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

ISMS e-Congress Huge Success – 2024 Congress in USA

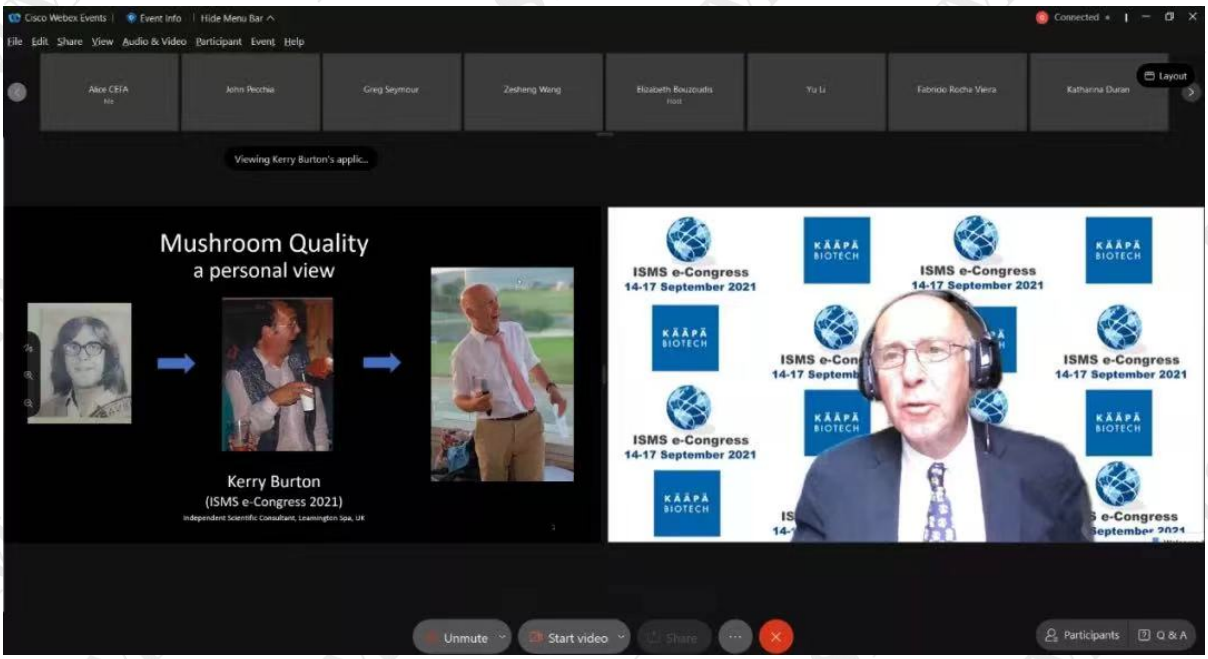
By Greg Seymour, President of ISMS

The live phase of the ISMS online e-Congress came to a close on Friday 17 September to widespread acclaim from the 288 delegates, authors, and presenters who took part in the event. Despite not being able to meet face-to-face in Vancouver, the audience spoke highly of the quality of the presenters and their presentations, the quality of the science, and the innovative online delivery format.

As one delegate commented, “I had a front seat with no distractions all week, enjoying a cup of tea and a sandwich while watching each day. It felt like I was in a one-on-one discussion with each presenter. While I can’t wait to catch up with everyone at the next live Congress, the online format sure had lots of good things going for it.”

One of the huge benefits is that the recordings of the live stage presentations including the Q&A sessions are now available on the 24/7 on-demand section of the e-Congress site, and will remain open to registered delegates until Sunday 17 October.

Registration is still open on the ISMS website for those who haven’t already registered. So if you weren’t able to make it live - you haven’t missed out on seeing and hearing some excellent cutting-edge research. As well as being able to watch the highly entertaining keynotes and live oral presentations, registered delegates can still view the 56 recorded oral videos, 58 posters, and the sponsor pages.



Kerry Burton gave a lecture titled Research into mushroom quality

The big news at the end of the final day was provided by Rachel Roberts, President of the American Mushroom Institute (AMI), when she announced that following discussions between AMI and ISMS, the 2024 ISMS Congress will be held in conjunction with the 2024 North American Mushroom Conference.

Rachel Roberts

An exact date and location for the event had yet to finalised but is likely to be in the northern autumn (fall) of 2024 somewhere in southern western USA. As soon as details are known they will be publicised widely. With the announcement by Mushrooms Canada last week that the NAMC scheduled for June 2022 in Vancouver has been cancelled, the 2024 combined event will be the first chance many of will get together at a major international mushroom conference.

The last ISMS Congress held in the US was also in conjunction the NAMC in Miami in 2004. That event was an outstanding success and Rachel was quick to assure the e-Congress audience that the 2024 event will be another highly memorable experience.

Delegates at the 2024 Congress can expect a truly innovative program with many of the learnings from the 2021 e-Congress incorporated into the 2024 event. Make a note in your diary now for what will be THE event of 2024.

