedelic experiences, and this really isn't the mushroom to go to for that," says Kevin Feeney, a lawyer and a cultural anthropologist at Central Washington University who has edited a compendium on *Amanita muscaria*.

People often seek it out for microdosing out of the belief that it helps anxiety, sleep and even more serious problems like addiction to benzodiazepines and alcohol, though there's little evidence from clinical research on its possible therapeutic properties in humans.

"[FDA] is clearly addressing this mushroom," Feeney says. "But to what degree are they addressing the other additives that are in these products?"

Feeney is also an adviser to Psyched Wellness, a company that sells *Amanita muscaria* products and is affected by the FDA decision. He says his comments do not reflect the company's views.

While the mushroom is poisonous, there are not many documented reports of overdose and death.

In its scientific review, FDA staff noted there were no "toxicity studies sufficient to establish the safe use" of the mushroom or its extracts, and that the available information "underscores their potential for serious harm and adverse effects on the central nervous system," including hallucinations, drowsiness, delirium and seizure.

Online retailer Rasmussen and others in the industry have said the mushroom can be prepared in ways that reduce undesirable effects. The FDA said there are no internationally recognized food standards to support safe processing and consumption.

Hauser, the Colorado-based lawyer, sees this as a cautionary tale of the "hands-off" approach that the FDA has taken with some natural substances that have a history of being used for medicinal, beneficial or spiritual purposes.

"This is one of the places where consumer demand is moving faster than the law, and businesses are going to try and meet that demand," she says. "When these products are unregulated and when there isn't consumer education, that's where you have real public safety issues."

Source: <https://www.npr.org/>

Newly Named Psychedelic Fungus Points to African Origins of World's Most Popular 'Magic Mushroom'

By environment reporter Peter de Kruijff



Psilocybe cubensis is the most commonly known type of magic mushroom which can be found all around the world.

(Flickr: Seattle.roamer, *P. cubensis*, CC_BY-NC-ND_2.0)

In short:

The closest wild relative to the world's most popular "magic mushroom" *Psilocybe cubensis* has been given a preliminary name: *Psilocybe ochraceocentrata*.

The two species shared a common ancestor 1.5 million years ago and may have originated in Africa.

What's next?

Further research is underway to try to pinpoint the exact origin and history of the spread of *P. cubensis*.

The fungus *P. cubensis* — colloquially known as cubes, gold tops or gold caps in Australia — is the most prolific hallucinogenic mushroom on the planet.

Its psychoactive compound psilocybin is an illegal drug in most parts of the world, so research into where the species came from and how it spread is limited.

But a new study, not yet peer reviewed but published on the biological sciences repository bioRxiv, suggests an ancestor of *P. cubensis* could have come from Africa before spreading far and wide.



The name of the new African species *P. ochraceocentrata* means pileus (cap) with a yellow-ochre centre. (Supplied: Cathy Sharp)

The study unveils a psychoactive mushroom that looks like *P. cubensis* but is new to Western science.

Samples of the unnamed species were collected in Zimbabwe and South Africa and their genetic blueprint compared to *P. cubensis*.

Study co-author Bryn Dentinger, the mycology curator at the Natural History Museum of Utah, said the new species, provisionally named *P. ochraceocentrata*, is the closest wild relative to *P. cubensis* discovered so far.

"We estimate they diverged [from a common ancestor] around 1.5 million years ago," he said.

"So, by comparison, they are roughly the same relatedness as chimps and bonobos are to each other.

"Knowing the closest wild relative of *P. cubensis* provides information on its origin and evolution."

Australian mycologist Alistair McTaggart, from the private company Psymbiotika Lab and who was not involved with new research, said the study supports the hypothesis that *P. cubensis* could have an African origin.

Dr McTaggart and Dr Dentinger agree that if the new species could be bred with *P. cubensis*, the hybrid offspring may lead to the development of new psilocybin therapies.



Natural History Museum of Utah mycology curator Bryn Dentinger. (Supplied: Bryn Dentinger)

How did 'gold top' mushrooms move around the world?

Psilocybes, a group which includes many species of psychedelic mushrooms with gills, first emerged 67 million years ago.

A common ancestor of *P. cubensis* and *P. ochraceocentrata* could have evolved alongside large herbivores in East Africa as far back as 1.8 million years ago, the study suggests.

"Bovids [cloven-hoofed grazing mammals] in particular were abundant and transforming the landscape to create and maintain grasslands and savannas in parts of Africa," Dr Dentinger said.

And it was about this time that the ancient human species *Homo erectus* started migrating out of Africa and into Eurasia alongside bovids.

Mushroom spores transported on bovid hoofs or dropped in poo could then explain how the ancestral *Psilocybe* species spread then diverged in Africa and Asia.

Modern magic mushroom observations



Source: iNaturalist

Broad ecological modelling for the study suggested *P. cubensis* could have been found in Africa, the Americas, Asia and Australasia between 2.55 million and 710,000 years ago.

The late Mexican mycologist and *Psilocybe* expert Gastón Guzmán thought *P. cubensis* arrived in the Americas with cattle and Europeans around the year 1500.

The new study suggests the mushrooms could have arrived before Europeans when bison migration waves started 190,000 years ago.



*The distribution of *P. cubensis* in America is similar to historic bison distribution ranges. (ABC Rural: Kim Honan)*

These are just theories, though. Dr Dentinger said where exactly the two mushroom species and their common ancestor originated was still speculative for the moment.

"We are also pursuing population genetic studies to try and pinpoint the origin and spread of *P. cubensis*," he said.

When did magic mushrooms reach Australia?

It's not clear when *P. cubensis* first arrived in Australia but a study last year suggested it was introduced with domesticated cattle.

One of the first Western recordings of suspected magic mushroom use in Australia came from the mycologist Sir John Burton Cleland.

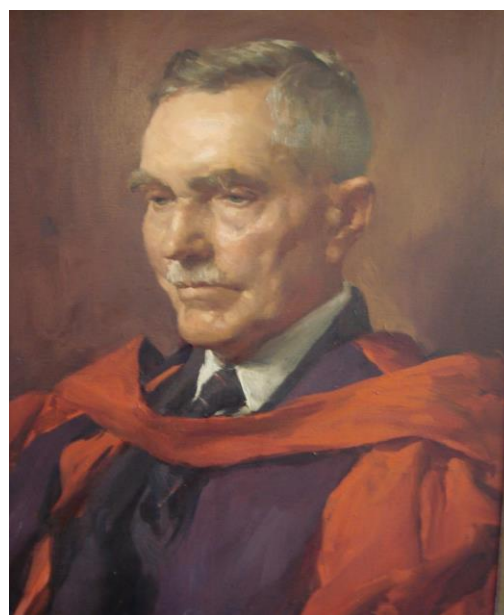
He wrote in 1934, in a South Australian fungi handbook, about how some "toadstools" gave rise to a kind of intoxication.

"A former colleague of mine told me how his parents ate once a dish of mushrooms," Cleland wrote.

"And as the meal progressed they gradually became more and more hilarious, the most simple remark giving rise to peals of laughter.

"The intoxication passed off without any unpleasant effects. Probably some poisonous kind had been included, possibly one of the dung-inhabiting species."

The mushrooms consumed at the dinner could have been a local



*Mycologist Sir John Burton Cleland.
(Wikimedia: University of Adelaide, John
Burton Cleland, CC BY-SA 3.0)*

Australian species but may have been *P. cubensis*.

Australasia is home to several species of endemic magic mushrooms, such as *P. subaeruginosa*, which are also known as "subs". They prefer to live on deteriorating wood over dung.

A recent study led by Dr McTaggart found subs, which have a high concentration of psilocybin and can cause temporary paralysis, have invaded parts of the Northern Hemisphere but are described as different species of mushrooms.

"This is one species in Australia and it should be a name applied to the Northern Hemisphere," he said.

Source: www.abc.net.au

Up-coming Events

International Mushroom Days, China 2025

International Mushroom Days, China 2025, the ultimate gathering for mushroom enthusiasts, is set to take place from April 14th to 16th, 2025 at Xiamen Fliport Hotel C&E Center, Fujian, China. Expo and multiple thematic conferences will be organized, covering a wide range of topics including rare edible mushroom cultivation techniques, professional equipment technology, brand building, and export trade. Get ready to embark on a thrilling journey into the world of mushrooms like never before.

This expo will adhere to the slogan of "Expand or Expire" and follow the guiding principles of "cross-industry alliances, cooperation and coordination, cross-border integration, complementary advantages, resource sharing, symbiosis, and common prosperity". We will unite various stakeholders including government, industry, enterprises, academia, and research institutions to connect resources along the entire edible fungi industry chain. Our aim is to establish a dual circulation of domestic and international trade in the Chinese edible fungi industry and create an international one-stop procurement platform for the entire edible fungi industry chain.

