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.

Honorable President: Prof. S.T.Chang, Prof.S.P. Wasser
President: Academician Li Yu
Executive President: Mr. Chen Hui
Secretary General: Mr. Liu Ziqiang

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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NEWSLETTER OF THE INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

Volume 1, Issue 17

Date-released: July 5, 2021

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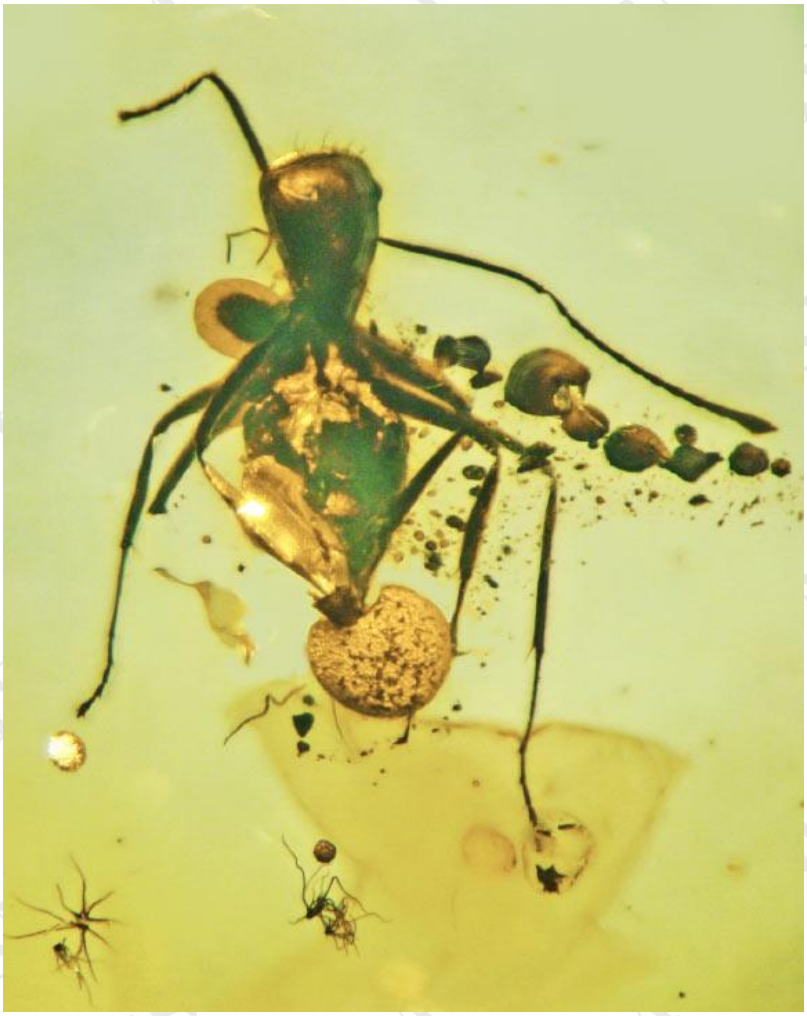
News Reports

Ancient Fungal Parasite of Ants Found Preserved in Baltic Amber

In a paper published this month in the journal *Fungal Biology*, a duo of paleontologists from the United States and France described a new genus and species of ancient parasitic fungus found in a piece of 50-million-year-old amber from Europe's Baltic region.



Allocordyceps baltica is coming out of the ant's rectum, and vegetative part of the fungus is emerging from its abdomen and neck. Image credit: George Poinar Jr., Oregon State University.

The newly-described species, named *Allocordyceps baltica*, is the oldest known fossil fungus of an ant.

"It's a mushroom growing out of a carpenter ant (tribe Camponotini)," said Professor George Poinar Jr., a researcher in the Department of Integrative Biology at Oregon State University.

“Ants are hosts to a number of intriguing parasites, some of which modify the insects’ behavior to benefit the parasites’ development and dispersion.”

“Carpenter ants seem especially susceptible to fungal pathogens of the genus *Ophiocordyceps*, including one species that compels infected ants to bite into various erect plant parts just before they die.”

Doing so puts the ants in a favorable position for allowing fungal spores to be released from cup-shaped ascomata — the fungi’s fruiting body — protruding from the ants’ head and neck. Carpenter ants usually make their nests in trees, rotting logs and stumps.

Allocordyceps baltica belongs to the fungi order Hypocreales and shares certain features with *Ophiocordyceps*, but also displays several developmental stages not previously reported.

“We can see a large, orange, cup-shaped ascoma with developing perithecia — flask-shaped structures that let the spores out — emerging from rectum of the ant,” Professor Poinar said.

“The vegetative part of the fungus is coming out of the abdomen and the base of the neck.”

“We see freestanding fungal bodies also bearing what look like perithecia, and in addition we see what look like the sacs where spores develop.”

“All of the stages, those attached to the ant and the freestanding ones, are of the same species.”

Allocordyceps baltica could not be placed in the *Ophiocordyceps* genus because ascomata in those fungi usually come out the neck or head of an ant and not the rectum.

“There is no doubt that *Allocordyceps baltica* represents a fungal infection of a carpenter ant,” Professor Poinar said.

“This is the first fossil record of a member of the Hypocreales order emerging from the body of an ant.”

“And as the earliest fossil record of fungal parasitism of ants, it can be used in future studies as a reference point regarding the origin of the fungus-ant association.”

Journal Reference:

George Poinar & Yves-MarieMaltier. *Allocordyceps baltica* gen. et sp. nov. (Hypocreales: Clavicipitaceae), an ancient fungal parasite of an ant in Baltic amber. *Fungal Biology*, published online June 5, 2021; doi: 10.1016/j.funbio.2021.06.002

Source: Sci-News.com

Study Finds Eating Two Mushrooms a Day could Lower Cancer Risk by 45 Percent

By Lily Canter

- Mushrooms contain high levels of antioxidants, and chemical components believed to strengthen the immune system. A study touts their anti-cancer properties
- Reviewing the study findings, scientists caution against the idea of 'miracle foods' and suggest mushrooms can be a component of a diet that lowers cancer risks

Eating 18 grams of mushrooms a day could lower the risk of cancer, a new study suggests.

Individuals who eat two medium-sized mushrooms daily have a 45 per cent lower risk of cancer compared to those who do not eat mushrooms, according to Pennsylvania State University research, published in Advances in Nutrition.

For centuries, Chinese medicine practitioners have used mushrooms, which are rich in vitamins, nutrients and antioxidants, as a treatment for illness including lung disease.

Some of the chemical compounds in mushrooms are believed to strengthen the immune system.

The Penn research examined 17 cancer studies from 1966 to 2020, analysing more than 19,500 cancer patients.

The team's findings showed that even though shiitake, oyster, maitake and king oyster mushrooms have higher amounts of the amino acid ergothioneine than white button, cremini and portobello mushrooms, people who incorporated any variety of mushrooms into their daily diets had a lower risk of cancer.

"Mushrooms are the highest dietary source of ergothioneine, which is a unique and potent antioxidant and cellular protector," said Djibril Ba, a graduate student in epidemiology at Penn State College of Medicine.

"Replenishing antioxidants in the body may help protect against oxidative stress and lower the risk of cancer."

"Mushrooms are the highest dietary source of ergothioneine, which is a unique and potent antioxidant and cellular protector," said Djibril Ba, a graduate student in epidemiology at Penn State College of Medicine.

"Replenishing antioxidants in the body may help protect against oxidative stress and lower the risk of cancer."

"Overall, these findings provide important evidence for the protective effects of mushrooms against cancer," said co-author John Richie, professor of public health sciences and pharmacology at the university.

"Future studies are needed to better pinpoint the mechanisms involved and specific cancers that may be impacted," he added.

Experts have urged caution in interpreting the research, simply calling the findings "interesting".

"It is important to consider mushroom intake within the broader context of an individual's dietary and physical activity-related behaviours. Our reviews, which are the most comprehensive examinations of the impact of lifestyle factors on cancer risk, find some evidence that consuming fruits and vegetables might reduce the risk of several cancers, and they may also reduce the likelihood of gaining excess weight which is itself a strong risk for several cancers," said Helen Croker, head of research interpretation at the World Cancer Research Fund.

She said it was also important to eat a wide variety of different fruits and vegetables to get the most benefits.

Sam Miller, head of nutrition for Pure Nutrition in Hong Kong, said it was “really important not to get too excited about the results of any single research paper”.

He noted that any consumption of fruit and vegetables would protect against certain cancers, with a higher intake associated with a lower risk of developing cancer across the lifespan.

“The results suggest to me that those who ate no mushrooms at all were quite likely to eat fewer vegetables overall than those who consumed the highest intake, meaning that the lowest intakes could be at higher risk of cancer regardless of mushroom intake,” he added.

Mushrooms are the highest dietary source of the antioxidant ergothioneine. Photo: Getty Images

Miller suggests eating more fruit and vegetables and to not “peg health hopes on one or two miracle foods”.

“The weight of evidence shows that they do not exist and there is no one food that will make you really healthy,” he said.

UK-based dietitian Fareeha Jay, who specialises in South Asian diets, said the research should be taken with “a pinch of salt” because it was based on analysis of observational studies and did not demonstrate cause and effect.

“With such promising results from the study, we must include mushrooms in our everyday diet – but also make sure that we are including whole grains, fibre, vegetables and fruit, as they can also be protective against certain cancers,” she added.

Mushrooms’ potential medicinal properties

Shiitake mushrooms are valued in some cultures as an anticancer agent and the whole dry mushroom is used in herbal remedies.

Complex sugar compound beta glucan, an active component of lentinan, is an extract of shiitake believed to stimulate the immune system and trigger certain cells and proteins in the body to attack cancer cells. In laboratory studies, it appears to slow the growth of some cancer cells.

In studies of mice, lentinan has been shown to stop bowel cancer cells growing. In laboratory tests, lentinan's protein stopped some fungal cells' growth. It also stopped leukaemia cells dividing.

Extract of maitake mushrooms (above) can stimulate the immune system, lower blood sugar levels and slow the growth of tumours. Photo: Shutterstock

In China a literature review of 12 studies looked at lentinan given with chemotherapy for lung cancer. They found that lentinan worked on the immune system and improved lung cancer patients' quality of life.

Maitake mushrooms are used in Japan and China to treat diabetes and hypertension. Laboratory studies have shown that maitake extract can stimulate the immune system, lower blood sugar levels and slow certain tumours' growth.

Phellinus linteus mushroom extract has been used for centuries in Eastern medicine because it is believed to refresh bodies and extend life.

Studies indicate that it slows the growth of breast cancer cells in the laboratory. It has also been shown to have anticancer effects on skin, lung and prostate cancer cells.

Journal Reference:

Djibril M Ba, Paddy Ssentongo, Robert B Beelman, Joshua Muscat, Xiang Gao, John P Richie. Higher Mushroom Consumption Is Associated with Lower Risk of Cancer: A Systematic Review and Meta-Analysis of Observational Studies. Advances in Nutrition, 2021; DOI: 10.1093/advances/nmab015

Source: www.scmp.com

Fungi Fashion is Booming as Adidas Launches New Mushroom Leather Shoe

By Anna Haines

Emerging foggy-eyed after a year spent indoors, you don't have to look far to notice—mushrooms are sprouting everywhere. Whether it's a reishi-infused serum to calm dry skin, lion's mane drops under the tongue to boost immunity or chaga coffee to curb quarantine fatigue—the humble fungus has never been so fashionable. The mushroom market is anticipated to reach a value of over $50 billion by 2025, according to Grand View Research, as people increasingly turn to nature for solutions to our late-stage pandemic needs. While some are ingesting mushrooms to support their bodies, others are wearing mushrooms to support the planet—literally.