Russian Mushroom Days 2021

By Aleksandr Khrenov

It will be more mushrooms, more competition and more activity.

Such few words can summarize discussions at Russian Mushroom Days 2021.

About 160 participants from 9 countries gathered at September 14-15 in Krasnodar EXPOGRAD SOUTH for 26th Russian Mushroom Days.

General Sponsor- Sylvan, Platinum Sponsor – Master Champ, Gold Sponsor – Agro-Project, Silver Sponsor – Christiaens Group.

Mr. Aleksandr Khrenov, General Director of Russian Mushroom School, Mr. Peter Zavgorodniy, the biggest exotic mushrooms producer at South of Russia and Mr. Andrey Zhuravel, Head of Plant and Mushroom Department at Kranodar Area Ministry of Agricultural have opened Russian Mushroom Days 2021.

They mentioned that Russian Mushroom Industry was grown last 3 year very fast and now Russia is a third mushroom producer in the Europe after Poland and Netherlands. In 2021 about 120 000 tons of mushrooms will be grown in Russia. There are big modern mushroom farms were built in the country. Russia has a wide diversity of raw materials for mushroom industry which could be used for different types of mushroom growing. Today level of cultivated mushrooms consumption is only 870 gr per head in Russian. There is still a big opportunity for local market developing. Cost of mushroom production let to expand a mushroom product export.

Krasnodar area is a leader among Russian regions in mushroom production. 25% of Agaricus, 10% of Pleurotus and 60% of exotic mushrooms are growing here.

EXPO «Equipmqnt and materials for mushroom growing and processing» introduced 21 company from Russia, Poland, Netherland, Italy, Spain, France and China.

First time we have more Russian then foreign companies at the Mushroom EXPO. Compost, spawn, peat, casing soil, packaging, shelves and picking trolley, equipment for Pleurotus and Exotic mushrooms production are produced in Russia now and supplied to Russian and foreign growers.

International Conference about Mushroom Business developing in Russia was organize in off-line and on-line format. Because of COVID limitations 4 from 23 speakers were not able to come to Russia they did presentations on-line. Main Conference topic was a situation and prospects of Russian local mushroom market. Three times production rising lead to price dropping more than 20%. At the same time raw materials, packing materials and labor cost seriously increased. How to keep a profit level of mushroom business and obtain it developing? Speakers offer few options: demand stimulating buy mushroom promotions, the product range expanding, standardization of mushroom grades, processing and addition value product creating.

At Section «Innovations from Russian Researchers» scientists from Moscow State University, Kuban State Agro University and Government Scientist and Research Center of Virology and Biotech “Vector” offered to growers ideas about spend compost processing, spawn production and medicine mushrooms products.

At sections «Agaricus Mushrooms Growing» and «Pleurotus and Exotic Mushrooms Growing» main Russian and foreign experts discussed important questions determining production stability, high yield and quality.

Conference was able on-line at Conference application.

Agaricus Section Sponsor-GTL Europe, Pleurotus and Exotic Mushrooms Section Sponsor -Technik.

First time at Russian Mushroom Days was arranged “MushroomBBQ-Show”. Three Great Chiefs from Krasnodar restaurants Ludmila Dikovskaya, Pavel Proskurin и and Vladimir Shabalin show master-class about mushroom cooking

at grill Weber. Carpaccio from Agaricus mushrooms, Enoki in the bacon, Burger with Portabelo, Sote from Beach mushrooms and Eringy were easy to cook and fantastically tasty.

After Chiefs Show, mushroom growers' teams started to fight for Prize -Professional Weber grill. «Voronezh Mushrooms», «South Mushroom Company», «Tula Mushroom Company», «Technik» and "Mushroom School Friends" try to surprise Chiefs buy mushroom dishes cooked at grill. All 3 Chiefs decide that best dishes were – Pleurotus sausages from "Technik" team.

Weber grill was provided by "Original – grill" Shop, Agaricus Mushrooms and Portobelo were provided by "Russian Mushrooms" farm, Pleurotus Mushrooms were provided by Rozmirskiy Farm. Shiitake, Eringy, Beach Mushrooms and Enoki were provided by "Eat Mushrooms" company.

Russian Mushroom Days confirmed a serious plan of Russian mushroom companies to solve today low-price period and continue to expand business. It is mean that more mushrooms will be produced in Russia, competition will be strong and more power and creative should be done for win in it.

Ukrainian Mushroom Days 2021

By Inna Ustylovska

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.

2021 Ukrainian Mushroom Days was held on 20-21st of October in Kyiv, the event includes TWO DAYS of ongoing CONFERENCE and EXHIBITION.

The organizer of the Exhibition-Conference is UMDIS Mushroom Information Agency of Eastern Europe.