Exhibition Area

The Expo will be held at the first and second floors of Xiamen Fliport Hotel C&E Center, with a total exhibition area of approximately 18,000 square meters. Two themed exhibition areas will be set up: the Intelligent Mushroom Equipments Hall (Hall A) and the Mushroom Products Hall (Hall B).

Booth Prices

Raw Space (without construction): 700 RMB/square meter (minimum order of 36 square meters).

Standard booth: 9 square meters (3 meters × 3 meters), equipped with lighting power supply, one display table, two chairs, two spotlights. The base price is 7000 RMB per booth. Booth with two-side open will incur an additional 10% fee.

Discount Policy

Enterprises that have participated in activities organized by the Edible Mushroom and Products Branch of the China



Xiamen Wutong Fliport Hotel and Xiamen Fliport C&E Center

Chamber of Commerce of Import and Export of Foodstuffs, Native Produce and Animal By-products (CFNA), or are members of the chamber, will enjoy a 10% discount.

Exhibition Contact

Contact: Sun Boyu +86-13683237198 (WeChat)

Phone: +86-010-87109859

Email: imd_expo@163.com



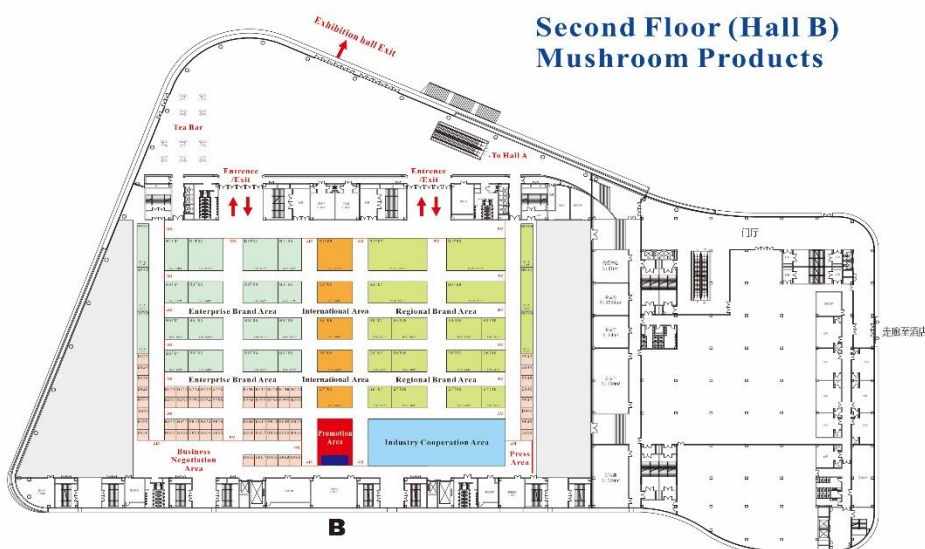
INTERNATIONAL MUSHROOM DAYS, CHINA 2025

April 14th - 16th, 2025 XIAMEN FLIPORT C&E CENTER, FUJIAN, CHINA

Ground Floor (Hall A) Intelligent Mushroom Equipments



Second Floor (Hall B) Mushroom Products



KEEP CALM & CARRY ON



INTERNATIONAL MUSHROOM DAYS, CHINA 2025

April 14th - 16th, 2025
Xiamen, China

For further information, please contact:

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Facebook:

[https://www.facebook.com/
ChineseMushroomDays](https://www.facebook.com/ChineseMushroomDays)

E-mail:

mushroomdays@hotmail.com



Registration online

Dutch Mushroom Days



Block the calendar

The Board of the Mushroomdays Foundation is pleased to inform you that the date of the next edition of the Mushroom Days has been set for **April 22-24, 2026**. The event will again take place in the **Brabanthallen** in **'s-Hertogenbosch**. This meets the preference of the exhibitors for a frequency of “every 3 years”. Also, for the same reason, the Mushroomdays Foundation has placed an option with the Brabanthallen for an edition on June 13-15, 2029.



After a very successful edition in 2023, there is no reason for the Mushroom Days Committee to opt for a substantially different format for the event, but (as always) to look for further optimization on a detailed level.

The Mushroom Days Committee plans to send out the first mailing for participation and registration in the 2nd quarter of 2025. We are very much looking forward to welcoming you all again in order to shape together this great global trade fair. We will keep you informed via our website www.mushroomdays.com.

Kind regards,

Piet Lempens

Chairman Mushroomdays Foundation.

Source: <https://champignondagen.nl/home-eng/>

The 11th International Conference on Mushroom Biology and Mushroom Products

(ICMBMP11)



**World Society for
Mushroom Biology
and Mushroom
Products**



The 11th International Conference on Mushroom Biology and Mushroom Products (ICMBMP11) will be held in Ghana, 2026, the chairman of the conference is Dr. Mary Obodai. Please stay tuned for the call for papers and conference programme.

ABOUT WSMBMP

The World Society for Mushroom Biology and Mushroom Products is an international organization devoted to the enhancement and application of knowledge related to basic and applied aspects of mushroom biology and mushroom products. Activities of the Society shall be conducted with the Constitution and Bye Laws and include: publishing the Society Bulletin, and other educational and scientific literature; organizing scientific meetings, symposia, workshops and training courses; representing mushrooms-related interests internationally and other means deemed appropriate.

CONTACT US

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Research progress

Recent progress in mushroom-derived ergothioneine: Techniques and applications

Yuwan Weng ^a, Min Zhu ^a, Huiguo Ma ^a, Xuechao Hu ^{a b}, Lujing Ren ^a

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^b*Jiangsu JanStar Biotechnology Co., Ltd., No. 6, Dongsheng West Road, Jiangsu, People's Republic of China*

Abstract: Ergothioneine (EGT), a vital naturally occurring water-soluble sulfur-containing amino acid and potent antioxidant, serves as one of the primary bioactive compounds found in mushrooms. Given its growing recognition and significance in the food industry, substantial efforts have recently been invested in the biosynthesis, extraction, and purification processes of EGT derived from mushrooms. Submerged fermentation of mushrooms to produce EGT is an eco-friendly method that offers shorter fermentation times and higher yields, making it ideal for large-scale production. However, it requires precise control of cultivation conditions to optimize EGT yield, along with efficient extraction and purification processes to remove impurities, ensuring bioactivity and maximizing its antioxidant and health benefits. With regard to existing research, this review uniquely emphasizes mushroom-derived EGT, focusing on the physiological roles of EGT, the biosynthesis mechanism in mushrooms, extraction and purification methodologies, and applications in food industries. These findings offer valuable insights and serve as a foundation for the large-scale production of EGT through the submerged fermentation of mushrooms, highlighting their potential applications in the food industry.

Food Bioscience, Volume 62, December 2024, 105533,

<https://doi.org/10.1016/j.fbio.2024.105533>

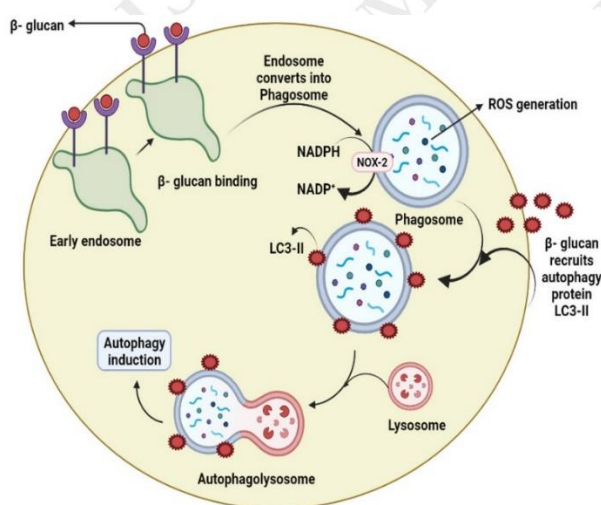
Exploring the Potential of Medicinal Mushroom β -Glucans as a Natural Frontier in Prostate Cancer Treatment

Rashmi Trivedi, Tarun Kumar Upadhyay

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Abstract: The global increase in cancer cases, particularly prostate cancer, poses a significant health challenge worldwide. Conventional treatments such as surgery, radiation therapy, hormone therapy, chemotherapy, and immunotherapy offer valuable options but are associated with limitations and potential side effects. As a result, there is growing interest in complementary therapies, including natural compounds such as β -glucans, derived from sources

such as yeast and mushrooms. In this review, we explored the potential therapeutic role of medicinal mushrooms β -glucan in prostate cancer treatment. β -glucans has demonstrated anti-cancer properties in preclinical studies, including inhibition of proliferation, induction of apoptosis, and modulation of immune responses. Studies in prostate cancer cell lines and animal models have shown promising results, with β -glucan inhibiting tumor growth, inducing DNA damage, and regulating tumor markers such as p53 and prostate specific antigen. β -glucans acts through various pathways, including stimulation of dendritic cells, modulation of cytokine secretion, suppression of myeloid-derived suppressor cells, and enhancement of immune responses. Moreover, β -glucans exhibits anti-androgenic and immune-modulatory effects, making it a promising candidate for prostate cancer treatment. In this study, we also focused on the mechanism of action of β -glucans through various pathways including tumor cell death by oxidative stress created through ROS generation and autophagy. Although preclinical studies support the potential therapeutic efficacy of medicinal mushrooms β -glucans, further research is needed to elucidate its clinical utility and safety in human trials.