Mushroom-based leather was used for the three stripes, heel tab overlay and signature branding of the Adidas Stan Smith. BOLT THREADS

Today marks the launch of Adidas' Stan Smith Mylo—the first shoe of its kind to be made with a mushroom-based material. Keeping in line with their sustainable ethos, Adidas has chosen their most famed shoe to make an environmental statement; the innovative renewable material was used to create the classic three stripes, heel tab overlay and signature branding the shoe is known for.

It's the latest use of Mylo, a mushroom-based material developed by biotechnology company Bolt Threads. Grown in a lab designed to replicate the forest floor, Mylo is developed from mycelium—the underground roots of mushrooms—to create a foamy mat that can then be finished in a variety of patterns, colors and textures, according to Jamie Bainbridge, the vice president of product development at Bolt Threads. The result is a flexible, breathable fabric that feels remarkably similar to animal leather.

The forest floor environment is replicated in the Bolt Threads lab to grow mycelium into a flexible, versatile foamy mat material. BOLT THREADS

The successful shoe application of the mushroom leather is largely thanks to the Mylo consortium: a partnership established in October of last year between Bolt Threads and Adidas, Stella McCartney, Lululemon and Kering (the French luxury group behind Yves Saint Laurent and Gucci). “It’s been a very unusual experiment, to gather four partners and say, ‘come along with us on a journey of development,’” Bainbridge tells Forbes. “The great thing about it, is that if I need to understand how this material will be used in shoe-making, I have a partner who makes shoes who I can call and we talk about the specifications of the material.”

“It’s been a very unusual experiment, to gather four partners and say, ‘come along with us on a journey of development,’” says Jamie Bainbridge, vice president of product development at Bolt Threads, describing the consortium with Stella McCartney, Adidas, Lululemon and Kering. BOLT THREADS

By having the brands just a phone call away, Bolt Threads has been able develop the new Stan Smith specifically for the needs of Adidas’ clientele. “The needs of a handbag are very different from the needs of a shoe,” Bainbridge tells Forbes.

“We’re supposed to take 10,000 steps a day—that means each one of your shoes has been flexed 10,000 times in a day.”

By partnering with Adidas, Bolt Threads has been able to finesse Mylo specifically for the functional needs of a shoe. BOLT THREADS

It’s this collaborative process that is enabling Mylo to turn science into fashion. They’ve been doing it with Stella McCartney since 2017, when they first began developing the mushroom-based Falabella bag, which premiered a year later at the V&A Fashioned from Nature exhibition in London. Last month Stella McCartney released the world’s first garment made of Mylo: a sensual-yet-athletic black top and utilitarian trouser, featuring the mushroom leather laid on recycled nylon scuba. The luxury house known for its planet-friendly approach is setting the stage for other fashion brands to follow suit. Hermès recently released a bag made from reishi fine mycelium while Allbirds has announced plans to develop a new shoe using ‘leather’ derived from rubber tree sap.

Stella McCartney recently released a black top and utilitarian trouser made of mushroom leather—the world’s first garment made of Mylo. BOLT THREADS

While there has been a “flurry of activity in the alternative leather space,” according to Bainbridge, up until recently, plant-based leathers have largely been limited to the world of high-end fashion. The biggest hurdle to making mushroom material mainstream? Bringing the product to scale. “Every time you go up in scale, you have big equipment changes, and that changes the proportions of the mixture, it changes everything about the dynamics of the material,” says Bainbridge. “You basically learn to make it over again at each scale.”

Jamie Bainbridge tells Forbes one of the greatest challenges for Bolt Threads has been bringing the mushroom leather to scale, “You basically learn to make it over again at each scale," the vice president of product development says.

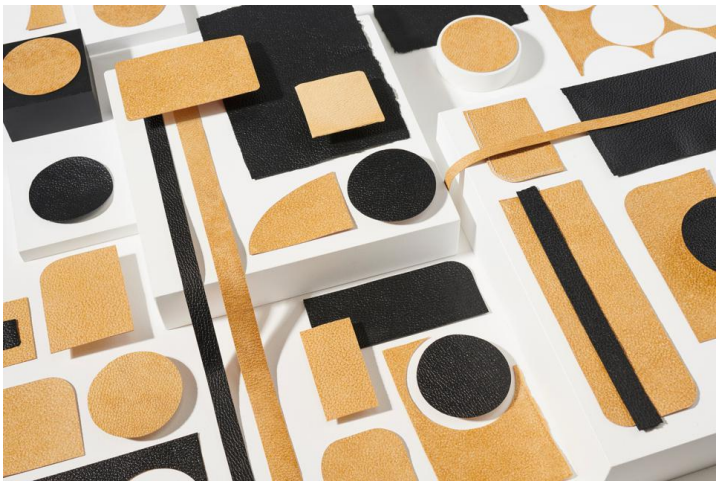
BOLT THREADS

Having committed partners on board seems to be a key ingredient to bringing mushroom leather to the masses. “Now we have a production facility, we’re getting to the point where we have large-scale production very soon,” says Bainbridge. The vice president is optimistic that the Adidas launch marks the beginning of that expansion, “This product that we’re revealing to the public is going to set the stage for taking it into a commercial product, Adidas is very clear that they will not show a product that they don’t have a line of sight for making in the near future,” Bainbridge says.

The new Mylo Adidas shoe marks the transition of mushroom leather from luxury fashion to the commercial market.

BOLT THREADS

But even if major retailers can create fabric made of fungi, will consumers buy it? “I’ve spent a career developing materials and I’ve never seen a material with this much pull, I’ve never seen anything like it,” says Bainbridge. Amidst a fashion industry increasingly concerned with its environmental footprint, it’s no surprise mushroom leather would draw interest. Compared to animal leathers, which consume significant amounts of natural resources in the year they take to produce, Mylo is produced in two weeks. And while there are plenty of non-animal leather alternatives available, most are made of plastic—mycelium-based textiles involve regenerative growing methods and contain less petrochemicals than their synthetic counterparts.



Compared to animal leathers that take at least a year to produce, mushroom-based Mylo is made in two weeks, with less petrochemicals than non-animal leathers. BOLT THREADS

“The planet can’t go on the way it has been,” Bainbridge tells Forbes. “You’re seeing it in every subject matter around sustainability—whether it’s climate change or carbon footprint—the public is gaining an understanding that they’ve got to change their ways.” If there was ever a moment for mushroom leather to take off, it would be now, as consumers become increasingly conscious about their impact. “There’s an understanding the world has gained in the last year of being locked up that perhaps we can’t go about business as usual,” says Bainbridge.

With consumers increasingly concerned about their impact on the planet, Jamie Bainbridge anticipates mushroom leather will continue to gain popularity, "the public is gaining an understanding that they’ve got to change their ways," she says. BOLT THREADS

But mushrooms are not just peaking interest as a material source, they're popping up in designs too. From button mushroom Chanel earrings to soft-edged fungi-shaped lamps to Bella Hadid's mushroom-engraved leather bag, mushrooms have become the go-to motif of the past year. "Fungi are having a moment, there's popular culture around it," says Bainbridge.

'Mycoschoen' by the Belgian shoe designer Kristel Peters, from the Somerset House exhibition, Mushrooms: The Art, Design and Future of Fungi. KRISTEL PETERS

After a year spent indoors, it makes sense that people are flocking to this symbol of nature. "We are at a moment of deep climate crisis and are very separated from our relationship to nature," says Francesca Gavin, curator of Mushrooms: The Art, Design and Future of Fungi, which exhibited early last year at the Somerset House in London. When asked if the trend is explained by a romanticization of nature, Bainbridge agrees, "It's staggering to watch what has happened to people's thinking around being outside, it's a whole new awareness for a lot of people."

'Mycelium + Timber' by Sebastian Cox and Ninela Ivanova from Mushrooms: The Art, Design and Future of Fungi exhibition at Somerset House last year. PETR KREJCI

Feeling powerless in the face of the pandemic, it's no surprise people are embracing one of nature's most resilient and self-sustaining organisms; one that symbolizes immortality. "Without fungi all ecosystems would die," Gavin tells Forbes. "Fungi provide a beautiful example of the fascinating importance of nature for human life to flourish."

But perhaps the fungi frenzy is about more than connecting to nature, and represents a larger desire to find comfort in our shared humanity. “Whether it’s trying to survive the pandemic together, seeing nature through a new lens, I think we’re all a little more connected these days,” says Bainbridge. Gavin echos this statement, “Mushrooms provide a contemporary metaphor for new ways of thinking and living in a more positive way with nature, they show how living in symbiosis with the world around us is the only route for survival.”

More than a desire to connect with nature, the mushroom boom might be explained by a cultural longing for a symbol of survival.

For fashion designers and sustainable textile producers that connection means embracing the presence of competition. Aside from Bolt Threads, Ecovative and MycoWorks are producing mycelium-based leathers too. But Bainbridge sees their fellow mushroom material-makers as united in the pursuit of a greener planet, “We’re glad to see others playing in the space too, there’s room for a lot of people, it makes each one of us stronger.”

Source: https://www.forbes.com

Up-coming Events

Russian Mushroom Days 2021

The Main Annual Event of Russian Mushroom industry.

Krasnodar

14-15 September 2021

Place: EXPOGRAD YUG

Basic hotel: Four Points Sheraton

ABOUT RUSSIAN MUSHROOM DAYS

Russian Mushroom Days is unique platform for everyone who works or wants to work in the rapidly developing Russian Mushroom Industry.

New contacts, new projects discussion, knowledge and experience exchange with people from European and Asian Mushroom Industries.

Knowledge and experience

More 200 participants from 20 countries— mushroom and compost farms, equipment, casing soil, package, pest and diseases control products producers, invest companies, banks and ministry representatives, Russian and foreign experts.

Analytics and innovation

During the Conference «Quality, variety, marketing» world leading and Russian experts will discuss worldwide mushroom market trends and local markets experiences with new mushroom products. In Expo «Mushroom growing, processing and packaging» companies from Russia, Europe and Asia will introduce their new products and projects.

EXPO

International Expo «Mushroom growing, processing and packaging» is one of main part of Russian Mushroom Days.

CONFERENCE

International Conference «Quality, variety, marketing» is one of main part of Russian Mushroom Days.

During Conference Russian-English simultaneous translation service will be provided.

SCHEDULE

September 14

10.00 – 13.30	**Registration** ***Lobby of the Four Points by Sheraton Hotel***
14.00 – 14.30	**Russian Mushroom Days opening** ***Expo Hall, Expograd Yug***
14.30 – 18.00	**EXPO** **Sponsor presentations** ***Expo Hall, Expograd Yug***
19:30 – 22.00	**BANQUET** ***Four Points by Sheraton Hotel***
15.00 – 17.30	**Section "Mushroom Science ISMS"** ***Small conference hall Expograd Yug, 2nd floor*** Live Stream

SCHEDULE

September 15

9.00 – 17.00	**Expo** ***Expo Hall, Expograd Yug***
9.00 – 12.00	**Section "Market, Marketing, Sales"** ***Big conference hall Expograd Yug, 2nd floor***
9.00 – 9.20	Russian mushrooms market 2021-2022
9.20 – 9.40	Russian oyster mushroom and exotic market 2021-2022
9.40 – 10.00	Mushrooms consumption in Russia today and tomorrow
10.00 – 10.20	Changes in retail
10.20 – 10.40	PR of mushrooms as categories
10.40 – 11.00	**Coffee break**
11.00 – 11.20	Mushrooms processing
11.20 – 11.40	Modern promotion channels
11.40 – 12.00	Cooking and HoReCa
12.00 – 15.00	**Mushroom BBQ-show** ***Open courtyard of Expograd Yug***
15.00 – 18.00	**Section "Oyster mushroom and exotic. Technology questions "** ***Conference hall Expograd Yug, 2nd floor***
15.00 – 18.00	**Section "Mushrooms. Technology questions"** ***Conference hall Expograd Yug, 2nd floor***
15.00 – 17.30	**Section "Mushroom Science ISMS"** ***Small conference hall Expograd Yug, 2nd floor*** Live Stream

ACCOMMODATION

FourPoints Sheraton hotel will be glad to take Russian Mushroom Days participants

*For more information:*https://dnirosgribovodstva.ru/

20th ISMS Congress 2021

The ISMS e-Congress will be held online from 14-17 September 2021. The 20th ISMS Congress in Vancouver had to be cancelled due to the Covid-19 pandemic. The next live ISMS Congress will be held in 2024 at a venue to be advised.