The event was sponsored by Agaris, Amycel, Agro-Project, World of Straw, Mexeo, Mushroom Team, Vierrebi, Alpie, DMP, GTL Europe, Hoving Holland.

This time Ukrainian Mushroom Days brought together not only Ukrainian, Russian and Belarusian farms – but delegations from the largest farms in Kazakhstan, Uzbekistan, Azerbaijan, Georgia, Armenia, Moldova, becoming an industry event not only for Eastern Europe, but also for Central Asia.

The event gathered **350 people from 20 countries**!

There were **55 companies-exhibitors**.

The program of Conference combined **27 speakers**, two great discussions with Monterey and Mushroom Council.

Mushroom Consumption May Lower Risk of Depression

By Tracy cox

Mushrooms have been making headlines due to their many health advantages. Not only do they lower one's risk of cancer and premature death, but new research led by Penn State College of Medicine also reveals that these superfoods may benefit a person's mental health.

Penn State researchers used data on diet and mental health collected from more than 24,000 U.S. adults between 2005 and 2016. They found that people who ate mushrooms had lower odds of having depression.

According to the researchers, mushrooms contain ergothioneine, an antioxidant that may protect against cell and tissue damage in the body. Studies have shown that antioxidants help prevent several mental illnesses, such as schizophrenia, bipolar disorder and depression.

"Mushrooms are the highest dietary source of the amino acid ergothioneine — an anti-inflammatory which cannot be synthesized by humans," said lead researcher Djibril Ba, who recently graduated from the epidemiology doctoral program at the College of Medicine. "Having high levels of this may lower the risk of oxidative stress, which could also reduce the symptoms of depression."

White button mushrooms, which are the most commonly consumed mushroom variety in the U.S., contain potassium, which is believed to lower anxiety. In addition, certain other species of edible mushrooms, especially Hericium erinaceus, also known as Lion's Mane, may stimulate the expression of neurotrophic factors such as nerve growth factor synthesis, which could have an impact on preventing neuropsychiatric disorders including depression.

According to the researchers, college-educated, non-Hispanic white women were more likely to eat mushrooms. The average age of surveyed participants was 45, and the majority (66%) were non-Hispanic white people. The investigators observed a significant association between mushroom consumption and lower odds of depression after accounting for socio-demographics, major risk factors, self-reported diseases, medications and other dietary factors. They said, however, that there was no clear additional benefit with relatively high mushroom intake.

“The study adds to the growing list of possible health benefits of eating mushrooms,” said Joshua Muscat, a Penn State Cancer Institute researcher and professor of public health sciences.

The team conducted a secondary analysis to see if the risk of depression could be lowered by replacing a serving of red or processed meat with a serving of mushrooms each day. However, findings show that this substitution was not associated with lower odds of depression.

Prior to this research, there have been few studies to examine the association between mushroom consumption and depression, and the majority have been clinical trials with fewer than 100 participants. The researchers said this study highlights the potential clinical and public health importance of mushroom consumption as a means of reducing depression and preventing other diseases.

The researchers noted some limitations that could be addressed in future studies. The data did not provide details on the types of mushrooms. As a result, the researchers could not determine the effects of specific types of mushrooms on depression. Food codes issued by the U.S. Department of Agriculture were used to determine mushroom intake; therefore, some entries may have been misclassified or inaccurately recorded.

John Richie and Xiang Gao from Penn State Cancer Institute; Laila Al-Shaar and Vernon Chinchilli from Penn State College of Medicine; and Robert Beelman from Penn State College of Agricultural Sciences also contributed to this research. The researchers declare no conflicts of interest or specific funding support.

Source: https://news.psu.edu/

Up-coming Events

2021 International Mushroom Days

Affected by the COVID-19, the 2021 International Mushroom Days, originally scheduled to be held at the end of November has been postponed to December 28th-30th in Xiamen Fliport C&E Center, China. The Expo will help rural revitalization, promote innovation and development of the whole industrial chain of Chinese edible mushroom, promote the integration of domestic and foreign trade, all-channel layout and sustainable development, and the high-quality products of the whole industrial chain of mushroom at home and abroad in the post-epidemic era.

2021 International Mushroom days is hosted by China Chamber of Commerce of I/E of Foodstuffs, Native Produce and Animal By-products (CFNA), organized by Xiamen Vissea Exhibition Service Co., LTD., Xiamen Wutong Fliport Hotel and Xiamen Fliport C&E Center.

As an upgraded version of the 2020 International Mushroom Days (Xiamen), the new Expo with an extended scale will occupy the first and second floor exhibition halls of Xiamen Fliport C&E Center. The organizing committee will pay more attention to the effective combination of the conference and exhibition, and make use of the space advantages to create an integrated exhibition. The first floor of the exhibition hall will be used as the Intelligent Manufacturing and Innovative Pavilion of Mushroom, which will display various equipment and supporting facilities, including raw and auxiliary materials, production, sterilization, inoculation, environmental simulation, packaging and processing. On the second floor, a mushroom industry revitalization hall will be set up to display the achievements of rural revitalization and the style of premium edible mushroom brand enterprises. The total scale of the Expo will be 15,000 square meters with about 600 international standard booths.