Keywords: immuno-modulatory, prostate cancer, complementary therapy, beta-glucans, active surveillance, medicinal mushrooms

International Journal of Medicinal Mushrooms, Volume 27, Issue 2, 2025, pp. 1-11

DOI: 10.1615/IntJMedMushrooms.2024056585

Bitter almond gum-fish gelatin conjugate coatings extend the storage of button mushrooms

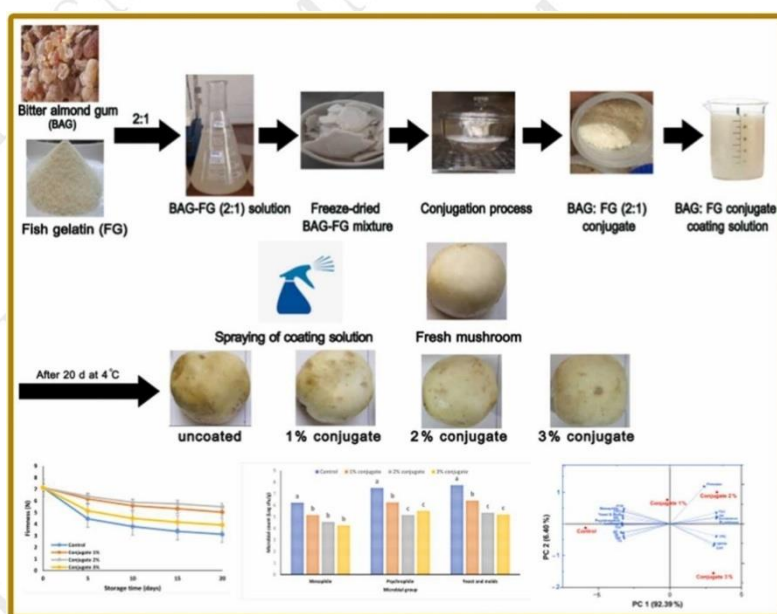
Chamran Moradi ^a, Ebrahim Hosseini ^{a 1}, Esmat Roustab ^b

^aDepartment of Food Science and Technology, Faculty of Agriculture, Kazerun Branch, Islamic Azad University, Kazerun, Iran

^bDepartment of Food Science and Technology, Faculty of Agriculture, Ferdowsi University of Mashhad, Mashhad, Iran

Abstract: Button mushrooms (*Agaricus bisporus*) have a short shelf-life due to high moisture content and lack of a protective layer, leading to browning and softening. This study aimed to investigate the effects of spraying different concentrations (1 %, 2 %, and 3 % w/v) of bitter almond gum: fish gelatin conjugate coating on the quality of fresh mushrooms during 20 d of cold storage. The results showed that the spray-coated samples maintained better quality

parameters than uncoated samples during storage. SEM micrographs confirmed formation coating on the surface of mushrooms and improvement in the microstructure. Mushrooms treated with 2 % conjugate showed considerable improvement in firmness retention, reduced browning, and sensory indices. At the same time, mushrooms coated with 3 % conjugate effectively retained phenolic content, DPPH radical scavenging, and enzyme activities. Lower microbial counts were observed in proportion to coating concentrations. The principal component and hierarchical cluster analyses were conducted to illustrate the effects of variable and conjugate concentration on extending the shelf-life of mushrooms and categorize the samples based on their performance. This study suggests that using conjugate coating can be a practical solution for prolonging the shelf life of button mushrooms and may also be beneficial for improving the post-harvest quality of other fruits and vegetables.



Postharvest Biology and Technology, Volume 222, April 2025, 113356

<https://doi.org/10.1016/j.postharvbio.2024.113356>

Mushroom-derived nutraceuticals in the 21st century: an appraisal and future perspectives

Hom-Singli Mayirnao ^a, Karuna Sharma ^a, Pooja Jangir ^a, Surinder Kaur ^b, Rupam Kapoor ^a

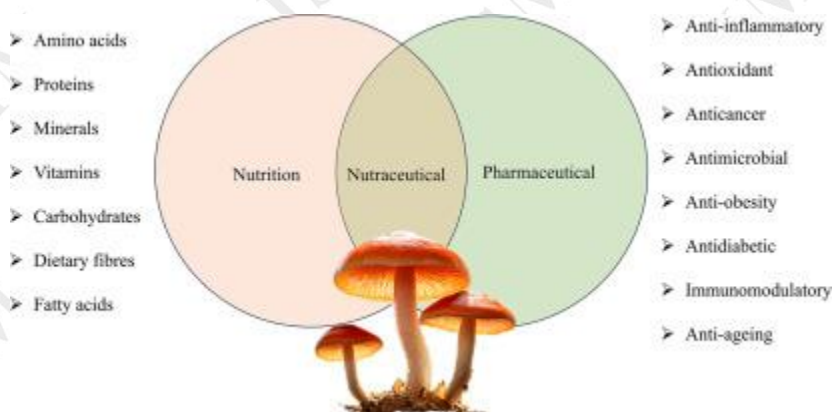
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^b*SGTB Khalsa College, University of Delhi, Delhi 110007, India*

Abstract: Mushrooms are not only delicious additions to various dishes but also possess several health benefits due to their diverse nutritional composition. They are a good source of essential nutrients including protein, vitamins, minerals, and dietary fibre, and are low in fats and calories. Comprehensive studies have been carried out with respect to the nutritive quality of wild and cultivated mushrooms. In recorded history, the purpose of mushroom cultivation was to meet household consumption and gradually, the combination of their nutritional quality and potential health benefits, and the growing interest in functional foods and natural remedies has led researchers to expand their focus towards nutraceutical innovation. The review highlights the utilitarian characteristics of mushrooms gaining popularity as source

of nutraceuticals. It summarizes the various factors influencing secondary metabolism. It also identifies knowledge gaps and proposes potential area where more research is needed for optimal use of their potential. Understanding the significance and potential applications of mushrooms can contribute to the development of new products and formulations that can stimulate economic growth and expand the market for mushroom-based nutraceuticals.

Graphical abstract



Keywords: Macrofungi, Food security, Nutrients, Bioactive compounds, Functional foods, Mushroom economics and production

Journal of Future Foods, Volume 5, Issue 4, July 2025, Pages 342-360,

<https://doi.org/10.1016/j.jfutfo.2024.07.013>

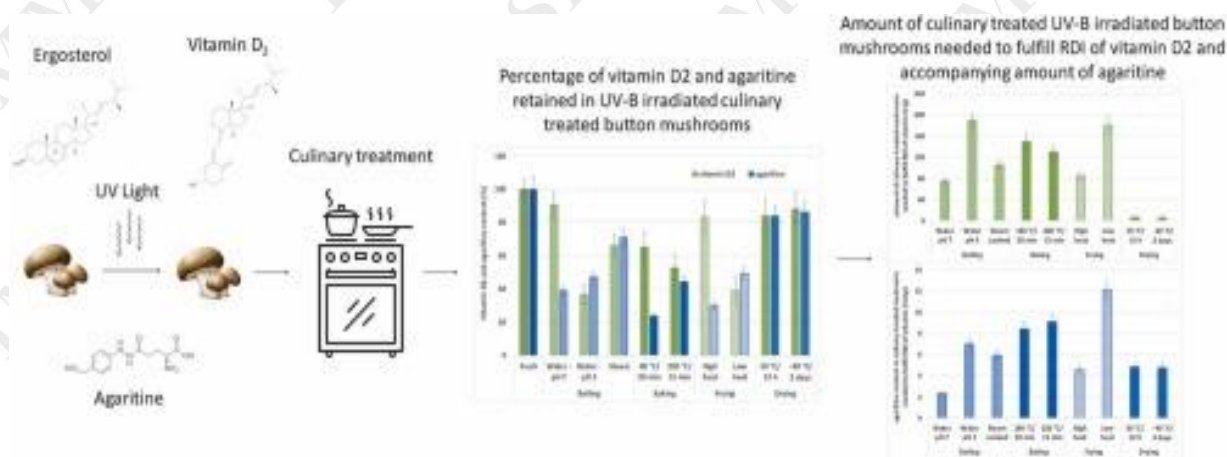
Influence of UV-B and culinary treatment on vitamin D2 and agaritine in button mushrooms