Overview of the e-Congress

The e-Congress will be held online each day from 12:00 UTC (GMT) to 14:30 from Tuesday 14 until Friday 17 September 2021.

Each day will begin with a 30-minute plenary session presentation on a topic of significant scientific or industry interest. The day will continue with two to three 2-hour concurrent sessions depending on the number of abstracts to be presented in each topic area.

Sessions will be synchronised so that delegates can easily move between sessions to hear presentations and questions related to abstracts they are interested in.

The timing and format of the concurrent sessions have been designed to enable maximum live participation for presenters and delegates around the world.

For those registered to attend, but unable to make it to the live sessions, they will be recorded and made available for viewing online after the event. Registration will be required to access this service.

Further Information: secretariat@isms.biz

Ukrainian Mushroom Days 2021

About the event

Ukrainian Mushroom Days is one of the biggest in Eastern Europe and the main in Ukraine event for the mushroom industry. The fair is attended by producers of cultivated mushrooms, compost, casing soil and spawn, also by suppliers of equipment for production, measurement, control and storage, producers of racks, nets, packaging, providers of services and others involved in the mushroom sector.

The event attracts companies that produce 95% of Ukrainian cultivated mushrooms and companies that produce 100% of Ukrainian compost. About 15% of participants are from Russia and Belarus. Totally nearly 40% are foreign guests from Uzbekistan, Kazakhstan, Moldova, as well as Poland, Netherlands, Germany, Italy, Great Britain, Ireland, Turkey, China and others.

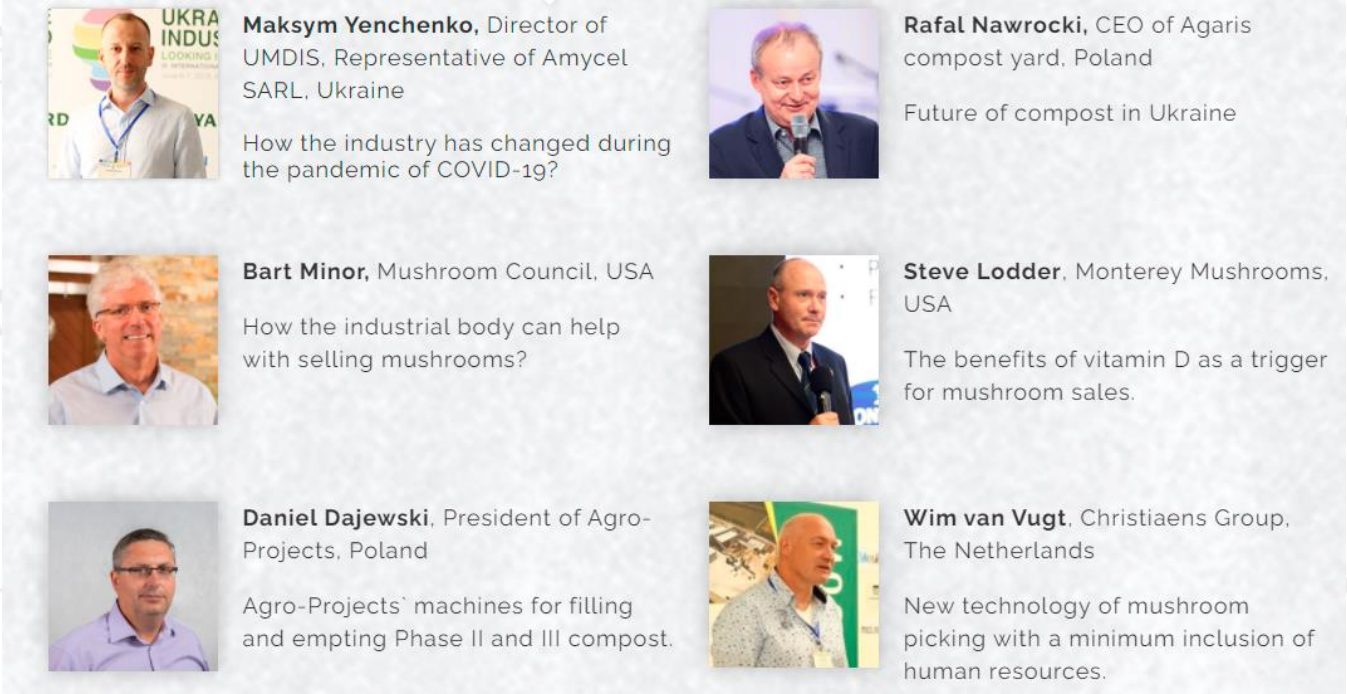
Ukrainian Mushroom Days are THREE ATTRACTIONS IN ONE.The event includes TWO DAYS of ongoing CONFERENCE and EXHIBITION. And the GALA DINNER PARTY on the first day. The THIRD DAY is free BONUS for participants from Platinum Sponsor – it is devoted to theTOUR to the largest compost yard.

The Conference for mushroom producers

20th – 21st of October

Ukrainian Mushroom Days conference is the big forum where mushroom producers from Ukraine and Eastern Europe meet experts, consultants and discuss the situation in the industry. We invite the best Ukrainian and international speakers to talk about the main and the most urgent topics.

SPEAKERS



Roman Stolper, consultant of Amycel SARL, Ukraine

Large and small errors in the design of a mushroom farm.

Bartosz Jan Skipor-Rybacki, consultant of Agrais, Poland

How to use chemical products for mushroom production without harm to the crop.

Igor Muzyka, Director of the GELEKA-M mushroom farm, Ukraine

Filling of the Phase 3 compost into the growing room with a head filling machine.

John Clay, Sales Director Europe at Amycel SARL, Great Britain

What determines the quality of the spawn?

Maksym Yenchenko, Director of UMDIS, Representative of Amycel SARL, Ukraine

Eastern European mushroom market.

Bart Minor, Mushroom Council, USA

How to make mushroom promotion and achieve good results?

Lina Turovska, Corporate Harvest Manager West in Highlinemushrooms, Canada

Effective organization of mushroom picking.

Roman Stolper, consultant of Amycel SARL, Ukraine

What is worth to know about composting process.

Alexander Melnik, Purchasing and Production Director at Ortika Frozen Foods, Russia, Ukraine

What's new in mushroom freezing technology.

Nikodem Sakson, consultant, Poland

Disinfection, sanitary condition of chambers and social rooms.

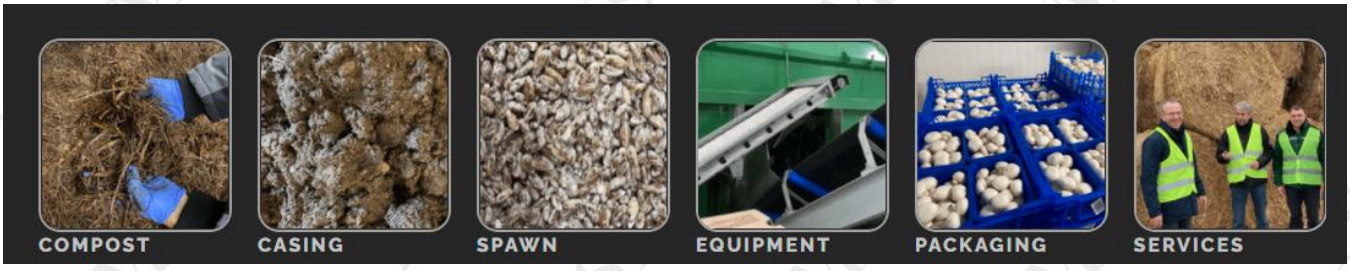
Artem Kovalenko, Owner of mushroom farm VKZ, Ukraine

How the cost of mushroom production has changed.

Exhibition for mushroom producers

20th – 21st of October

From balers for collecting straw to trays for packing mushrooms – suppliers of any goods and services that a mushroom farm needs. The exhibition usually gathers 50 companies-exhibitors from Ukraine, Russia, Poland, Netherlands, Italy, Turkey, China and other countries



The Gala Dinner Party

Evening, 20th of October

On the first day we invite all participants and exhibitors for the Gala Dinner.

It is the big banquet with artists, popular singers, dances, competitions, and much fun. The awards of the industry are being presented at this event.

Gala Dinner is the great opportunity to become closer friends with your partners.

Participation in Gala Dinner is free for all participants and exhibitors of Ukrainian Mushroom Days.

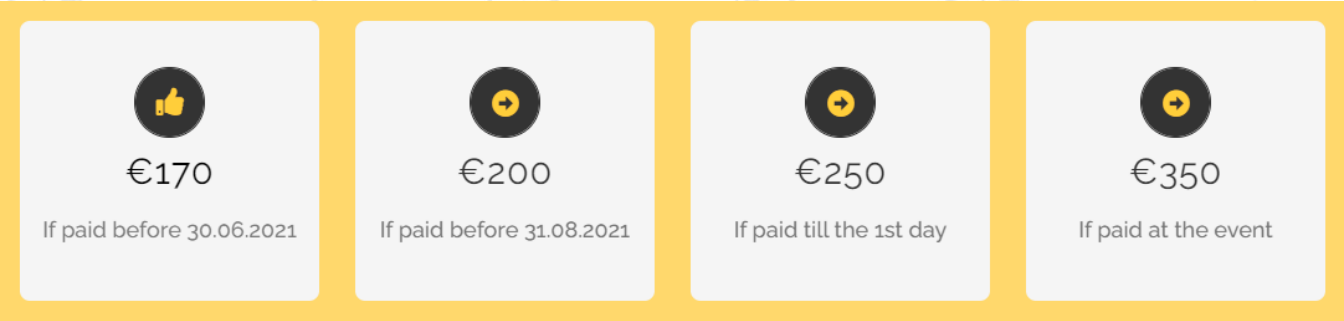
Tour to Agaris, the largest compost yard of Ukraine

22nd of October

Agenda:

- Gathering near main entrance of Mercury Kyiv Congress Hotel and departure
- Arrival to Agaris plant
- Seeing the plant
- Departure and arrival to Kyiv

Registration



Ukrainian Mushroom Days are taking place on 20th-21th of October in Kyiv, in Mercure Kyiv Congress Hotel 4*

If you have any questions, please, call or text by messenger **Inna Ustylovska**

+380935690941, info@mushroomdays.in.ua

For more information: www.mushroomdays.in.ua

26th North American Mushroom Conference 2022

Join us in Vancouver - June 12-14, 2022!

In light of the current pandemic and ongoing group gathering and travel restrictions, Mushrooms Canada and its North American Mushroom Conference partners have made the decision to postpone the 26th North American Mushroom Conference until June 2022. We thank all those who have shown their continued support for the conference during this time. More details will be shared in the coming months and we hope to see you all again soon!

North American Mushroom Conference

Mushrooms Canada will be hosting North American Mushroom Conference at the Parq Vancouver in June 2022. Expand your knowledge and improve your daily business operation by gathering the most current industry information on mushroom production technology, food safety, and consumer marketing at the North American Mushroom Conference.