Xiamen Wutong Fliport Hotel and Xiamen Fliport C&E Center

NAMC 2022 in Vancouver Cancelled

In light of the continuing pandemic and ongoing group gathering and travel restrictions, Mushrooms Canada and its North American Mushroom Conference partners have made the difficult decision to cancel the 2022 (26th) North American Mushroom Conference in Vancouver, Canada. This decision was made at the borard meeting on 22 September.

A statement by the organisers Mushrooms Canada and the NAMC comittee on 23 September read: "As the conference date approaches, we have been seeing previously lifted government restrictions reintroduced and many re-opening plans put on pause, all of which could significantly impact conference participation. Ultimately, this uncertainty left us with a tough decision, but one we feel we had to make. We thank all those who have shown their continued support for the conference during this challenging time. More details will be shared in the coming months about the 2024 North American Mushroom Conference hosted by the American Mushroom Institute and we look forward to seeing you there."

The statement also said, that sponsors or exhibitors who already signed up for the NAMC 2022, will be refunded.

The NAMC was scheduled before to be held in June 2021 in conjunction with the ISMS Congress, but was postponed because of COVID to 2022. Big events in the mushroom industry have been struggling with the pandemic and its (travel) restrictions for some time now. The ISMS Congress was held last week in an online format (report in Mushroom Business magazine no 108). At this e-Congress, it was announced that the 2024 ISMS Congress will be held in conjunction with the NAMC in the (Western) USA.

Usually, the NAMC is organised every two years (alternately in the US and Canada), so the 2024 edition will be the 26th. There is an (unconfirmed) chance that the 27th NAMC will be held in Vancouver in 2026 after all.

Further Information: https://mushroomconference.org/

The Dutch Mushroom Days in the Spring of 2022

The next edition of the Mushroom Days will probably be held in the spring of 2022.

The Mushroom Days Foundation announced this in a letter to their exhibitors. The event is scheduled for Wednesday March 30, Thursday March 31 and Friday April 1 in the Brabanthallen in Den Bosch in the Netherlands. That still seems a long way ahead, but the Mushroom Days Foundation is looking forward with great optimism and therefore wants to start with the preparations. But because of the Covid-19 pandemic there will be a slight difference. For this edition of the Mushroom Days there is unfortunately a limited set-up time due to a prior mega event. The desired hall is therefore only available on Monday around noon. This entails a different method than the exhibitors are used to.

A tightly controlled structure will require a clear on time final participation, the size of the stand and all desired facilities. Unfortunately it will not be possible to organize meetings for exhibitors to present their plans, nor for questions and room for discussion. The exhibitors were invited by letter to indicate whether they are positive about the intention to hold the 36th edition in the spring of 2022.

The Mushroom Days Foundation is once again looking forward to making it a success and inviting visitors with a warm welcome.

Source: https://mushroommatter.com/

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

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

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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 0.1 nM 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 disease model.

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

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A Systematic Review on Bioactivity of Brazilian Mushrooms (Agaricomycetes)

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Abstract: The medicinal properties of Agaricomycetes mushrooms have been explored for millennia. Several biological activities produced by mushrooms have been evaluated worldwide. Therefore, this systematic review aims to present the studies that evaluated the biological activities demonstrated by mushrooms from Brazil. To select the articles, PubMed, Scopus, ScienceDirect and Google Scholar databases were used, with publications between the years 2001-2018, using the key words "mushrooms," "medicinal properties," "extracts," and "Brazil." The articles were selected according to three inclusion criteria: made with mushrooms from Brazil; title and summary with assessment of biological activity of basidioma or mycelium extracts; title and summary with evaluation of biological activity of isolated compound. Exclusion criteria were: work not done in Brazil; review articles; duplication of articles and abstracts and full texts irrelevant to the topics in question. A total of 31 articles were selected. According to the way used to assess biological activities, 54.8% evaluated from basidioma extract, 32.3% from isolated compound and 12.9% from mycelium extract. A total of 12 biological activities were evaluated, the most frequent were antioxidant (22%), anti-inflammatory (12.2%), anticancer (9.8%), antimicrobial (9.8%), and cytotoxic (7.3%). A total of 22 species of Agaricomycetes were evaluated in the studies, *Agaricus blazei (=A. brasiliensis)* the most studied (35.5%), mainly for antigenotoxic and anticlastogenic/antimutagenic activities. The most common isolated compounds of Agaricomycetes evaluated were β-glucan, fucogalactane, mannogalactoglucan, amaurocin, and polysaccharides. Agaricomycetes studied in Brazil are promising for medicinal applications.