Lenka Libenská, Aliaksandra Kharoshka, Jana Pulkrabová, Věra Schulzová, Lucie Drábová ¹

University of Chemistry and Technology, Prague, Faculty of Food and Biochemical Technology, Department of Food Analysis and Nutrition, Technická 3, Prague 166 28, Czech Republic

Abstract: This study investigated the effects of different culinary treatments on the levels of vitamin D2 and agaritine in irradiated white button mushrooms. In addition, the intake of this vitamin via mushroom dishes was evaluated. In fresh irradiated white button mushrooms, the vitamin D2 content was $21.5 \pm 2.4 \mu\text{g}/100 \text{ g}$ fresh weight, 42 % of which was in the cap skin. The highest losses of vitamin D2 (63 %) were found in samples boiled in acidic water. In contrast, the lowest losses were found in samples boiled in non-acidified water. In the baking and frying experiments, vitamin D2 retention depended more on the cooking time than on the temperature. This resulted in high-heat frying being the second-best treatment for retaining vitamin D2 content in the samples. In the case of agaritine, no effect of UV treatment on its content was observed, and cooking treatment reduced its consumption. At the same time, the formation of toxic degradation products was not observed. The Recommended Daily Intake (RDI) of vitamin D can be achieved by consuming about 75–190 g of cooked, irradiated white button mushrooms, which can thus be an important dietary source of this vitamin.

Graphical Abstract



Journal of Food Composition and Analysis, Volume 137, Part A, January 2025, 106879

<https://doi.org/10.1016/j.jfca.2024.106879>

Health Risk Assessment for Ingestion of Edible Mushrooms Contaminated by Chromium

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^bCentro de Investigaciones Biológicas, Área Académica de Biología, Instituto de Ciencias Básicas e Ingenierías, Universidad Autónoma del Estado de Hidalgo, México

^cDepartamento de Botánica, Instituto de Biología, Universidad Nacional Autónoma de México, México

Abstract: A health risk assessment was carried out to determine the probability of damage and carcinogenic effects from consumption of five mushroom species (*Boletus edulis*, *Cantharellus cibarius*, *Lactarius indigo*, *Ramaria flava*, and *Sarcodon calvatus*) potentially contaminated by chromium (Cr), based on data reported by López-Vázquez and Prieto-García (2016) in Hidalgo state [López-Vázquez E, Prieto-García F. Minerals and toxic elements in wild mushrooms species from regions of Hidalgo state in Mexico. Asian J Chem. 2016;28(12):2725–30]. The evaluation was carried out based on an environmental risk indicator: potential ecological risk; and two health risk indicators: the hazard quotient, non-cancer damage and the risk of increase of individual cancer. The results showed that there is a high probability of carcinogenic damage for the three regions where older adults and pregnant are the most vulnerable sectors. Due to the traditional use of edible mushrooms in Mexico, the evidence of bioaccumulation of heavy metals of toxicological interest in mushroom species, as well as the notable damage to health due to the consumption of contaminated species; the monitoring and implementation of standards that regulate their consumption and ensuring their food safety is essential. More research is required to support the use of these evaluations.

Keywords: heavy metals, chromium, bioaccumulation, edible and medicinal mushrooms, health risk, Mexico

International Journal of Medicinal Mushrooms, Volume 27, Issue 1, 2025, pp. 41-49

DOI: 10.1615/IntJMedMushrooms.2024055570

Prevalence and characterization of *Listeria monocytogenes* isolated from online market-purchased enoki mushrooms (*Flammulina velutipes*) in the Republic of Korea

Sang-Woo Lee ^a, Sa-Rang Park ^a, Se-Gyeong Yoon ^a, Hyun-Dong Cho ^a, Mi-Kyung Lee ^a, Sun-Young Lee ^b, Jae-Hyun Yoon ^a

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^bDepartment of Food and Nutrition, Chung-Ang University, 4726 Seodong-dearo, Anseong-si, Gyeonggi-do, 17546, Republic of Korea

Abstract: The aim of this study was to characterize the microbiological quality of enoki mushrooms (*Flammulina velutipes*) commercially sold via online market retailers in the Republic of Korea and to identify the antibiotic susceptibility and genetic variability of *Listeria monocytogenes* isolates. A total of 100 enoki mushrooms were purchased online from 20 different sellers. As a result, 86–100% of the samples had a mean load of total aerobic bacteria (TAB), coliform, and yeast/mold (Y/M) which reached 5.32 ± 1.52 , 3.89 ± 1.85 , and 4.23 ± 1.14 log CFU/g, respectively. Seven samples positive for *L. monocytogenes* were detected among 100 online market-purchased enoki mushrooms, followed by the enrichment step of the isolates. Among the nine *L. monocytogenes* isolates, the highest proportion (67%; 6/9) was serogrouped as 12 a-3a. It also was found that six isolates (i.e. BMI₅₋₁, BMI₅₋₃, BMI₅₋₄, BMI₅₋₅, BMI_{B5-1}, and BMI_{B5-3}) were capable of amplifying *prfA*, *actA*, *hlyA*, *inlA*, and *inlC*. An antibiotic susceptibility test using the disc diffusion method revealed that all the *L. monocytogenes* isolates were susceptible to antibiotics (amoxycillin-clavulanic acid, gentamicin, and kanamycin) commonly used for the resolution of listeriosis infections, while being resistant to aztreonam and nalidixic acid.

Keywords: Antibiotic susceptibility, Enoki mushroom, *Listeria monocytogenes*, Serotyping

LWT, Volume 215, 1 January 2025, 117235

<https://doi.org/10.1016/j.lwt.2024.117235>

Single and Multi-Objective Optimization of the Red Pine Mushroom *Lactarius deliciosus* (Agaricomycetes) Extraction Conditions Using Artificial Intelligence Methods and Biological Activities of Optimized Extracts

Ayşenur Gürgen ^a, Mustafa Sevindik ^{a,b}

^aUniversity of Osmaniye Korkut Ata, Faculty of Engineering and Nature Sciences, Department of Industrial Engineering, Osmaniye, Türkiye

^bUniversity of Western Caspian, Department of Life Sciences, Baku, Azerbaijan

Abstract: In this study, the biological activities of *Lactarius deliciosus* were determined. Experimental studies were carried out using a soxhlet device, in the range of 40–70°C extraction temperature, 3–9 h extraction time and 0.5–2 mg/ml extraction conditions. A total of 64 different extracts were obtained using four different values of each variable and

the total antioxidant status (TAS) and total oxidant status (TOS) values of these extracts were determined. The obtained data were modeled using artificial neural networks (ANN). Both single-objective and multi-objective optimization processes were performed using the best ANN model selected among the established models. Single-objective optimization was performed with genetic algorithm (GA), and multi-objective optimization was performed using the Non-Dominated Sorting Genetic Algorithm (NSGA-II) algorithm. Extracts obtained from the extraction conditions suggested by the optimization algorithms were used for biological activities. As a result of the analyzes, TAS values of the single-objective optimization extract (1st) and multi-objective optimization extract (2nd) prepared under optimum conditions of the mushroom were determined as 7.468 ± 0.055 and 6.128 ± 0.049 mmol/L, TOS values were 13.161 ± 0.168 and 10.056 ± 0.106 $\mu\text{mol/L}$ and OSI values were 0.176 ± 0.003 and 0.164 ± 0.003 , respectively. It was found to be effective against bacterial and fungal strains at concentrations of 50–200 $\mu\text{g/mL}$. In addition, mushroom extracts were found to have strong cytotoxic effects against A549 cancer cell line. Acetylcholinesterase activity of the 1st and 2nd extracts of the mushroom were determined as 24.80 ± 0.82 and 32.71 ± 0.91 $\mu\text{g/mL}$, butyrylcholinesterase activity was determined as 51.24 ± 0.80 and 57.10 ± 0.51 $\mu\text{g/mL}$, respectively. In our study, it was determined that *L. deliciosus* extracts obtained under optimum conditions had strong biological activities.

Keywords: antimicrobial, anticancer, antioxidant, *Lactarius deliciosus*, optimization, red pine mushroom, medicinal mushrooms

International Journal of Medicinal Mushrooms, Volume 27, Issue 2, 2025, pp. 59-73

DOI: 10.1615/IntJMedMushrooms.2024057054

International Journal of Medicinal Mushrooms Call for Papers

We would like to invite you to submit an article to the International Journal of Medicinal Mushrooms (IJM), published by Begell House Publishers. As a leader in this field, we feel you would be an excellent fit as a contributor to this journal.