About Vancouver

Consistently ranked as one of the most beautiful places to live, Vancouver offers a bustling city nestled within the mountains and the ocean.

The city is renowned for its natural beauty and cultural diversity. For thousands of years the Coast Salish people have called the area now known as Vancouver home, and their history and cultural traditions, deep respect for nature, and spirituality are all tightly woven into the city's cultural fabric.

At a Glance Agenda

SUNDAY | JUNE 12	
MORNING / AFTERNOON	• **Registration Opens** • **Sponsor/ Expo Set Up**
EVENING	• **Reception**
MONDAY | JUNE 13	
MORNING	• **Breakfast & Expo** • **NAMC Sessions**
AFTERNOON	• **Lunch & Expo** • **NAMC Sessions**
TUESDAY | JUNE 14	
MORNING	• **Breakfast & Expo** • **NAMC Sessions**
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EVENING	• **NAMC Gala Dinner**
WEDNESDAY | JUNE 15	
MORNING / AFTERNOON	• **Optional Tours**

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Website: www.mushroomconference.org

The 11th International Medicinal Mushroom Conference 2022

At the moment, the COVID-19 outbreak is still ongoing all over the world, it is recommended to follow preventive measures in order to reduce the risk of occurrence and transmission of this infection. The organizers of 11th International Medicinal Mushroom Conference decide to postpone the conference to the year 2022 in Belgrade, Serbia, which was supposed to be held in 2021.

International Medicinal Mushroom Conference

The International Medicinal Mushroom Conference (IMMC) is also known as the "Olympic Games of Edible and Medicinal Mushrooms". It is a platform for all medicinal mushroom researchers to come and discuss basic and currently important scientific questions, share the results of individual studies, make new or renew friendships, and work together to develop a new chapter in medicinal mushrooms.

The awareness of the international movement for the medicinal mushroom industry made a marked important milestone when the International Journal of Medicinal Mushrooms (IJMM) was launched in 1999 by Begell House Inc. (USA). This organized effort then led to the inaugural International Medicinal Mushroom Conference held in Kiev, Ukraine, in 2001, where it was agreed that there would be an IMMC every two years. The IMMC2 was held in Pattaya, Thailand, in 2003; the IMMC3 took place in Port Townsend, Washington, USA, in 2005; the IMMC4 was held in Ljubljana, Slovenia, in 2007; the IMMC5 in Nantong, China, in 2009; the IMMC6 in Zagreb, Croatia, in 2011; the IMMC7 in Beijing, China, in 2013; the IMMC8 was held in Manizales, Colombia, 2015, and the IMMC9 was held in Palermo, Italy 2017.

IMMC10

The 10th International Medicinal Mushroom Conference (IMMC10), led by Professor Yu Li, Chairman of International Society for Medicinal Mushrooms (ISMM) and the Academician of Chinese Academy of Engineering, was successfully held at Alphay International Conference Center (AICC), in Nantong, China on September 19-22, 2019. A lot of activities including the 297th Chinese Engineering Science and Technology Symposium--Forum for the Fungal Health Industry, Professor Shu-Ting Chang's Symposium on Academic Thoughts, the founding workshop of the Health Industry Branch and the Lingzhi Industry Branch of the Mycological Society of China etc., were also organized during the conference. More than 500 professionals from 43 countries and regions participated in the event.

The major activities of IMMC10 included key-note speeches, scientific forums, poster sessions, exhibitions of edible and medicinal mushroom products, and so on. The scientific symposia involved biodiversity, genetics and breeding, cultivation and fermentation, biochemistry and pharmacology, medicinal mushrooms in veterinary medicine and agriculture, clinical practice, nutritional and medicinal value, industrialization.

About Belgrade

Belgrade is the capital and largest city of Serbia. It is located at the confluence of the Sava and Danube rivers and the crossroads of the Pannonian Plain and the Balkan Peninsula. Nearly 1.7 million people live within the administrative limits of the City of Belgrade, a quarter of the total population of Serbia.

Belgrade is one of the oldest continuously inhabited cities in Europe and the World. One of the most important prehistoric cultures of Europe, the Vinča culture, evolved within the Belgrade area in the 6th millennium BC.

The city has direct flights to over 72 destinations, visa free for EU countries, plus Turkey, Russia, Georgia, Moldova, Ukraine, Azerbaijan, Belarus, Iran, Israel, Kazakhstan, China, Mongolia, India, Japan, USA.

If you have any questions or require assistance please contact Prof. dr Miomir Niksic at miomir.niksic@gmail.com.

Research progress

High-throughput sequencing view on the magnitude of global fungal diversity

Petr Baldrian, Tomáš Větrovský, Clémentine Lepinay & Petr Kohout

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Abstract: High-throughput DNA sequencing has dramatically transformed several areas of biodiversity research including mycology. Despite limitations, high-throughput sequencing is nowadays a predominant method to characterize the alpha and beta diversity of fungal communities. Across the papers utilizing high-throughput sequencing approaches to study natural habitats in terrestrial ecosystems worldwide, > 200 studies published until 2019 have generated over 250 million sequences of the primary mycological metabarcoding marker, the nuclear ribosomal internal transcribed spacer 2 (ITS2). Here we show that at a 97% sequence similarity threshold, the total richness of non-singleton fungal taxa across the studies published so far is 1.08 million, mostly Ascomycota (56.8% of the taxa) and Basidiomycota (36.7% of the taxa). The Chao-1 estimate of the total extant fungal diversity based on this dataset is 6.28 million taxa, representing a conservative estimate of global fungal species richness. Soil and litter represent the habitats with the highest alpha diversity of fungi followed by air, plant shoots, plant roots and deadwood with Chao-1 predictions, for samples containing 5000 sequences, of 1219, 569, 392, 228, 215 and 140 molecular species, respectively. Based on the high-throughput sequencing data, the highest proportion of unknown fungal species is associated with samples of lichen and plant tissues. When considering the use of high-throughput sequencing for the estimation of global fungal diversity, the limitations of the method have to be taken into account, some of which are sequencing platform-specific while others are inherent to the metabarcoding approaches of species representation. In this respect, high-throughput sequencing data can complement fungal diversity predictions based on methods of traditional mycology and increase our understanding of fungal biodiversity.

Keywords: High-throughput sequencing, Metabarcoding, Internal transcribed spacer, Alpha diversity, Meta-analysis

Fungal Diversity Volume 108, Issue 1, May 2021. https://doi.org/10.1007/s13225-021-00472-y

Suppression of obesity and inflammation by polysaccharide from sporoderm-broken spore of Ganoderma lucidum via gut microbiota regulation

Tingting Sang, Chengjie Guo, Dandan Guo, Jianjun Wu, Yujie Wang, Ying Wang , Jiajun Chen, Chaojie Chen, Kaikai Wu, Kun Na, Kang Li, Liu Fang, Cuiling Guo, Xingya Wang*

College of Pharmaceutical Science, Zhejiang Chinese Medical University, Hangzhou, China

Abstract: *Ganoderma lucidum* has been shown to have anti-obesity effects. However, polysaccharide extracted from the sporoderm-broken spores of *Ganoderma lucidum* (BSGLP) against obesity and its underlying mechanisms have never been reported. In the current study, we showed that BSGLP inhibited high-fat diet (HFD)-induced obesity, hyperlipidemia, inflammation, and fat accumulation in C57BL/6 J mice. BSGLP improved HFD-induced gut microbiota dysbiosis, maintained intestinal barrier function, increased short-chain fatty acids production and GPR43 expression, ameliorated endotoxemia, manifested by reduced serum lipopolysaccharide level, and increased ileum expression of tight junction proteins and antimicrobial peptides. Fecal microbiota transplantation study confirmed that BSGLP-induced microbiota change is responsible, at least in part, for obesity inhibition. Besides, BSGLP notably alleviated HFD-induced upregulation of TLR4/Myd88/NF-κB signaling pathway in adipose tissue. Collectively, our study showed for the first time that BSGLP might be used as a prebiotic agent to inhibit obesity and hyperlipidemia through modulating inflammation, gut microbiota, and gut barrier function.

Keywords: Obesity, Gut microbiota, Endotoxemia, Sporoderm-broken spores, *Ganoderma lucidum* polysaccharide

Carbohydrate Polymers Volume 256, 2021, 117594, ISSN 0144-8617, https://doi.org/10.1016/j.carbpol.2020.117594.

Edible mushrooms as a novel trend in the development of healthier meat products

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Abstract: One of the challenges in modern society is the reduction of meat consumption as well as the formulation of new meat products, considering health and sustainability aspects. In this regard, mushrooms are considered a promissory source of bioactive compounds to be used in the production of healthier meat products. Mushrooms have antimicrobial and antioxidant properties, which can improve the self-life of meat products. This review shows that a substantial improvement in terms of protein, dietary fiber and ash content in meat products can be achieved by incorporating different types of mushrooms without significantly affecting their physico-chemical properties. Moreover, due to high percentage of dietary fiber, easily digestible protein and a meat-like texture, mushroom is an interesting choice to replace salt, phosphates, protein and fat in the formulation of meat products. Finally, the presence of high contents of free amino acids in mushroom can enhance the sensorial properties of meat products.

Current Opinion in Food Science, Volume 37, 2021, Pages 118-124, https://doi.org/10.1016/j.cofs.2020.10.004.

Healthy function and high valued utilization of edible fungi

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Base of Edible Mushroom Processing Technology Integration of Ministry of Agriculture and Rural Affairs, Changchun 130118, China; [3]*Engineering Research Center of Grain Deep-processing and High-effeciency Utilization of Jilin Province, Changchun 130118, China;* [4]*Engineering Research Center of Chinese Ministry of Education for Edible and Medicinal Fungi, Jilin Agricultural University, Changchun 130118, China*

Abstract: Edible fungi are large fungi with high added value that can be utilized as resources. They are rich in high-quality protein, carbohydrate, various vitamins, mineral elements and other nutrients, and are characterized by high protein, low sugar, low fat and low cholesterol. In addition, edible fungi contain a variety of bioactive substances, such as polysaccharides, dietary fiber, steroids, polyphenols, and most of these compounds have antioxidant, anti-tumor and other physiological functions. This review comprehensively discusses the bioactive components and functional characteristics of edible fungi (such as antioxidant, anti-aging, hypolipidemic activities, etc.). Then the recent developments and prospect in the high-valued utilization of edible fungi are discussed and summarized. The objective of this review is to improve the understanding of health-promoting properties of edible fungi, and provide reference for the industrial production of edible fungi-based health products.

Keywords: Edible fungi, Functional components, Processing and utilization, High valued utilization

Food Science and Human Wellness, Volume 10, Issue 4, 2021, Pages 408-420, https://doi.org/10.1016/j.fshw.2021.04.003.