Keywords: medicinal mushrooms, *Agaricus blazei (=, A. brasiliensis)*, antioxidant, B-glucans, Brazil
International Journal of Medicinal Mushrooms, 2021, 23 (11) DOI: 10.1615/IntJMedMushrooms.2021040410

The normal cell proliferation and wound healing effect of polysaccharides from *Ganoderma amboinense*

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Abstract: To study the cell proliferation and wound healing activity of polysaccharides from *Ganoderma amboinense* (GAMPS), the polysaccharide was extracted by water extraction and alcohol precipitation method, and its monosaccharide composition and molecular weight were analyzed. The effects of different concentrations of GAMPS on the cell proliferation were determined by cell survival rate test, and the wound healing ability of GAMPS to NIH/3T3 cells was detected. The preliminary evaluation of the antioxidant ability of GAMPS was conducted by the oxygen radical absorbance capacity (ORAC). The results showed that the GAMPS was composed of glucose, mannose, and galactose at a molar ratio of 67.62:14.07:7.50, and the weight-average molecular weights were 5.439 $\times 10^6$ and

1.704×10^5g/mol by using high-performance gel-permeation chromatography-multiple angle laser scatter (HPGPC-MALS) analysis. GAMPS (0.2 μg/μL) showed the strongest proliferation ability to THP-1 cells, with cell survival rate of 178.7%. The wound healing effect of GAMPS (0.1 μg/μL) was obvious on NIH/3T3 and 3.75 μg/μL of GAMPS showed the strongest total antioxidant ability. All the results indicate that GAMPS promotes cell proliferation, and has cell wound healing effect and strong antioxidant activity. The results provide theoretical foundation for the development and utilization of GAMPS.

Keywords: *Ganoderma amboinense*, mycelium polysaccharide, Proliferation promotion, Wound healing, Antioxidant activity

Food Science and Human Wellness, 2021, 10(4): 508-513. DOI:10.1016/j.fshw.2021.04.013.

Culinary–medicinal mushrooms: a review of organic compounds and bioelements with antioxidant activity

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Abstract: There are about 3000 species of mushrooms, which have a high amount of substances that are beneficial to human health, such as antioxidants. It is well known that oxidative stress plays an important role in the etiopathogenesis of many diseases, including cancer, cardiovascular disorders, and diseases of the central nervous system. One way to prevent homeostasis disorders that occur as a result of excessive production of pro-oxidative substances is to include the ingredients having antioxidant properties in the diet. Several compounds, such as those with phenolic and indole derivatives as well as carotenoids and some vitamins, exhibit antioxidant activity. These substances are present in many foods, including mushrooms. In addition, they have certain unique compounds that are not found in other sources (e.g., norbadione A). The present work discusses selected ingredients exhibiting antioxidant activity, which are found in various species of mushrooms as wells as describes the content of these compounds in the extracts obtained from mushrooms using artificial digestive juice.

Keywords: Antioxidant activity, Culinary, Medicinal mushrooms, Gastric juices, Oxidative stress

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Fresh Mushroom Preservation Techniques

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Abstract: The production and consumption of fresh mushrooms has experienced a significant increase in recent decades.

This trend has been driven mainly by their nutritional value and by the presence of bioactive and nutraceutical components that are associated with health benefits, which has led some to consider them a functional food. Mushrooms represent an attractive food for vegetarian and vegan consumers due to their high contents of high-biological-value proteins and vitamin D. However, due to their high respiratory rate, high water content, and lack of a cuticular structure, mushrooms rapidly lose quality and have a short shelf life after harvest, which limits their commercialization in the fresh state. Several traditional preservation methods are used to maintain their quality and extend their shelf life. This article reviews some preservation methods that are commonly used to preserve fresh mushrooms and promising new preservation techniques, highlighting the use of new packaging systems and regulations aimed at the development of more sustainable packaging.

Keywords: fresh mushrooms, nutraceutical value, preservation, sustainable packaging

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***Trametes robiniophila* Murr in the treatment of breast cancer**

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Abstract: Breast cancer is the leading cause of cancer death among women across the world. *Trametes robiniophila* Murr (Huaier), a traditional herbal medicine, has been used in China to protect human health for about 1600 years. Recent years, Huaier had been proven to be effective for multiple types of malignancies. This systematic review focused on breast cancer treatment, summarizing the curative function of Huaier aqueous extract and polysaccharides in preclinical researches. Huaier could markedly inhibit breast cancer progression with low toxicity, enhance immune response and increase the sensitivity to radiation and chemotherapy. The therapeutic effect of Huaier granule in clinical studies was also included. This review amalgamated the current studies and highlighted the promising role of Huaier and its polysaccharides as complementary alternative medicine in breast cancer treatment.