IJM is a monthly peer-reviewed journal that was launched in 1999 and is indexed in major databases, including PubMed, EBSCO, Scopus, Science Citation Index Expanded (also known as Sci-Search®), BIOSIS Database, Current Contents®/ Agriculture, Biology, and Environmental Sciences, INSPEC, Embase, Current Awareness in Biological Sciences (CABS), and Chemical Abstracts, (CAS). The journal has a five-year impact factor of 1.4 and an H-index of 37.

The mission of IJM is to be a source of information that draws together all aspects of the exciting and expanding field of medicinal mushrooms - a source that will keep you up to date with the latest issues and practice.

The journal publishes original research articles and critical reviews on a broad range of subjects pertaining to medicinal mushrooms, including systematics, nomenclature, taxonomy, morphology, medicinal value, biotechnology, and much more. Papers on new techniques that might promote experimental progress in the aforementioned field are also welcomed. In addition to full-length reports of original research, the journal publishes short communications and interesting case reports, together with literature reviews.

More information about the journal can be found at <https://www.begellhouse.com/journals/medicinal-mushrooms.html>

If you would like to contribute, please submit your paper to Editor-in-Chief Solomon P. Wasser at spwasser@research.haifa.ac.il. Please feel free to contact me at spwasser@research.haifa.ac.il if you have any questions or need any assistance, or reach out to Begell House Publishers at journals@begellhouse.com.

Sincerely,

Solomon P. Wasser

Editor-in-Chief, International Journal of Medicinal Mushrooms

International Centre for Biotechnology and Biodiversity of Fungi

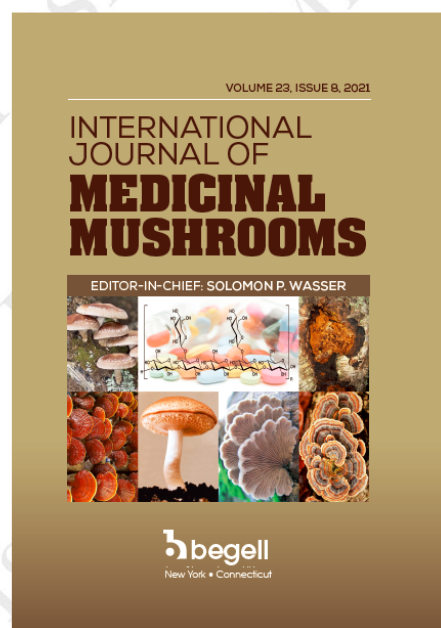
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For More Information and Submission

<https://www.begellhouse.com/journals/medicinal-mushrooms.html>



International Journal of Medicinal Mushrooms

2025, Vol. 27, Issue no.1

THE GIANT POLYPORE MUSHROOM *MERIPILUS GIGANTEUS* (AGARICOMYCETES): PROMISING MEDICINAL APPLICATIONS (A REVIEW)

Katarzyna Sulkowska-Ziaja, Mateusz Korczyński, Monika Trepka, Katarzyna Kala, Bożena Muszyńska

OPTIMIZATION OF SUBMERGED FERMENTATION CONDITIONS FOR POLYSACCHARIDE PRODUCTION IN SPECIES OF THE GENUS *GANODERMA* (AGARICOMYCETES) AND COMPARATIVE ANALYSIS OF THE ANTIOXIDANT ACTIVITIES OF DIFFERENT STRAINS

Shanshan Luo, Yilin Luo, Yi Yuan, Jiliang Zhou, Wei Huang, Xiaomin Wu, Tian-Xu Cao, Ping Du

QUANTITATIVE LC-QTOF-MS ANALYSIS OF MYCOCHEMICALS IN *AMANITA MUSCARIA*, *PSILOCYBE* SPP. (AGARICOMYCETES), AND CONSUMER PRODUCTS

Kumar Katragunta, Bharathi Avula, Amar G. Chittiboyina, Hemant Lata, Ikhlas A. Khan

HEALTH RISK ASSESSMENT FOR INGESTION OF EDIBLE MUSHROOMS CONTAMINATED BY CHROMIUM

Sharon Alethia de Lucio-Flores, Juan Carlos Gaytan-Oyarzun, Roberto Garibay-Orijel, Griselda Pulido-Flores

METHANOLIC EXTRACT OF *MORCHELLA ESCULENTA* (ASCOMYCOTA) PREVENTS CHEMOTHERAPY-RELATED CARDIOTOXICITY IN TUMOR-BEARING MICE

Sneha Das, Anit Mathew, Kainoor Krishnankutty Janardhanan

PREPARATION AND CHARACTERIZATION OF A NOVEL MAGNETIC MOLECULARLY IMPRINTED POLYMER CAPABLE OF ISOLATING AND PURIFYING CORDYCEPIN FROM A SUBMERGED CULTURE OF THE CATERPILLAR MEDICINAL MUSHROOM *CORDYCEPS MILITARIS* (ASCOMYCETES)

Yitong Qi, Jiahao Luo, Liying Zhang, Chuanjian Fang, Xiuyun Zhang, Chunchao Han

ANTIFUNGAL PROPERTIES OF *POLYCEPHALOMYCES NIPPONICUS* (ASCOMYCETES) AGAINST *CANDIDA ALBICANS*: POTENTIAL FOR NOVEL THERAPEUTIC DEVELOPMENT

Sutthiwan Thammawat, Winita Fowsantear, Kusavadee Sangdee, Aphidech Sangdee

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Points and Reviews

Exploring the Potential of Medicinal Mushroom β -Glucans as a Natural Frontier in

Prostate Cancer Treatment

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ABSTRACT: The global increase in cancer cases, particularly prostate cancer, poses a significant health challenge worldwide. Conventional treatments such as surgery, radiation therapy, hormone therapy, chemotherapy, and immunotherapy offer valuable options but are associated with limitations and potential side effects. As a result, there is growing interest in complementary therapies, including natural compounds such as β -glucans, derived from sources such as yeast and mushrooms. In this review, we explored the potential therapeutic role of medicinal mushrooms β -glucan in prostate cancer treatment. β -glucans has demonstrated anti-cancer properties in preclinical studies, including inhibition of proliferation, induction of apoptosis, and modulation of immune responses. Studies in prostate cancer cell lines and animal models have shown promising results, with β -glucan inhibiting tumor growth, inducing DNA damage, and regulating tumor markers such as p53 and prostate specific antigen. β -glucans acts through various pathways, including stimulation of dendritic cells, modulation of cytokine secretion, suppression of myeloid-derived suppressor cells, and enhancement of immune responses. Moreover, β -glucans exhibits anti-androgenic and immune-modulatory effects, making it a promising candidate for prostate cancer treatment. In this study, we also focused on the mechanism of action of β -glucans through various pathways including tumor cell death by oxidative stress created through ROS generation and autophagy. Although preclinical studies support the potential therapeutic efficacy of medicinal mushrooms β -glucans, further research is needed to elucidate its clinical utility and safety in human trials.

KEY WORDS: immuno-modulatory, prostate cancer, complementary therapy, β -glucans, active surveillance, medicinal mushrooms

ABBREVIATIONS: CTL, cytotoxic T lymphocyte; MAPKs, mitogen-activated protein kinases; NF-KB, nuclear factor kappa B; NO, nitric oxide; PAMPs, pathogen associated molecular patterns; ROS, reactive oxygen species; WHO, World Health