Identification of existing pharmaceuticals and herbal medicines as inhibitors of SARS-CoV-2 infection

Jia-Tsrong Jan[1], Ting-Jen Rachel Cheng[1], Yu-Pu Juang[2], Hsiu-Hua Ma[1], Ying-Ta Wu[1], Wen-Bin Yang[1], Cheng-Wei Cheng[1], Xiaorui Chen[1], Ting-Hung Chou[3], Jiun-Jie Shie[3], Wei-Chieh Cheng[1], Rong-Jie Chein[3], Shi-Shan Mao[1], Pi-Hui Liang[1,2], Che Ma[1], Shang-Cheng Hung[1], and Chi-Huey Wong[1,4]

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Abstract: The outbreak of COVID-19 caused by SARS-CoV-2 has resulted in more than 50 million confirmed cases and over 1 million deaths worldwide as of November 2020. Currently, there are no effective antivirals approved by the Food and Drug Administration to contain this pandemic except the antiviral agent remdesivir. In addition, the trimeric spike protein on the viral surface is highly glycosylated and almost 200,000 variants with mutations at more than 1,000 positions in its 1,273 amino acid sequence were reported, posing a major challenge in the development of antibodies and vaccines. It is therefore urgently needed to have alternative and timely treatments for the disease. In this study, we used a cell-based infection assay to screen more than 3,000 agents used in humans and animals, including 2,855 small molecules and 190 traditional herbal medicines, and identified 15 active small molecules in concentrations ranging from 0.1nM to 50 μM. Two enzymatic assays, along with molecular modeling, were then developed to confirm those targeting the virus 3CL protease and the RNA-dependent RNA polymerase. Several water extracts of herbal medicines were active in the cell-based assay and could be further developed as plant-derived anti–SARS-CoV-2 agents. Some of the active compounds identified in the screen were further tested in vivo, and it was found that mefloquine, nelfinavir, and extracts of *Ganoderma lucidum* (RF3), *Perilla frutescens*, and *Mentha haplocalyx* were effective in a challenge study using hamsters as diseasemodel.

Keywords: SARS-CoV-2, drug repurposing, antiviral, cell-based and animal studies

PNAS Vol. 118 2021 No. 5 e2021579118 https://doi.org/10.1073/pnas.2021579118

Antitumor, immunomodulatory and antiangiogenic efficacy of medicinal mushroom extract mixtures in advanced colorectal cancer animal model

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Abstract: Due to frequent drug resistance and/or unwanted side-effects during conventional and targeted cancer treatments, development of multi-target therapies is an important research field. Medicinal mushrooms' isolated specific compounds and mushroom extracts have been already proven as non-toxic multi-target inhibitors of specific oncogenic pathways, as well as potent immunomodulators. However, research on antitumor effects of multiple-species extract mixtures was limited so far. The aim of this study was therefore, a study of medicinal mushroom preparations AGARIKON.1 and AGARIKON PLUS on colorectal cell lines in vitro and colorectal mice model in vivo. We found a significant antiproliferative and pro-apoptotic effect of tested medicinal mushroom preparations on colorectal (HCT-116, SW620) tumor cell lines, while the effect on human fibroblast cell line (WI-38) was proliferative emphasizing a specificity towards tumor cell lines. We further investigated the effect of the medicinal mushroom preparations AGARIKON.1 and AGARIKON PLUS in various combinations with conventional cytostatic drug 5-fluorouracil in the advanced metastatic colorectal cancer mouse model CT26.WT. AGARIKON.1 and AGARIKON PLUS exhibited immunostimulatory and antiangiogenic properties in vivo which resulted in significantly increased survival and reduction in tumor volume. The antitumor effects of AGARIKON.1 and AGARIKON PLUS, with or without 5-fluorouracil, are based on M1 macrophage polarization enhancement, inhibition of M2 and tumor-associated macrophage (TAM) polarization, effects on T helper cell Th1/Th2/Th17 cytokine profiles, direct inhibition of CT26.WT tumor growth, inhibition of vascular endothelial growth factors (VEGF) and metalloproteinases 2 and 9 (MMP-2 and MMP-9) modulation. The administration of AGARIKON.1 and AGARIKON PLUS did not show genotoxic effect. This data provides good basis for an expanded translational study.

Keywords: colorectal cancer; medicinal mushrooms; immunotherapy; multi-target; combination therapy; 5-fluorouracil; survival; angiogenesis; macrophage polarization

Molecules 2020, 25, 5005; doi:10.3390/molecules25215005

Life cycle assessment of a circular, urban mushroom farm

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Abstract: Modern food systems incur many environmental impacts, which can be mitigated by the application of circular economy principles, such as the closing of material and energy loops and the upcycling of waste products. Mushroom farming provides a relevant case in this direction because organic waste can be used for substrate as an input in the cultivation process, which produces valuable outputs such as edible foodstuffs and soil amendment. Few studies evaluate the actual environmental impacts of circular food production systems and assess their efficacy with respect to more linear alternatives. To address this research gap, we quantified the environmental impacts of a circular, urban mushroom farm next to Paris, France. We used life cycle assessment to study the production of 1 kg of fresh oyster mushrooms (*Pleurotus ostreatus*), from the generation of substrate materials through delivery to the distribution center. Our goals were to quantify the environmental impacts of a novel type of food production system, to find the aspects of production that contribute most to these impacts, and to assess the advantages and disadvantages of circular economy for this case study. In terms of climate change impact, the product system emitted 2.99–3.18 kg CO_2-eq./kg mushroom, and on-farm energy use was the top contributor to all impact categories except land use. Surprisingly, 31% of the climate change impacts came from transport throughout the supply chain, despite the local nature of the farm. Circular economy actions helped optimize the environmental performance by minimizing impacts from the use of materials, which were mostly upcycled. This suggests that further improvements could be made by reducing energy consumption on the farm or by making the transport schemes more efficient, rather than continuing to focus on the type and source of materials used. This circular, urban farm had similar climate change impacts to classical, more linear systems, but these impacts could be largely reduced by implementing appropriate actions. These were identified and discussed with the farmers, factoring in their feasibility.

Keywords: Life cycle assessment; Mushroom; Circular economy; Urban agriculture; Industrial ecology; Sustainable food systems

Journal of Cleaner Production, Volume 288, 2021, 125668, https://doi.org/10.1016/j.jclepro.2020.125668.

Novel hypoglycemic compounds from wild mushroom *Paxillus involutus*

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Abstract: Wild mushrooms are an important source of secondary metabolites possessing a broad range of biological activities. In this study, eight new compounds, named furanopaxin A–F (1–6), deoxybisinvolutone (7), and coumarinvol (8) along with two known compounds were isolated from fruiting bodies of the wild mushroom *Paxillus involutus* (Batsch) Fr. Their structures were established based on HR-ESI-MS and 1D and 2D NMR spectroscopic data. The results of hypoglycemic assays indicated that compounds 5–8 possessed significant α-glucosidase inhibitory activities, with IC_{50} values ranging from 14.65 ± 1.68 to 47.55 ± 1.47 μM, and each compound could enhance glucose consumption in insulin-resistance HepG2 cells. Further analysis by molecular docking implied that compounds 5–8 could interact with the amino acid residues of α-glucosidase, supporting the hypoglycemic activity of the compounds.

Keywords: *Paxillus involutus*; Chemical composition; Hypoglycemic activity; Molecular docking

Bioorganic Chemistry, Volume 112, 2021, 104984, https://doi.org/10.1016/j.bioorg.2021.104984.

Nutritional impact of adding a serving of mushrooms to USDA Food Patterns – a dietary modeling analysis

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Abstract: Mushrooms are part of vegetables and are important source of nutrients and bioactive compounds. The objective was to assess the nutritional impact of adding a serving of mushrooms in USDA Food Patterns using a similar approach to that used by USDA for Dietary Guidelines.

A composite of commonly consumed raw mushrooms (white, brown/crimini and portabella; at 1:1:1 ratio) and raw speciality mushrooms (oyster mushrooms) were used for modeling. The United States Department of Agriculture (USDA) Food Data central database (*https://fdc.nal.usda.gov/*) was used to obtain nutrient profiles of mushrooms. Nutritional profiles of USDAs Food Patterns were obtained from the Scientific Report of the 2015 Dietary Guidelines Advisory Committee, Appendix E-3 (*https://health.gov/dietaryguidelines/2015-scientific-report/15-appendix-E3/*) and dietary modeling was accomplished by adding nutrients from mushrooms.

Addition of an 84 g serving of commonly consumed raw mushrooms to USDA Food Patterns resulted in about 1% increase in calories, less than 5% increase in macronutrients, 2–3% increase in fiber, 8–12% increase in potassium, 12–18% increase in riboflavin, 11–26% increase in niacin, 11–23% selenium and 16–26% increase in copper depending upon the pattern type and calorie level. Mushrooms exposed to UV light to increase vitamin D levels to 200 IU/serving also increased vitamin D by 67–90% in USDA Food Patterns. Addition of oyster mushroom also additionally increased 8–11% vitamin D and 10–16% choline in USDA Food Patterns. Addition of mushrooms had minimal effect on sodium (1% or less increase) and no effect on saturated fat or cholesterol in USDA Food Patterns. Based on published data, a serving of commonly consumed mushrooms would also be expected to add 2.2 mg ergothioneine and 3.5 mg glutathione to the USDA Food Patterns.

Addition of mushrooms to USDA Food Patterns increased several micronutrients including shortfall nutrients (such as potassium, vitamin D and choline), and had a minimal or no impact on overall calories, sodium or saturated fat.

Keywords: healthy US-style food pattern, healthy Mediterranean-style pattern, healthy vegetarian pattern, white mushrooms, crimini mushrooms, portabella mushrooms, oyster mushrooms

Food & Nutrition Research 2021, 65: 5618, http://dx.doi.org/10.29219/fnr.v65.5618

Medicinal Mushrooms against Influenza Viruses

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Abstract: This review provides results obtained by scientists from different countries on the antiviral activity of medicinal mushrooms against influenza viruses that can cause pandemics. Currently, the search for antiviral compounds

is relevant in connection with the coronavirus disease 2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Medicinal mushrooms contain biologically active compounds (polysaccharides, proteins, terpenes, melanins, etc.) that exhibit an antiviral effect. The authors present the work carried out at the State Research Center of Virology and Biotechnology Vector in Russia, whose mission is to protect the population from biological threats. The research center possesses a collection of numerous pathogenic viruses, which allowed screening of water extracts, polysaccharides, and melanins from fruit bodies and fungal cultures. The results of investigations on different subtypes of influenza virus are presented, and special attention is paid to *Inonotus obliquus* (chaga mushroom). Compounds produced from this mushroom are characterized by the widest range of antiviral activity. Comparative data are presented on the antiviral activity of melanin from natural *I. obliquus* and submerged biomass of an effective strain isolated in culture against the pandemic strain of influenza virus A/California/07/09 (H1N1 pdm09).

Keywords: *Inonotus obliquus*, influenza viruses, SARS-CoV-2 coronavirus, antiviral activity, polysaccharides, melanin, biotechnology, medicinal mushrooms

JournalsInternational Journal of Medicinal Mushrooms, Volume 23, 2021 Issue 2;

DOI: 10.1615/IntJMedMushrooms.2020037460

Cordyceps cicadae **polysaccharides inhibit human cervical cancer hela cells proliferation via apoptosis and cell cycle arrest**

Jiao Xu[1,2], Zhi-Cheng Tan[1,2], Zhong-Yuan Shen[1,2], Xing-Jia Shen[1,2], Shun-Ming Tang[1,2*]

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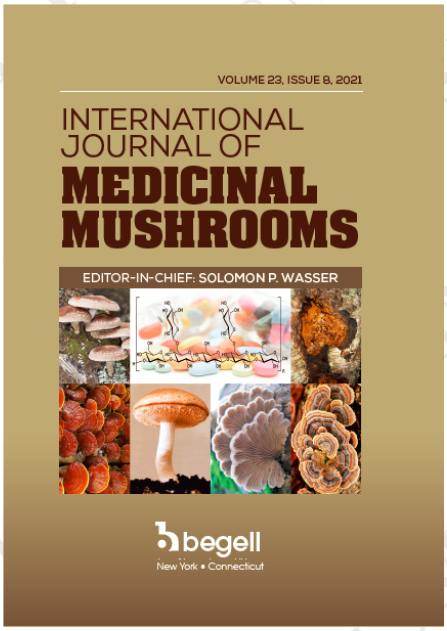
Abstract: The present study presented the extraction and purification of polysaccharides from artificially cultured *Cordyceps cicadae* and wild *Cordyceps cicadae* by pre-soaking ultrasonic water extraction. The effects of different concentrations of polysaccharides on proliferation and cytotoxicity of Hela cells were detected by MTT and LDH methods. The results showed that the proliferation of Hela cells was inhibited by polysaccharides treatment (25μg/mL-1600μg/mL). The results of flow cytometry further confirmed that polysaccharides blocked the cell cycle in the S phase and promoted apoptosis. RT-qPCR and Western Blot were used to study the mRNA and protein expression of genes related to cell cycle and apoptosis signaling pathway. The results showed that polysaccharides treatment inhibited the expression of Cyclin E, Cyclin A and CDK2 and up regulated the expression of P53. Further, activation of Caspase cascade reaction, up regulation of death receptor, and the ratio of pro-apoptotic factor/anti-apoptotic factors, thus caused the cell cycle arrest and induced the apoptosis. The above research results lay a foundation for extending the anti-cancer effects of natural plant resources with low toxicity and high efficiency.