Keywords: Huaier, Polysaccharides, Breast cancer, Traditional Chinese medicine, Anti-tumor therapy

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Fermentation of *Pleurotus ostreatus* and *Ganoderma lucidum* mushrooms and their extracts by the gut microbiota of healthy and osteopenic women: potential prebiotic effect and impact of mushroom fermentation products on human osteoblasts

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Abstract: Recent data have highlighted the role of the gut microbiota and its several metabolites in maintaining bone health. Thus, gut microbiota manipulation, e.g., by prebiotics, might offer a plausible target in the fight against bone degenerative diseases. This study aimed (a) to investigate the in vitro prebiotic potential of *Ganoderma lucidum* and *Pleurotus ostreatus* mushrooms in healthy and osteopenic women and (b) to explore the impact of mushroom fermentation products on human osteoblasts. *G. lucidum* LGAM 9720 and *P. ostreatus* IK 1123 lyophilized mushroom-powders (2% w/v) and their hot-water extracts (1% w/v) were fermented in a 24 h static batch culture model by using faecal inocula from healthy (n = 3) or osteopenic (n = 3) donors. Gut microbiota analysis (qPCR) and measurement of short chain fatty acids (SCFAs) were performed during fermentation, and 24 h-prebiotic indexes were calculated. Evaluation of the effects of fermentation products on bone metabolism parameters (OPG: osteoprotegerin; and RANKL: receptor activator of nuclear factor kappa B ligand) in osteoblast cultures was also performed. Our data suggest that the origin of the gut microbiota inoculum plays a major role in the viability of osteoblasts. The treatments using *P. ostreatus* mushroom-powder and *G. lucidum* mushroom-extract had positive effects based on gut microbiota and SCFA analyses. Both mushrooms exhibited lower RANKL levels compared to controls, whereas their extracts tended to enhance the osteoblastic activity. In conclusion, mushrooms that are rich in beta-glucans may exert beneficial in vitro effects on bone physiology by alterations in the gut microbiota and/or SCFA production.

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Antiviral Bioactive Compounds of Mushrooms and Their Antiviral Mechanisms: A Review

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Abstract: Mushrooms are used in their natural form as a food supplement and food additive. In addition, several bioactive compounds beneficial for human health have been derived from mushrooms. Among them, polysaccharides, carbohydrate-binding protein, peptides, proteins, enzymes, polyphenols, triterpenes, triterpenoids, and several other compounds exert antiviral activity against DNA and RNA viruses. Their antiviral targets were mostly virus entry, viral genome replication, viral proteins, and cellular proteins and influenced immune modulation, which was evaluated through pre-, simultaneous-, co-, and post-treatment in vitro and in vivo studies. In particular, they treated and relieved the viral diseases caused by herpes simplex virus, influenza virus, and human immunodeficiency virus (HIV). Some mushroom compounds that act against HIV, influenza A virus, and hepatitis C virus showed antiviral effects comparable to those of antiviral drugs. Therefore, bioactive compounds from mushrooms could be candidates for treating viral infections.

Keywords: mushroom, bioactive compound, virus, infection, antiviral mechanism

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Nephrotoxic Mushroom Poisoning: Global Epidemiology, Clinical Manifestations, and Management

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Abstract: Because mushroom poisonings are increasing worldwide after ingestions of known, newly described, and formerly considered edible species, the objectives of this review are to describe the global epidemiology of nephrotoxic mushroom poisonings, to identify nephrotoxic mushrooms, to present a toxidromic approach to earlier diagnoses of nephrotoxic mushroom poisonings based on the onset of acute renal failure, and to compare the outcomes of renal replacement management strategies. Internet search engines were queried with the keywords to identify scientific articles on nephrotoxic mushroom poisonings and their management during the period of 1957 to the present. Although hepatotoxic, amatoxin-containing mushrooms cause most mushroom poisonings and fatalities, nephrotoxic mushrooms, most commonly *Cortinarius* species, can cause acute renal insufficiency and failure. Several new species of nephrotoxic mushrooms have been identified, including *Amanita proxima* and *Tricholoma equestre* in Europe and *Amanita smithiana* in the United States and Canada. In addition, the edible, hallucinogenic mushroom *Psilocybe cubensis* has been noted recently via mass spectrometry as a rare cause of acute renal insufficiency. Renal replacement therapies including hemodialysis are often indicated in the management of nephrotoxic mushroom poisonings, with renal transplantation reserved for extracorporeal treatment failures.