I. INTRODUCTION

Cancer is the leading cause of death worldwide. A study showed the prediction of World Health Organization (WHO) forecasting a significant increase in cancer cases globally by 2050, with over 35 million new cases expected a 77% rise from 2022 levels.¹ Prostate cancer stands as one of the most prevalent malignancies affecting men worldwide, with significant implications for public health and healthcare systems globally. According to the latest data from the World Health Organization (WHO), prostate cancer ranks as the second most frequently diagnosed cancer and the fifth leading cause of cancer-related deaths among men worldwide.² Although it predominantly affects older men, recent epidemiological shifts have unveiled concerning trends of diagnosis among younger populations. This emerging pattern prompts critical inquiries into potential early-life risk factors and genetic susceptibilities that might contribute to the disease's onset at an earlier age.³ As the disease advances, symptoms such as urinary difficulties (such as frequent or painful urination), blood in the urine, erectile dysfunction, and localized discomfort or pain in the pelvic area or lower back may manifest.⁴ There are many anticancer drugs available in the markets for the treatment of cancer, but most of these have many complications and side effects in various types of cancer, as well as these, are not target-specific so there is the need to develop novel therapeutics for cancer. The development of new drugs should be target-specific, less toxic, and effective so that we can develop more efficient therapies with minimal side effects. For the development of these therapies, there are a variety of natural sources available that have novel bioactive components that elicit anticancer properties. The anti-cancer potential of medicinal mushrooms β -glucans can be triggered by the immune-stimulatory activity⁵ by control of cancerous cell proliferation and survival.⁶ β -glucan works as an adjuvant for conventional cancer treatment practices and promotes the immune effector cells by working as pathogen-associated molecular patterns (PAMPs). Moreover, it is observed that a combination of yeast-derived soluble β -glucan and lipopolysaccharide could enhance the IL-10, IL-8, TNF- α , and tissue factor concentration.⁷ In an *in vitro* study on *Hericium erinaceus*, mushroom β -glucan showed the induction of apoptosis in prostate cancer cells by modulating oxidative stress.⁸ In a study, it was found that β -glucan has a supplementary role in the oncology vaccine, which shows both a potent cytotoxic T lymphocyte (CTL) response and humoral response. Additionally, the combination therapy of β -glucan may enhance natural immunity against adaptive anti-tumor immunity. Treatment with β -glucan may therefore provide a more effective means of developing long-term tumor-specific T-cell immunity by targeting both granulocytes and CTLs to eliminate tumors and prevent tumor recurrence.⁹ Lentinan β -glucan (LNT) (a B1,3-glucan) isolated from *Lentinus edodes* is a form of β -glucan that contains two branches of B1,6 glucose and is the first medicinal mushroom to enter the field of modern biotechnology. Due to its unique triple helix conformation, LNT appears to exert a significant antitumor effect.¹⁰ Compared with chemotherapy alone, lentinan chemo-immunotherapy can prolong the survival time of patients with advanced gastric cancer.¹¹

Complementary therapies for prostate cancer are increasingly sought after due to the limitations and side effects associated with conventional treatments. Because resistance to standard therapies can develop over time, there is a growing need to explore alternative approaches that target resistant cancer cells and improve treatment outcomes. Natural and complementary therapies provide additional options for patients seeking a holistic approach to their care, though further research is required to evaluate their efficacy and safety. The quest for alternative therapies in prostate

cancer treatment reflects a desire to improve outcomes, minimize side effects, and enhance the quality of life for affected individuals. Natural sources have garnered attention for their potential efficacy in prostate cancer treatment, offering complementary options to conventional therapies.¹² Several compounds found in fruits, vegetables, and herbs have shown promise in inhibiting cancer growth and promoting overall health. β -glucan, polysaccharides found in the cell walls of many fungi, have demonstrated anti-cancer properties by modulating the immune system and reducing inflammation. Studies suggest that β -glucan may help inhibit the progression of prostate cancer by enhancing immune responses and suppressing tumor growth.¹³ Although natural sources such as β -glucan show promise in preclinical studies, more research is needed to elucidate their efficacy and safety in human trials. Integrating these compounds into a balanced diet and lifestyle may offer potential benefits in prostate cancer prevention and treatment.

II. β -GLUCAN STRUCTURE AND PROPERTIES

TABLE 1: β -glucan sources and bioactive compounds and their effect on a variety of prostate cancer cell

Source	Bioactive compound	Target cells	Mode of action	Refs.
<i>Agaricus blazei</i>	Blazeispirols	Prostate cancer	Inhibited cell proliferation in both androgen-dependent and androgen-independent prostate cancer cells. It induced significant lactate dehydrogenase leakage, increased caspase 3 activity, and promoted DNA fragmentation, particularly in aggressive androgen-independent PC3 cells.	14
<i>Grifola frondosa</i>	Carmustine (BCNU), Grifron-D	Prostate cancer	BCNU exert cytotoxicity by alkylation of nitrogenous bases of DNA in combination with β -glucan of maitake.	15
		Prostate cancer	Grifron-D exhibited <i>in vitro</i> anti-tumor and immune-modulatory activities against prostate cancer cells.	16
<i>Ganoderma lucidum</i>	β -glucan Polysaccharide	Prostate cancer	Boosted the effectiveness of docetaxel and flutamide, making prostate cancer cells more responsive to these treatments.	17
		Prostate cancer	Inhibited cell growth, the cell cycle, and cell migration in prostate cancer, potentially through the PRMT6 signaling pathway suggesting that it could act as a tumor suppressor and may have therapeutic potential in prostate cancer treatment.	18
		Prostate cancer	Induces cytotoxicity, ROS accumulation, and apoptosis in PC-3 prostate cancer cells by inhibiting STAT-3 translocation, reducing BCL-2 and cyclin-D1 expression, and increasing Bax, caspase-3, and caspase-9 levels.	19
<i>Dictyophora indusiata</i>	β -glucan	Colony stimulating factor	β -glucan polysaccharide show enhancement in mitogenic and colony stimulating factor.	20
<i>Inonotus obliquus</i>	β -glucan	Prostate cancer	Reduced macrophage cells activity and showed efficient cytotoxic activity <i>in vitro</i> for the treatment of prostate cancer.	21
<i>Agaricus brazei</i>	β -glucans	Human peripheral lymphocytes	DNA damage protective effect induced by H_2O_2 and trp-p-2 has been shown in dose dependent manner.	22
<i>Schizophyllum commune</i>	Schizophyllan, Sizofiran	Prostate cancer	Inhibited the growth of the human prostate cancer cells DU145 and prostate carcinoma epithelial cell line (22RV1).	23
	Carboxymethylated curdlan	Cancer cells	Carboxymethylated curdlan have its role in cancer therapy as an important carrier for epirubicin which is a drug used in chemotherapy for cancer treatment.	24

TABLE 1: (continued)

<i>Lentinus lepideus</i>	PG101	Prostate cancer	Apoptosis was induced in prostate cancer cells via caspase activation and, in a xenograft assay, it effectively reduces the viability of tumors formed by DU145 and PC3 cells in mice.	25
<i>Hericium erinaceus</i>	Polysaccharide	Prostate cancer	Significant anti-proliferative activity on prostate cancer cell lines, particularly LNCaP and PC3, with an IC ₅₀ of 0.61 mg/mL in LNCaP cells was reported.	26
	β -glucan	Lymphocytes	β -glucan from <i>Hericium erinaceus</i> showed lymphocyte proliferation and it upregulated many inflammatory cytokines.	27
<i>Lentinus edodes</i>	Lentinan	Myeloid cells	Lentinan binds to receptor present on myeloid cells and induces PI3K, MAPk, Akt pathways.	28
	β -D-glucans	Prostate cancer	<i>Lentinus edodes</i> derived β -D-glucans demonstrated efficient anticancer activity against prostate cancer cells DU145.	29
	1,3 1,6 β -glucans	Prostate cancer	Prostate cancer patients maintained stable prostate-specific antigen (PSA) levels.	30
<i>Astraeus hygrometricus</i>	β -glucans	Macrophages and NK cells	β -glucans increase production of NO and interleukins from macrophages as well as enhanced phagocytosis and NK cell activation.	31
<i>Grifola frondosa</i>	β -glucan	Prostate cancer	β -glucan derived from <i>Grifola frondosa</i> reported to induce cell death in the <i>in vitro</i> prostate cancer cells PC3.	32
<i>Agaricus bisporus</i>	β -1,3-1,6-glucan	Immune cells	Help in the reduction of prostate cancer by decreasing the immunosuppressive factors present in immune cells.	33

Polysaccharides are a digestible and indispensable component present in a variety of foods that provide essential calories and glucose necessary for regular bodily functions along with various health benefits. One extensively studied and well-documented bioactive polysaccharide is β -glucan having monomer units linked through glycosidic bonds at B (1 \rightarrow 3), (1 \rightarrow 4), and/or (1 \rightarrow 6) positions, forming either branched or unbranched structures.³⁴ β -glucan is recognized as a bioactive functional food component due to its various biological effects, including its ability to lower cholesterol, regulate blood sugar, modulate the immune system, demonstrate anti-tumor properties, act as an antioxidant, and reduce inflammation.³⁵ β -glucan are biologically active components found in various sources such as bacteria, oats, yeast, algae, and barley and due to their great structural variation, they are supposed to have a higher biological information for various complicated and important signaling pathways as shown in Table 1.³⁶ β -glucan whether ingested through food or supplements, bypasses gastric digestion, reaches the small intestine, gets absorbed by the intestinal epithelium or macrophages, and interacts with immune cells in the Peyer's patches and distal lymphoid organs. Specific receptors such as Toll-like receptors (TLRs) and C-type lectin-like receptors, notably dectin-1, primarily found on monocyte/macrophages, neutrophils, dendritic cells, and natural killer cells initiate intracellular signaling, activating the NF- κ B resulting in the production of cytokines, nitric oxide (NO), and reactive oxygen species (ROS).³⁷