Keywords: Artificially cultured *Cordyceps cicadae*, Polysaccharides, Cell cycle, Apoptosis

Food and Chemical Toxicology, Volume 148, 2021, 111971, https://doi.org/10.1016/j.fct.2021.111971.

International Journal of Medicinal Mushrooms Call for Papers

About *International Journal of Medicinal Mushrooms*



International Journal of Medicinal Mushrooms is a journal covering the technologies/fields/categories related to Applied Microbiology and Biotechnology (Q3); Drug Discovery (Q3); Pharmacology (Q3). It is published by Begell House Inc.. The overall rank of *International Journal of Medicinal Mushrooms* is 10594. According to SCImago Journal Rank (SJR), this journal is ranked 0.471. SCImago Journal Rank is an indicator, which measures the scientific influence of journals. It considers the number of citations received by a journal and the importance of the journals from where these citations come. SJR acts as an alternative to the Journal Impact Factor (or an average number of citations received in last 2 years). This journal has an h-index of 30. The best quartile for this journal is Q3.

The ISSN of *International Journal of Medicinal Mushrooms* journal is 15219437. An International Standard Serial Number (ISSN) is a unique code of 8 digits. It is used for the recognition of journals, newspapers, periodicals, and magazines in all kind of forms, be it print-media or electronic. *International Journal of Medicinal Mushrooms* is cited by a total of 618 articles during the last 3 years (Preceding 2020).

International Journal of Medicinal Mushrooms Impact Score 2020-2021

The impact score (IS) 2020 of *International Journal of Medicinal Mushrooms* is 1.92, which is computed in 2021 as per its definition. *International Journal of Medicinal Mushrooms* IS is increased by a factor of 0.05 and approximate percentage change is 2.65% when compared to preceding year 2019, which shows a **rising** trend. The impact score (IS), also denoted as Journal impact score (JIS), of an academic journal is a measure of the yearly average number of citations to recent articles published in that journal. It is based on Scopus data.

Aims and Scope

The rapid growth of interest in medicinal mushrooms research is matched by the large number of disparate groups that currently publish in a wide range of publications. The *International Journal of Medicinal Mushrooms* is the one source of information that will draw together all aspects of this exciting and expanding field - a source that will keep you up to date with the latest issues and practice. The *International Journal of Medicinal Mushrooms* 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. Letters to the editor on topics of interest to readers are also published.

For More Information and Submittion

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

Cover of the issue n8 and list of forthcoming papers

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50 North St
Danbury, CT 06810

ISSN: 1521-9437 Print
ISSN: 1940-4344 Online

International Journal of
Medicinal Mushrooms

2021, Vol. 23, Issue no.5

International Journal of
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2021, Vol. 23, Issue no.6

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Medicinal Mushrooms

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Points and Reviews

Mushrooms and immunity

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ABSTRACT

In the wide field of nutraceuticals, the effects of mushrooms on immunity, cancer and including autoimmunity have been proposed for centuries but in recent years a growing interest has led scientists to elucidate which specific compounds have bioactive properties and through which mechanisms. Glucans and specific proteins are responsible for most of the biological effects of mushrooms, particularly in terms of immunomodulatory and antitumor results. Proteins with bioactive effects include lectins, fungal immunomodulatory proteins (FIPs), ribosome inactivating proteins (RIPs), ribonucleases, laccases, among others. At the present status of knowledge, numerous studies have been performed on cell lines and murine models while only a few clinical trials have been conducted. As in most cases of dietary components, the multitude of variables implicated in the final effect and an inadequate standardization are expected to affect the observed differences, thus making the available evidence insufficient to justify the treatment of human diseases with mushrooms extracts. We will herein provide a comprehensive review and critically discussion the biochemical changes induced by different mushroom compounds as observed in *in vitro* studies, particularly on macrophages, dendritic cells, T cells, and NK cells, compared to *in vivo* and human studies. Additional effects are represented by lipids which constitute a minor part of mushrooms but may have a role in reducing serum cholesterol levels or phenols acting as antioxidant and reducing agents. Human studies provide a minority of available data, as well illustrated by a placebo-controlled study of athletes treated with β-glucan from *Pleurotus ostreatus*. Variables influencing study outcomes include different mushrooms strains, growing conditions, developmental stage, part of mushroom used, extraction method, and storage conditions. We foresee that future rigorous research will be needed to determine the potential of mushroom compounds for human health to reproduce the effects of some compounds such as lentinan which a metaanalysis demonstrated to increase the g cancer and which a metaanalysis demonstrated to increase the in the improvement of the patients quality of life.

Keywords: Immunity, Leukocytes, Cytokines, Mushrooms, Glucans, Nutraceutical

1. Introduction

Mushrooms and/or their extracts have been advocated as potential immune modulators, including for immunotherapy, treatment of cancer and immune regulation in autoimmunity. Fungi and mushrooms are extremely abundant worldwide with great diversity. Their number is approximately 1.5 million [1] and the number of mushroom species on earth is estimated to be around 150,000–160,000, with only 10% known to science. Therefore, we are familiar with 1% of the world fungal biota. Approximately 2000 species are safe and 700 have pharmacological properties, but not all of these are edible. The majority of mushrooms belongs to the class of Basidiomycetes, a few are Ascomycetes [2,3].

What we intend for 'mushroom' is a 'macrofungus', i.e. a fungus visible to human eye. It is usually the fruiting body (basidiocarp), consisting of a stipe and a cap. It produces spores that undergo germination, become mycelium and when mating with compatible hyphae form the primordia, which will develop into a fruiting body (Fig. 1) [4].

Mushrooms have been used for medical purposes since pre-historical times [5]. The 3500 year-old mummy discovered in 1991 in an Italian Alps receded glacier had a mushroom among his possessions, perhaps as a laxative for intestinal parasite disease [6]. Through centuries, mushrooms have had an important part in the culture of the civilizations, such as ancient Greece, Rome, China and India, for their medical, nutraceutical, dietary and psychotropic properties. Oriental medical tradition still relies on the use of mushroom for remedies preparation [7]. Scientific studies on the mechanisms underlying their medical properties were lacking until the last decades, when progresses have been made and molecular studies, clinical trials, papers, journals and congresses have been dedicated to mushrooms [2].

2. Mushroom type and composition

The gross composition of mushrooms is water (90%), and the remaining 10% consists of protein and amino acids (10%–40%) including primarily leucine, valine, glutamine, glutamic and aspartic acids, fats (2%–8%), mainly linoleic, oleic and palmitic fatty acid, carbohydrates (3%–28%) such as chitin, glycogen, trehalose and mannitol, fibers (3%–32%), and ash (8%–10%), the fraction of dry matter that remains after incineration, mainly composed of salts and metals, such as potassium, calcium, phosphorus, magnesium, iron, zinc and copper. Mushrooms also contain vitamins such as thiamine, riboflavin, niacin, tocopherol and vitamin D and antioxydants. Growth features, stage, harvest and storage condition may influence the chemical composition and the nutritional value of edible mushrooms [7–9]. While in the last centuries whole mushrooms were used for treatment and analysed in early studies, it is now ascertained that medical properties are attributable to polysaccharide fractions, some specific proteins or other bioactive compounds. They have been identified and purified from fruit bodies, cultured mycelium and cultured broth and studies now focus on their activities [7]. Medicinal mushrooms appear to have several functions, including immunomodulating, antitumor, antioxidant, cardioprotective, hypocholesterolemic, antiviral, antibiotic, anti-parasitic, antifungal, hepatoprotective and hypoglycemic effects [2]. In this review we will focus on the effects on immunity. Bioactive beneficial properties have been found in both edible and non-edible mushrooms. For example, *Ganoderma* and *Coriolus* are considered as medicinal but not edible. The most common medicinal mushrooms are listed in Table 1 [7].

3. Mushroom bioactive compounds

3.1 Polysaccharides

Polysaccharides are the mushroom-derived molecules with the most biologically potent effects and numerous studies

have been performed on hundreds of different species. Glucans are the main polysaccharides found in mushrooms, as they constitute the fungal cell wall, and are excreted into the cell growth medium, therefore their recovery, purification and characterization is generally feasible [7,10]. As glucans are recognized by different immune cells, their effects are pleiotropic and several experiments have tried to elucidate them. Different methods are available to extract and purify glucans, potentially affecting their activities [11]. The most common type of glucan and the most important for biological activities consists of a backbone of D-glucose-linked β-(1→ 3) frequently branched at O-6 by β-D-glucose residues as side chains (hereafter referred to as β-glucan) [10]. A large variability can be observed in mushroom species and its concentrations range from 0.21 to 0.53 g/100 g dry weight [12]. In addition, α- and mixed D-glucans can be found [11], even though the majority are β-glucans, including lentinan from *Lentinus edodes*, schizophyllan from *Schizophyllum commune*, krestin from *Coriolus versicolor*, grifolan from *Grifola frondosa* and scleroglucan from *Sclerotinia sclerotiorum* [13].

Glucans cannot be synthesized and their structure includes pathogen-associated molecular patterns (PAMPs), a highly conserved pattern able to induce the immune response. Different membrane receptors, the pattern-recognition receptors (PRRs), can recognize PAMPs, such as Dectin-1, complement receptor 3 (CR3), NOD-like (NLR), RIG-Ilike (RLR), and Toll-like receptors (TLR) [14,15]. These are found on macrophages, monocytes, neutrophils, dendritic cells (DCs) and natural killer (NK) cells [14] and bind with the highest affinity the polymers with the greatest molecular weight, such as schizophyllan and scleroglucan [13]. After binding, the signal is transduced through direct receptor activation and/or cellular pathway activation. Studies in animal models demonstrate that a possible mechanism could be the glucan-induced clustering of Dectin-1, with subsequent recruitment of downstream proteins activating the nuclear factor kappa-light-chain-enhancer of activated B cells (NF-κB) and mediating the transcription of genes [16]. Dectin-1 is one of the most important innate immune receptors for glucans and notably knock out mice for this receptor show an increased susceptibility to chemically induced colitis, as a consequence of altered responses to fungi. Moreover, in humans, a polymorphism in the gene for Dectin-1 is linked to a severe form of ulcerative colitis [17]. Other studies *in vitro* showed how the macrophage response to β-glucans could be influenced by the inflammatory milieu. In fact, immune cells can be activated by membrane PRRs, by direct membrane binding or by intracellular PRRs, depending on factors as priming with lipopolysaccharide (LPS) and various cytokines and different inflammatory pathways are initiated [18].