Keywords: orellanine, orellanus syndrome, allenic norleucine, rhabdomyolysis, mushroom-induced

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Application of Identification and Evaluation Techniques for Edible Mushrooms: A Review

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Abstract: Edible mushrooms are healthy food with high nutritional value, which is popular with consumers. With the increase of the problem of mushrooms being confused with the real and pollution in the market, people pay more and more attention to food safety. More than 167 articles of edible mushroom published in the past 20 years were reviewed in this paper. The analysis tools and data analysis methods of identification and quality evaluation of edible mushroom species, origin, mineral elements were reviewed. Five techniques for identification and evaluation of edible mushrooms were introduced and summarized. The macroscopic, microscopic and molecular identification techniques can be used to identify species. Chromatography, spectroscopy technology combined with chemometrics can be used for qualitative and quantitative study of mushroom and evaluation of mushroom quality. In addition, multiple supervised pattern-recognition techniques have good classification ability. Deep learning is more and more widely used in edible mushroom, which shows its advantages in image recognition and prediction. These techniques and analytical methods can provide

strong support and guarantee for the identification and evaluation of mushroom, which is of great significance to the development and utilization of edible mushroom.

Keywords: Chromatography, deep learning, edible mushroom, quality evaluation, spectroscopic

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Chemistry and Toxicology of Major Bioactive Substances in Inocybe Mushrooms

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Abstract: Mushroom poisoning has always been a threat to human health. There are a large number of reports about ingestion of poisonous mushrooms every year around the world. It attracts the attention of researchers, especially in the aspects of toxin composition, toxic mechanism and toxin application in poisonous mushroom. *Inocybe* is a large genus of mushrooms and contains toxic substances including muscarine, psilocybin, psilocin, aeruginascin, lectins and baeocystin. In order to prevent and remedy mushroom poisoning, it is significant to clarify the toxic effects and mechanisms of these bioactive substances. In this review article, we summarize the chemistry, most known toxic effects and mechanisms of major toxic substances in *Inocybe* mushrooms, especially muscarine, psilocybin and psilocin. Their available toxicity data (different species, different administration routes) published formerly are also summarized. In addition, the treatment and medical application of these toxic substances in *Inocybe* mushrooms are also discussed. We hope that this review will help understanding of the chemistry and toxicology of *Inocybe* mushrooms as well as the potential clinical application of its bioactive substances to benefit human beings.

Keywords: *Inocybe* mushroom; muscarine; psilocybin; psilocin; toxicology

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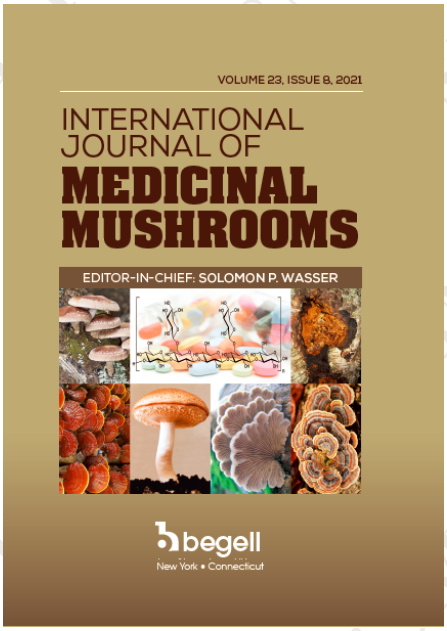

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Aims and Scope

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.

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Points and Reviews

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/Califor- nia/07/09 (H1N1 pdm09).

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

ABBREVIATIONS: AIDS, acquired immunodeficiency syndrome; **CoV**, coronavirus; **COVID-19**, coronavirus disease 2019; **H1N1 pdm09**, pandemic strain of influenza virus A/California/07/09; **HIV**, human immunodeficiency virus; **HSV**, herpes simplex virus; **IC_{50}**, half-maximal inhibitory concentration; **MDCK**, Madin-Darby canine kidney; **MERS**, Middle East respiratory syndrome; **PSK**, krestin; **PSP**, polysaccharide peptide; **SARS**, severe acute respiratory syndrome; **SARS-CoV-2**, severe acute respiratory syndrome coronavirus 2; **SRC VB**, State Research Center of Virology and Biotechnology

I. INTRODUCTION

Viruses causing influenza are characterized by high genetic variability, which leads to the appearance of mutants resistant to antiviral drugs. This review provides information on pandemics caused by respiratory viruses in the 21st century. Characteristics of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which leads to coronavirus disease 2019 (COVID-19) and severe infections of the human respiratory tract, are also described. Due to the high variability of SARS-CoV-2, it is still difficult to judge the effectiveness of drugs that were previously used against influenza viruses (e.g., oseltamivir, zinamivir).

Mushrooms, many of which are edible, contain a wide range of different biologically active com- pounds. Many of these compounds exhibit antiviral activity and have an immunomodulatory effect. Particularly relevant now is the search for antiviral compounds in connection with the COVID-19 pandemic caused by SARS-CoV-2.

This review presents the research completed thus far on the antiviral activity of mushrooms. We pay attention to the research carried out at the State Research Center of Virology and Biotechnology (SRC VB) Vector in Russia, where a collection of strains of higher Basidiomycetes and Ascomycetes mushrooms, newly isolated from habitats in Siberia, were established for the first time. It was possible to screen water from the SRC VB Vector collection.