β -glucan found in grains is not digested in the stomach or intestines after consumption and has a strong ability to bind water, forming sticky gels in the gastrointestinal tract. This process slows down the emptying of the stomach, which in turn delays the breakdown of starch by enzymes and hampers the absorption of digestible carbohydrates in the intestines. As a result, there is a reduction in post-meal glucose levels in the blood and a decrease in insulin secretion. This mechanism potentially contributes to a lower incidence of type II diabetes.³⁸ Soluble β -

glucan after being recognized by cell surface receptors activates the signal cascade transmission that leads to heightened phagocytosis, faster antigen presentation, increased production of reactive oxygen species (ROS), and secretion of cytokines or chemokines by immune cells. This dual activation of both innate and adaptive immune responses serves to positively stimulate the immune system thereby maintaining a balanced immune environment within tumors, enhancing the immune system's ability to reject tumors, and ultimately exhibiting anti-tumor activity.³⁹ β -glucan are also considered as “biological response modifiers” because of their immuno-modulatory, healing, antiviral, antibacterial, anticoagulant, and antitumor activities as shown in Fig. 1.⁴⁰ In addition, β -D-glucan is also a modulator of NK cytotoxicity and can stimulate the activation of tumor cells by NK cells through the production and release of pro-inflammatory cytokines and complement activation.⁴¹

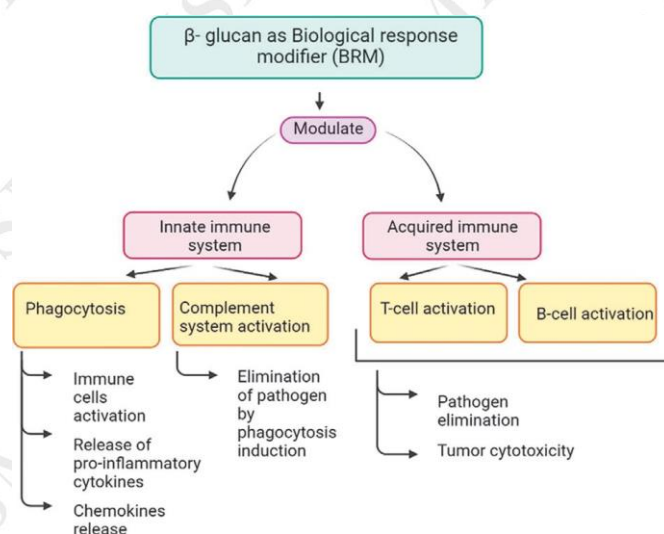


FIG. 1: Potential of β -glucans as biological response modifiers (BRMs) through the modulation of innate and acquired immune systems

III. β -GLUCANS FOR THE TREATMENT OF PROSTATE CANCER

β -glucans has emerged as a potential therapeutic agent in prostate cancer treatment. β -glucans derived from a variety of mushrooms is a glucose polymer and is considered a biological response modifier with proven effects on adaptive and innate immune systems. Carboxymethyl-glucan is a soluble form of β -glucan having a variety of effects for the treatment of cancer.⁴² *In vitro* studies using prostate cancer cell lines have demonstrated the anti-proliferative, anti-metastatic, and immune-stimulatory effects of β -glucan, including induction of apoptosis, inhibition of proliferation, and enhancement of immune cell activity. Furthermore, β -glucan derived from mushrooms has also been found to suppress myeloid-derived suppressor cells. These cells increase during tumor development and are responsible for the formation of tumor microenvironment to promote tumorigenesis and their suppression leads to increased immunity against the development of tumor. β -glucan derived from white button mushrooms was also found anti-androgenic and immune-modulatory potential.⁴³ Moreover, in a study, prostate cancer cells LNCaP were co-cultured with dendritic cells and glucan for the evaluation of cytokine release, maturation marker expression, and superoxide production. The findings showed that LNCaP cells were able to secrete IL-12 along with partial maturation of dendritic cells. Glucan was found to increase the secretion of IL-12 in the co-cultured LNCaP and dendritic cells however, superoxide production in glucan stimulated

dendritic cells was decreased. Glucan-treated co-cultured LNcaP and dendritic cells were also found to activate the production of IFN- γ by natural killer cells and the generation of helper T-cells from CD4+ lymphocytes.⁴⁴ Some of the *in vitro* and *in vivo* studies are discussed here that are showing that β -glucan have a significant potential for the treatment of prostate cancer.

A. *In Vitro* Studies

In a study, β -glucan derived from *Agaricus blazei* was able to inhibit cell proliferation in both androgen-dependent and androgen-independent prostate cancer. Its oral administration was found to inhibit tumor growth in the mice in which the tumor was developed by the injection of PC3 cells.⁴⁵ Benign prostatic hyperplasia is an atypical cause of mortality in men in their 50s. *Antrodia cinnamomea* is a source of β -glucan named antrodan that works by collagen deposition and alleviating the prostatic epithelial hyperplasia thereby resulting in increased cholesterol biosynthesis and suppression of low-density lipids. This leads to the suppression of benign prostatic hyperplasia.⁴⁶ A study investigated the efficacy of carboxymethyl-glucan, in protecting against DNA damage in advanced prostate cancer (PCa) patients undergoing androgen deprivation therapy. There was a significant reduction in DNA damage post-treatment, ranging from 18% to 87%, with an average of 59%.⁴⁷

β -glucans also modulate immune cell response by regulation of cytokine secretion. One *in vitro* study reported that β -glucan derived from *Grifola frondosa* has the potential to induce apoptosis in prostate cancer cells by altering oxidative stress.⁴⁸ One more *in vitro* study for the treatment of hormone-refractory prostate cancer through β -glucan reported that β -glucan effectively induces apoptosis through various signaling pathways by caspase-3 activation and modulating Bcl-2. This study also showed that vitamin C and carmustine enhance the cytotoxic effect of β -glucan for prostate cancer cells *in vitro*.⁴⁹ Another *in vitro* study used the β -glucan as a carrier molecule for the loading of quercetin for the treatment of prostate cancer. The study found that β -glucan enhanced the potential of quercetin by slowing down its release from β -glucan thereby inhibiting the growth of the prostate cancer cell line PC3.⁵⁰

Moreover, a study reported that *in vitro* β -glucan treatment have the potential to trigger the trained immunity in peripheral blood monocytes that were received from the prostate cancer patients those previously didn't receive any treatment.⁵¹ One more study reported that lentinan, β -glucan derived from *Lentinus edodes* inhibited the growth of prostate cancer cells DU145 up to 42%.⁵² Another study focused on effect of β -glucan and quercetin loaded β -glucan derived from *Agaricus bisporus* showed that β -glucan have efficient anticancer activity against prostate cancer cell line PC3 and it works as a good carrier molecule for the quercetin to target prostate cancer more effectively.⁵⁰

B. *In Vivo* Studies

A study explored the direct effects of *Agaricus blazei* on human prostate cancer, both *in vitro* and *in vivo*. It demonstrated inhibitory effects on cell proliferation in androgen-dependent and androgen-independent prostate cancer cell lines. It also induced lactate dehydrogenase leakage and enhanced caspase 3 activity and DNA fragmentation, particularly in androgen-independent PC3 cells, and significantly suppressed tumor growth in severe combined immune-deficient mice with PC3 tumor xenografts.⁵³ Research investigated the tumor-regulating effects of β -D-glucan on tumor markers p53 and prostate-specific antigen in a nitroso is amine-induced prostate tumor model in Wistar rats. Administration of β -D-glucan at varying doses led to significant down-regulation of p53 and PSA levels, along with a reversal of histological distortions, in a dose-dependent manner.⁵⁴ A study found that β -glucan-enriched

with *A. blazei* broth induced apoptosis and anti-angiogenesis in a mouse model of prostate cancer.⁵⁵ A study used C57BL/6 mice were treated with white button mushroom β -glucan in prostate cancer model. It was found to lower the dihydrotestosterone induced activation of androgen receptor and prostate specific antigen expression by disrupting the expression of transmembrane protease serine 2.⁵⁶