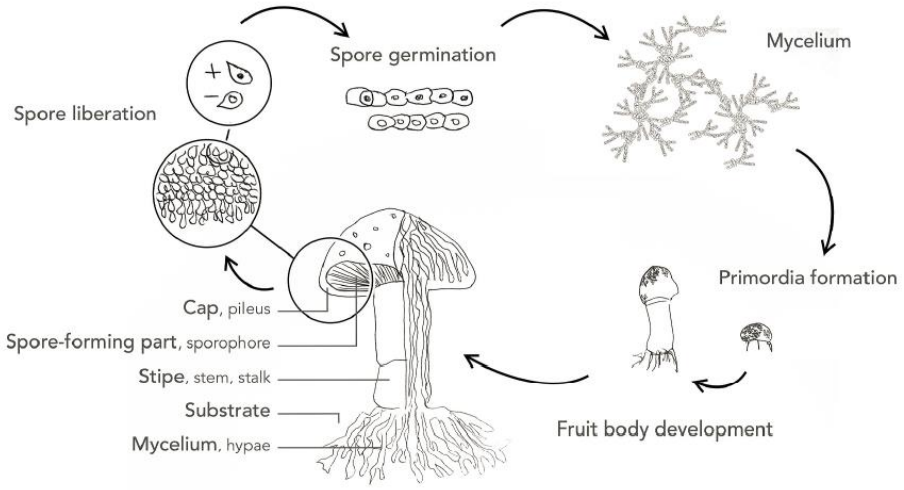

Fig. 1. Schematic representation of mushrooms life cycle.

The route of administration of glucans has been an issue, and the bioavailability after oral intake remains debated, with only intraperitoneal or intravenous applications being considered adequate. However, further experiments showed that orally given glucan has similar effects to an injected dose [19] and that the gut-associated lymphoid tissue is the principal site of interaction between mushroom extracts and immune cells, which have membrane PRRs [20].

Table 1 Classification of the most common medicinal mushrooms.

Genus	Latin name	Common name	Family	Class
Agaricus	*A. bisporus* *A. blazei* *A. subrufescens*	White mushroom Sun mushroom Almond mushroom	Agaricaceae	Basidiomycetes
Lentinus	*Lentinula edodes* *L. polychrous*	Shiitake	Tricholomataceae	Basidiomycetes
Pleurotus	*P. ostreatus* *P. nebrodensis* *P.citrinopileatus* *P. sajor-caju*	Oyster mushrooms	Pleurotaceae	Basidiomycetes
Ganoderma	*G. lucidum*	Reishi	Ganodermataceae	Basidiomycetes
Schizophyllum	*S. commune*	Button mushroom	Schizophyllaceae	Basidiomycetes
Trametes	*Coriolus (or Trametes) versicolor*	Turkey tail	Polyporaceae	Basidiomycetes
Grifola	*G. frondosa*	Maitake	Polyporaceae	Basidiomycetes
Sclerotinia	*S. sclerotiorum*	Cottony rot	Sclerotiniaceae	Ascomycetes

3.2. Effects of polysaccharides on macrophages

Macrophages play a role in tissue homeostasis, immune surveillance, response against pathogens and in the resolution of inflammation. They are able to secrete cytokines and mediators and to polarize to M1, eliciting a cytotoxic immune response, or to M2, with homeostatic and anti-inflammatory effects [21,22]. In macrophages, the β-glucans immunomodulatory action involves the activation of NF-κB [23] and stimulates the generation of reactive oxygen species (ROS) and nitric oxide (NO), which contribute to the death of microorganisms. The effect

on cytokines has been demonstrated in several studies on different mushrooms mostly for β-glucan, in both murine and human macrophages, showing increased expression of interleukin (IL)-1, IL-6, tumor necrosis factor (TNF)-α and other pro-inflammatory cytokines and decreased expression or no induction of anti-inflammatory factors, as IL-10 [24–32]. Table 2 depicts the detailed effects of glucans on macrophages in different studies and Fig. 2 illustrates them.

Macrophage stimulation by glucans appears to be important in murine models to mitigate chemotherapy-induced myelosuppression [33, 34], to induce wound healing [35], as a defence against viral [36] and bacterial infections, i.e. against Salmonella [37] and Cryptococcus [38], as well as against cancer [39,40].

In a few studies α-glucan effect was examined. An α-glucan from *Grifola frondosa* was administered to diabetic mice, leading to reduction of NO and IL-1 macrophages production, improvement of glucose, triglycerides, cholesterol and free fatty acid levels and amelioration of ultrastructural changes of pancreatic β-cells, suggesting a protective role on pancreatic islets [41].

Table 2 Effects of mushroom glucans on macrophages.

Mushroom	Type of glucan	Type of macrophages	Pro- or anti-inflammatory effects	Other effect	Ref
Ganoderma australe	β-glucan	Murine	Pro-inflammatory		[25]
Polyporus rhinocerus	β-glucan (PRA-1p)	Murine	Pro-inflammatory		[26]
Pleurotus sajor-caju	β-glucan	Murine	Pro-inflammatory		[27]
Amillariella mellea	β-glucan	Murine	Pro-inflammatory		[28]
Volvariella volvacea	α-glucan	Murine	Pro-inflammatory		[30]
Macrocybe lobayensis	Crude polysaccharide	Murine	Pro-inflammatory		[31]
Russula senecis	Crude polysaccharide	Murine	Pro-inflammatory		[32]
Grifola frondosa	MT-α-glucan (400,000–450,000Da)	Murine	Anti-inflammatory	Improvement of glucose, triglycerides, cholesterol and free fatty acid levels. Amelioration of ultrastructural changes of pancreatic β-cells	[41]
Lentinus edodes	β-glucan (LeP-N2)	Murine	Pro-inflammatory		[42]
Grifola frondosa	β-glucan	Murine	Anti-inflammatory		[50]
Pleurotus ostreatus	Mushroom concentrate	Murine	Anti-inflammatory		[52]
Lentinula edodes	β-glucan (lentinan)	Murine	Anti-inflammatory		[53]
Xylaria nigripes	Polysaccharides	Murine	Anti-inflammatory		[54]
Agrocybe chaxingu	β-glucan	Murine	Anti-inflammatory	Topical application reduced ear-induced edema in mice	[55]
Grifola frondosa	β-glucan	Murine	Anti-inflammatory		[56]
Lentinula edodes	β-glucan (lentinan)	Human	Anti-inflammatory		[29]
Ganoderma lucidum, Lentinula edodes and *Grifola frondosa*	Three extracts from nine commercial preparation, with high β-glucan-α-glucan ratio	Human	Pro-inflammatory		[43]
Pleurotus citrinopileatus	Polysaccharide fraction (450 kDa)	Human	Anti-inflammatory		[44]
Agaricus subrufescens (syn. Agaricus blazei Murill) and Coprinus comatus	Zymosan, curdlan and polysaccharide extract	Human	Pro-inflammatory		[45]
Cordyceps militaris	Aqueous extract, alkaline extract, β-(1 → 3)-D-glucan	Human	Pro or anti-inflammatory effects, depending on aqueous or alkaline extraction		[46]
Lentinus edodes	'in house' lentinan and commercial extract	Human	Anti-inflammatory		[51]

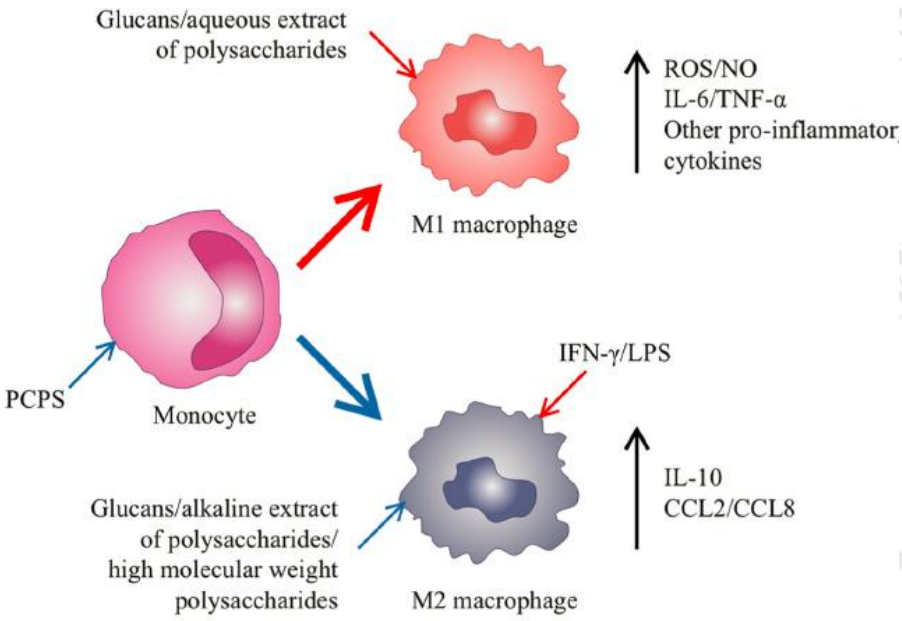

Fig. 2. Effects of mushroom polysaccharides on monocytes and macrophages. Mushroom polysaccharides seem to have a pro-inflammatory activity, inducing M1 macrophages. On the other hand, if monocytes are stimulated with glucans as PCPS at early stages, the differentiation in M2 anti-inflammatory macrophages is promoted.

Of note, in a recent study Li and Colleague obtained a β-glucan (LeP- N2) from *Lentinus edodes* and showed its ability to activate macrophages with ROS and NO production in a dose-dependent manner, with no cytotoxicity until the dose of 100 μg/mL [42].

In a study on human macrophages, nine commercially available preparations from three mushroom species, *Ganoderma lucidum*, *Lentinula edodes*, and *Grifola frondosa*, were analysed for β- and α-glucan contents and three

extracts were selected based on the highest β-glucan contents. These extracts led to a dose-dependent increase in cytokine expression in both non-LPS and LPS stimulated macrophages, with a synergistic effect on the expression of IL-1α, IL-6 and TNF-α and an antagonistic effect on the expression of IL-10. A combined mushroom formula had EC50 values lower than 100 μg/mL and even lower in TNF-α expression from LPS treated macrophages compared to the individual extracts, suggesting a potential synergistic effect of the mushroom formulas [43].

As already mentioned, the capability of mushrooms to stimulate the production of pro-inflammatory cytokines is likely dependent on complex factors, among which an important variable is the stage of maturation of immune cell precursors. In fact, a polysaccharide derived from *Pleurotus citrinopileatus* (PCPS) showed anti-inflammatory effect on macrophages, modulating the monocyte-to-macrophage differentiation early, at the monocyte stage, promoting the development of alternative activated macrophages with anti-inflammatory properties. The response of PCPS-treated monocytes to interferon (IFN)-γ + LPS led to reduced levels of TNF, IL-6 and CCR2 and a tendency to increase IL-10, CCL2 and CCL8, with anti-inflammatory effect. Therefore, an early stimulation of macrophage precursor with mushroom glucans might induce a long- lasting anti-inflammatory effect [44]. Zymosan and mushroom polysaccharide extracts led to a different response of THP-1 monocytes compared to macrophages, the latter producing higher levels of cytokines upon stimulation [45].