IV. WORKING MECHANISM AND MODE OF ACTION OF β -GLUCANS

β -glucans exert their anticancer effects through multiple mechanisms, primarily by modulating the innate and adaptive immune responses. These polysaccharides are recognized as PAMPs by pattern recognition receptors (PRRs) on immune cells.⁵⁷ β -glucan binds to the dectin-1, complement receptor 3 (CR3), CD11b/ CD18 to show its effect. Dectin-1 is a trans-membrane receptor present on many macrophages and dendritic cells and responsible for β -glucan recognition on macrophages, dendritic cells, and neutrophils. When β -glucan binds to the dectin-1 receptor, it activates downstream signaling pathways, including the spleen tyrosine kinase (Syk) pathway, leading to the activation of nuclear factor kappa B (NF- κ B) and mitogen-activated protein kinases (MAPKs) as shown in Fig. 2. This activation enhances phagocytosis, antigen presentation, and cytokine production by macrophages and dendritic cells, thereby promoting T-cell activation and differentiation.⁵⁸ Activated receptor works as antigen-presenting cells (APC) and activates CD4 + and CD8 + T cells to produce pro-inflammatory cytokines such as tumor necrosis factor (TNF) α , anti-tumor cytokine interferon γ (IFN γ), granzyme B and perforin, leading to tumoricidal activity.³⁰ Activated dectin-1 further leads to the conversion of normal immunosuppressive M2 macrophages into M1 macrophages. This switching leads to the activation of M1 macrophages resulting in the activation of Th-1 type T-cells. Th1 T-cells have activated macrophages and lead to various activities such as pro-inflammatory cytokine production, ROS generation, and induction of apoptosis.⁵⁹

Moreover, β -glucans promote the activation and cytotoxicity of NK cells, which play a crucial role in immune surveillance against cancer cells. NK cells recognize and eliminate cancerous cells through various mechanisms, including the release of cytotoxic granules containing perforin and granzymes, as well as the engagement of death receptors such as Fas ligand (FasL) and tumor necrosis factor-related apoptosis-inducing ligand (TRAIL). Additionally, β -glucans can enhance the production of pro-inflammatory cytokines, such as interleukin-1 β (IL-1 β), interleukin-6 (IL-6), TNF- α , and interferon-gamma (IFN- γ), which promote antitumor immune responses and inhibit tumor proliferation.⁶⁰

β -glucans exhibit their anticancer effects through various molecular pathways, including the activation of apoptosis and cell cycle arrest mechanisms. Upon β -glucan stimulation, various intracellular signaling pathways are triggered, such as the p38 MAPK and JNK pathways, leading to the activation of pro-apoptotic factors such as Bax and Bak, and the inhibition of anti-apoptotic proteins such as Bcl-2 and Bcl-xL.⁶¹ This results in the release of cytochrome c from mitochondria, subsequent activation of caspase-9 and caspase-3, and ultimately results in the induction of apoptosis in cancer cells. Furthermore, β -glucans induce cell cycle arrest by targeting key regulators of cell cycle progression. For instance, β -glucans can upregulate cyclin-dependent kinase inhibitors (CDKIs) such as p21 and p27, leading to the inhibition of cyclin-CDK complexes essential for cell cycle progression.⁶² Additionally, β -glucans may downregulate the expression of cyclins such as cyclin D1 and cyclin E, further inhibiting cell cycle progression at specific checkpoints. This modulation of cell cycle regulators by β -glucans effectively halts the proliferation of cancer cells, promoting their elimination.⁶³ β -glucans also possess direct cytotoxic effects on cancer cells by inducing apoptosis, cell cycle arrest, and autophagy as shown in Fig. 3. They can also inhibit tumor angiogenesis by suppressing the secretion of pro-angiogenic

factors and disrupting endothelial cell function.

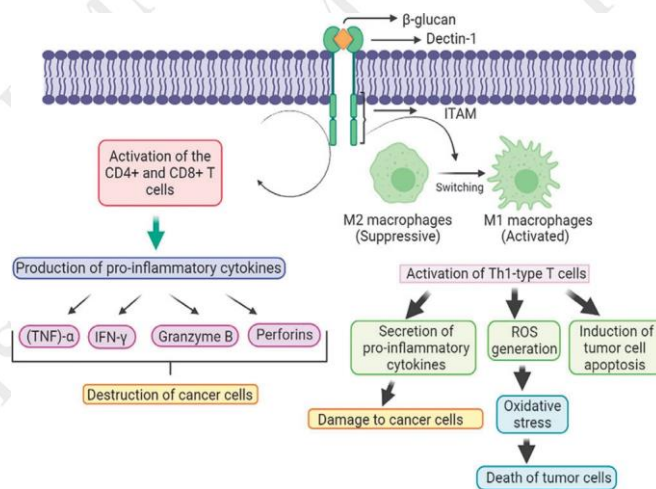


FIG. 2: Working mechanisms of dectin-1 receptor after binding with β -glucan. It can activate the pathways responsible for production of pro-inflammatory cytokines or leads to the activation of helper T-cells. Both pathways can ultimately lead to tumor cell death.

A study reported that orally administered β -glucan has the potential to directly interact with mucosa followed by uptake by M cells. This uptake results in the interaction with dendritic cells and macrophages being circulated in the body.⁵¹ Moreover, in prostate cancer, β -glucan binds dectin-1 receptor leading to the stimulation of dendritic cells. This stimulation results in secretion of a variety of interleukins including IL1, IL6 and IL23 along with T-cell differentiation.⁶⁴ Another study reported that β -glucan bind to the antigen presenting cells and activate these cells to migrate lymph nodes and bone marrow where they degrade, and their degradation product binds to the neutrophils or complement receptor 3 in bone marrow. This binding results in activation of the neutrophils or complement receptor 3. On the other hand, activated antigen presenting cells produce pro-inflammatory cytokines thereby induce lymphocytes.⁶⁵ To exert their effects on prostate cancer, β -glucan stimulates dendritic cells through the dectin-1 resulting in the secretion of a variety of interleukins including IL1 and IL6 leading to the differentiation of CD4+ cells into T helper cells. This study found that dendritic cells stimulated by β -glucan can prime T-lymphocytes to activate B-cells resulting in IgG and IgA antibody secretion.

V. CONCLUSIONS

The exploration of β -glucans as a potential therapeutic agent in prostate cancer treatment represents a promising avenue for future research and clinical applications. This review highlights the mechanisms through which β -glucan exerts its anti-cancer effects, including immune modulation, tumor inhibition, and modulation of tumor markers. Various studies have shown encouraging results, demonstrating the ability of β -glucans to inhibit tumor growth and induce apoptosis in prostate cancer cells. The holistic approach offered by β -glucan complements conventional treatment modalities and may help mitigate the limitations and side effects associated with standard therapies. However, further research is needed to fully explore the clinical efficacy and safety of β -glucans in human trials. Integration of β -glucans into prostate cancer treatment holds the potential to improve patient outcomes and enhance the quality of life for

affected individuals. Overall, β -glucans represents a natural frontier in prostate cancer therapy, offering a promising avenue for the development of novel treatment strategies that couple the power of nature to combat prostate cancer.

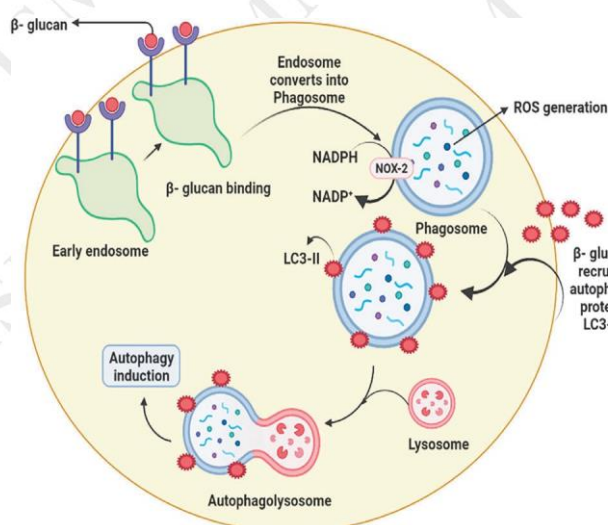


FIG. 3: Binding of β -glucan to the receptors present on endosome converts it into phagosome. NADPH converted into NADP^+ with the help of enzyme NADPH oxidase present on phagosomal membrane which in turn results in free radical production in phagosome leading to recruitment of autophagy complex. β -glucan binding recruits autophagy protein LC3-II on the surface of phagosome. This phagosome fuses with lysosome leading to the formation of autophagolysosome, resulting in autophagy induction.

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Call for Papers

Aiming to build the relationship between the members and the Society, the publication of the newsletters was proposed before the launching of the Society. The newsletters represent one of the key official publications from the Society. Contents of the newsletters will include notifications of the decisions made by the committee board, reviews or comments contributed by ISMM committee members, conferences or activities to be organized, and the status updated in research, industrialization, and marketing for medicinal mushrooms. The newsletters will be released quarterly, by the first Monday of every January, April, July, and October, with possible supplementary issues as well. The Newsletter is open to organizations or professionals to submit news, comments, or scientific papers relating to medicinal mushroom research, marketing, or industry.

Contact information

For any inquiry in membership enrollment, subscribing to ISMM newsletters, upcoming activities and events organized by ISMM, or submitting news reports, statements, or manuscripts to the Society, please contact the secretariat's office in Beijing, China.

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