Other factors implicated in the bioactivity of mushroom polysaccharides are their composition and structure. It has been demonstrated that polysaccharides derived from the Ascomycete *Cordyceps militaris* have different effects depending on the type of extraction. The aqueous extract, which is more rich of mannose and galactose and poor of glucose, stimulates a pro-inflammatory response, while the alkaline extract, with a higher amount of glucose and a lower content of the two other monosaccharides, show the inhibition of inflammatory genes, as observed for the purified β-(1 → 3)-D-glucan [46]. Moreover, when analysed in detail, the effect of glucans might be dual with pro-inflammatory properties in some pathways and inhibitory in others. In this regards, Ahn and Colleagues described that lentinan had an effect on inflammasome activation and cytokine maturation in murine bone marrow-derived macrophages. Lentinan up-regulated pro-inflammatory cytokines and the expression of the inflammasome components NLRP3 and pro-IL-1β. However, lentinan also selectively inhibited the IL-1β maturation in response to AIM2 inflammasome activation, ameliorated LPS-induced lethality and reduced IL-1β secretion induced by Listeria monocytogenes-mediated AIM2 inflammasome activation. Therefore, while stimulating the expression of pro-inflammatory cytokines, it selectively attenuates the cytokine maturation in response to AIM2 inflammasome activation. The Authors suggest lentinan as an *anti*-inflammasome agent, especially for AIM2 inflammasome [47]. On the contrary, in previous studies, other glucans as paramylon and zymosan failed to modulate IL-1β secretion [48,49]. It could be possible that polysaccharides have different effect depending on the type of glucans, their chemical structures, the method for extraction, the cells and the setting used to study their effects and a multitude of variables not yet completely understood. For example, a high molecular weight fraction from *Grifola frondosa* inhibits TNF-α, IL-6 and NF-κB activation in LPS-induced macrophages. On the base of chemical and enzymatic analyses, a glucan with a β-(1 → 4)-linked backbone and β-(1 → 6)-linked branches has been identified and may contribute to the anti-inflammatory activity, interacting with TLR2 rather than Dectin-1 or CR3 receptors [50]. Murphy and Colleagues compared an 'in house' lentinan and a commercial extract and reported that the latter has higher amounts of α-glucans and less β-glucans while both reduce cytokine-induced NF-κB activation in human alveolar epithelial A549 cells, with the 'in house' extract being more potent. However, in activated THP-1 derived macrophages, the commercial extract is more effective in attenuating

pro-inflammatory cytokine producti , IL-8, IL-2, IL-6, IL-22), transforming growth factor (TGF)-β -10.

Moreover, it reduces the oxidative stress-induced early apoptosis, while the 'in house' extract attenuated late apoptosis [51]. Other studies support the observation of anti-inflammatory properties of glucans on macrophages, thus reducing the production of NO and cytokines even after stimulation [52–56]. Of note, an *Agaricus blazei Murill* extract, known to be pro-inflammatory *in vitro*, showed reduction of cytokines levels in human whole blood of healthy volunteers after oral intake of the extract for several days [57].

Taken altogether, the unconclusive and in some cases conflicting results account for the great heterogeneity of mushrooms, derived polysaccharides, extraction techniques, biological pathways involved and underline the importance of rigorous studies and trials to settle the issue.

3.3. Effects of polysaccharides on dendritic (DCs) and T cells

DCs have an important role in immune defence, contributing to antigen presentation to cluster of differentiation (CD)4+ and CD8+ T cells, thus stimulating acquired immune response against pathogens and tumor cells [58]. The immunomodulatory effects of glucans on DCs are mediated by Dectin-1 for some compounds [59], by TLR4 for others [60] and the intracellular signaling appears to be transduced through the MEK-ERK cascade [61]. The effects of glucans on DCs and T cells *in vitro* are reported in Table 3 and illustrated in Fig. 3.

The α-glucan YM-2A, isolated from *Grifola frondosa*, was shown to have an impact on maturation and function of DCs, increasing the expression of maturation markers, as major histocompatibility complex (MHC) class II molecules, CD80 and CD86, in dose-dependent manner, increasing IL-12p40, TNF-α, and IL-6 production by DCs, but not IL-10 and promoting CD4 and CD8 lymphocytes proliferation and production of IFN-γ. In addition, it had an adjuvant effect on a vaccine against murine tumors, increasing IFN-γ producing T cells thus reducing tumor growth and improving survival in murine models [59].

A soluble β-glucan D-fraction extracted from *Grifola frondosa*, in combination with a TLR9 agonist, synergistically increases the surface expression of CD80, CD86 and MHC class II and cytokine production in DCs, but not IL-10, generating a polarized type 1 T cell response. As for α-glucan, it acts as an anti-tumor, increasing DCs in the tumor site and inducing activation of CD4 and CD8 T lymphocytes [62]. A different study on *Grifola frondosa* demonstrated that labelled MD-extract administered orally to tumor-bearing mice is captured by macrophages and DCs in the Peyer's patches, transported to the spleen significantly changing the cellular composition, increasing the number of CD4, CD8, B, NK cells and DCs, while decreasing the number of splenic myeloid-derived suppressor cells. It also induces the immune response against cancer by increasing the IFN-γ expression in Peyer's patches, spleen tumor and mesenteric lymph nodes. Moreover, the proliferation of T lymphocytes induced by MD/tumor lysate DCs was higher than that induced by tumor lysate alone-stimulated DCs [63].

A similar effect can be obtained with schizophyllan [64] and with sparan derived from *Sparassis crispa*, which increased maturation and cytokine production in murine DCs and promote T lymphocyte proliferation and activation with release of IFN-γ [60]. A *Ganoderma lucidum* extract activates DCs, induces secretion of IL-23 but not IL-12 and promotes the differentiation of Th17 cells. T cells produce large amounts of IL-17 but not of IFN-γ, different from cells cultured with LPS-stimulated DCs [61]. An extract from *Agaricus brasiliensis* induces the production IL-6 and TNF-α from bone marrow

derived DCs in a dose dependent manner, in the presence of exogenous granulocyte macrophage-colony stimulating factor (GM-CSF). In addition, DCs have a crucial role in stimulating IFN-γ production by splenocytes [65].

The DCs and T cells-mediated immunomodulating potential of mushrooms is effective in murine models of colitis, where *Grifola frondosa* and *Agaricus bisporus* extracts stimulate IL-23 [66], malaria parasite infection, with lentinan-induced DCs maturation and Th1 immune response [67], allergy, with Th1 polarization and reduced IgE production elicited by *Agaricus blazei Murill* extract [68]. In addition, paramylon, a β-1,3-D-glucan isolated from *Euglena gracilis Z*, has been shown to inhibit the development of atopic dermatitis in mice models [69]. Through activation of DCs in the Peyer's patches and induction of T-cell response, the oral administration of glucan fractions inhibits tumor growth and improves survival rate in murine models of colon carcinoma and melanoma [70].

In human DCs a mushroom extract leads to significant dose- dependent elevation of IL-8, CCL4, granulocyte-colony stimulating factor (G-CSF), TNF-α, IL-1β and IL-6. The increase of G-CSF, TNF-α and IL-1β is greater than those induced by LPS, whereas IL-2, IL-8 and IFN-γ levels are similar after extract and LPS stimulation. IL-5, IL-10, IL-12 and IL-13 are not increased by the same mushroom extracts [71]. In a different study, human DCs analysed *in vitro* show no cytokine production and no increase of maturation markers, albeit T cells stimulated by glucans and immunoglobulin against viral antigens are significantly elevated [72].

Table 3 Effects of mushroom glucans on dendritic cells and lymphocytes.

Mushroom	Type of glucan	Type of DCs	Effects on DC and lymphocytes	Other effects	Ref
Grifola frondosa	α-glucan YM-2A	Murine	DC maturation, CD4 and CD8 lymphocytes stimulation	Enhanced DCs vaccine as an adjuvant	[59]
Grifola frondosa	Soluble β-glucan D-fraction	Murine	DC maturation, CD4 and CD8 lymphocytes stimulation	Enhanced DCs anti-tumor effect	[62]
Grifola frondosa	MD-fraction	Murine	DC maturation, CD4 and CD8 lymphocytes stimulation	Reduction of tumor volume	[63]
Schizophyllum commune	Schizophyllan K3-SPG	Murine	CD8 lymphocyte stimulation		[64]
Sparassis crispa	Sparan (1,3-β-D-glucan)	Murine	DC maturation, T lymphocyte stimulation		[60]
Ganoderma lucidum	Water soluble extract	Murine	DC maturation, CD4 lymphocyte stimulation		[61]
Agaricus brasiliensis	1,6-β-glucan with a small amount of 1,3-β-glucan extract	Murine	Splenocyte stimulation		[65]
AndoSan™ extract (82.4% from *Agaricus blazei Murill*, 14.7% from *Hericium erinaceum* and 2.9% from *G. frondosa*)	Moisture 5.8 g, protein 2.6 g, fat 0.3 g, carbohydrates 89.4 g (of which β-glucan constitutes 2.8 g) and ash 1.9 g	Human		Pro-inflammatory cytokine release	[71]
Pleurotus sajor-caju	β-glucan extract	Human	CD4 and CD8 lymphocytes stimulation	IgG neutralizing antibodies to HPV (in mice)	[72]

Legend. DCs: dendritic cells. CD: cluster of differentiation. IgG: immunoglobulin G. HPV: human papilloma virus.

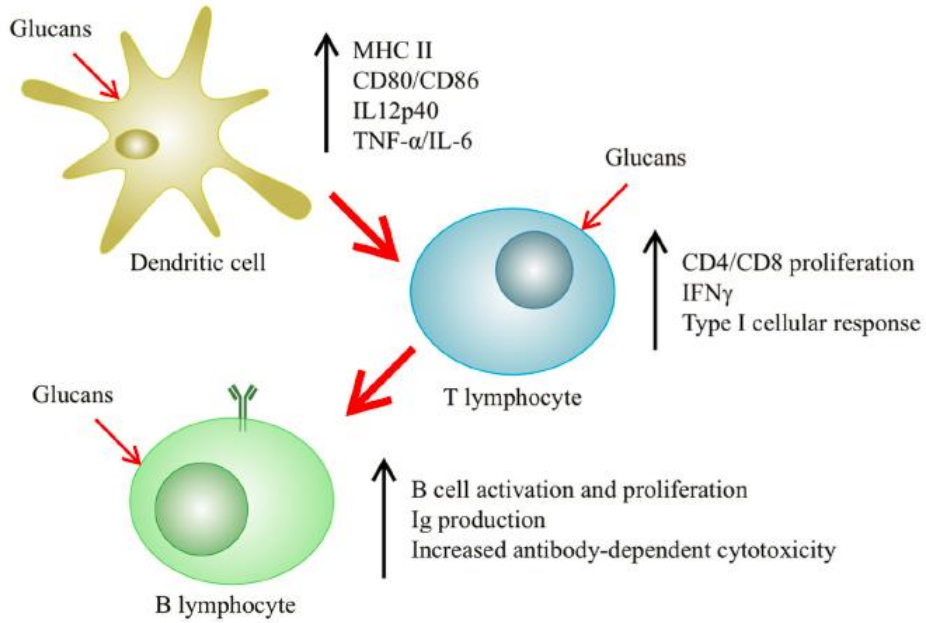

Fig. 3. Effects of mushroom glucans on dendritic cells and lymphocytes. Glucans activate dendritic cells and T lymphocyte proliferation and polarization towards a type 1 immune response. B cells are also activated and Ig production is increased after glucans stimulation. Legend. MHC II: major histocompatibility complex class II. CD: cluster of differentiation. IL: interleukin. TNF: tumor necrosis factor. IFN: interferon. Ig: immunoglobulin. Red arrows indicate pro- inflammatory stimuli. . (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

The molecular structure of glucans and their ability to stimulate DCs to activate acquired immune response led to test their potential role in enhancing vaccine delivery and efficacy. Glucans are good antigen carriers and can be used for nasal delivery of vaccines, as they are up- taken in the nasal-associated lymphoid tissue [73,74]. Moreover, it has been shown that carbon nanotubes binding lentinan are able to increase antigen accumulation in cells and potentiate cellular and humoral immunity [75]. It has also been demonstrated that the intravenous injection of K3-fraction from schizophyllan, but not a TLR9 agonist alone, is accumulated in the tumor microenvironment and stimulates immunogenic cell death of malignant cells through IFN and IL-12 production [76]. The glucan-induced maturation of DCs into more immunostimulatory cells is a promising tool for a more efficient immunotherapy against cancer.

(...to be continued)

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