The half-maximal inhibitory concentration (IC; inhibiting pandemic virus reproduction by 50%) of melanin obtained from a submerged culture of *Inonotus obliquus* (Ach. ex Pers.) Pilát strain F-1244 (Hymenochaetaceae, Agaricomycetes) was four times lower than that of melanin from natural *I. obliquus* (10 μg/mL and 40 μg/mL, respectively).

Electron microscopy examination has shown that melanin disrupts replication of the pandemic strain of influenza A/California/07/09 (H1N1 pdm09) virus in Madin-Darby canine kidney (MDCK) cell culture.

I. obliquus grows very slowly in nature, and its reserves are depleted. Therefore, a biotechnological method for obtaining *I. obliquus* biomass based on effective strains will facilitate the production of drugs against influenza viruses, including pandemic strains.

II. PANDEMICS CAUSED BY RESPIRATORY VIRUSES

The 21st century has seen two pandemics caused by respiratory viruses. These are the 2009 H1N1 flu pandemic and the ongoing COVID-19 pandemic caused by SARS-CoV-2.

Influenza viruses belong to the family Orthomyxoviridae comprising seven genera. Representatives of four genera alpha-, beta-, gamma-, and delta influenza viruses, corresponding to the former genera A, B, C, and D cause flu-like diseases. The family contains RNA viruses with a negative genome, which is represented by single-stranded segments of RNA of negative polarity. Transcription and replication of the genome occurs in the nucleus of an infected cell.[1,2]

Influenza A viruses are most widespread in nature. Besides humans, they infect birds, pigs, horses, marine mammals, bats, and some other animals. Influenza A viruses are divided into subtypes based on the properties of two surface proteins: hemagglutinin (H) and neuraminidase (N). There exist 18 different sub- types of hemagglutinin and 11 different subtypes of neuraminidase: H1 H18 and N1 N11, respectively.[1,2] The 2009 pandemic was caused by the influenza A/H1N1 pdm0 virus. Molecular genetic analysis revealed that the pandemic influenza virus was the result of genetic recombination of human and animal vi- ruses, which may have occurred in pigs, although there is no

evidence of direct pig-to-human transmission of this virus. However, it is highly likely that pigs were a “mixing vessel" for the generation of new human influenza A viruses.[3]

In December 2019, several medical institutions in the Chinese city of Wuhan (Hubei Province) re- ported patients with pneumonia.[4] Clinical manifestations resembled symptoms of severe acute respiratory syndrome (SARS), a disease that appeared in 2002 in a neighboring region, Guangdong Province, caused by SARS-CoV coronavirus.[5] On January 7, 2020, a new strain of coronavirus was isolated. It was named SARS-CoV-2 due to its similarity to SARS-CoV in structure. Both pathogens belong to the family Coronaviridae. All known coronaviruses are divided into four genera, including α-, β -, γ -, and δ-CoV. Representatives of the first two genera can infect mammals, while γ -andδ-CoV infect mainly birds. Six coronaviruses were previously known to infect humans; they cause mild respiratory symptoms similar to the common cold. Two β -coronaviruses, SARS-CoV and MERS-CoV, lead to severe and potentially fatal infections of the human respiratory tract. The new SARS-CoV-2 coronavirus caused the COVID-19 pandemic.

The symptoms of influenza and COVID-19 are similar, including fever, chills, cough, sore throat, myalgia, headache, fatigue, and sometimes diarrhea, nausea, and vomiting. As a result, it is very difficult to differentiate these diseases only by symptoms. COVID-19 is often accompanied by sputum formation and shortness of breath, but not in all cases and not in all patients. In addition, these symptoms are also found in influenza. Therefore, the diagnosis must be based on the results of laboratory tests, mainly PCR data on the presence of virus RNA in nasal and pharyngeal smears. Compared with other acute respiratory viral infections, more characteristic symptoms of COVID-19 likely are loss of smell (full or partial) and impaired taste (anosmia, hyposmia, and dysgeusia).[6]

There are highly effective drugs against influenza viruses, such as oseltamivir (Tamiflu; Genentech, South San Francisco, CA) and zanamivir (Relenza; GlaxoSmithKline, Research Triangle Park, NC). Unfortunately, drug-resistant mutants appear over time due to the high variability of influenza virus. Regarding coronavirus, it is not yet clear which drugs are effective in treating COVID-19. Some medical providers use a combination of lopinavir and ritonavir, which is effective in treating human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), SARS, and MERS; chloroquine, which is used to treat malaria and autoimmune diseases; or ribavirin, which is being tested in treating SARS and MERS.[7]

III. THERAPEUTIC POTENTIAL OF MEDICINAL MUSHROOMS

More than 200 medicinal functions are thought to be produced by medicinal mushrooms and fungi,[8-10] including antitumor, immunomodulating, antioxidant, radical scavenging, cardiovascular, cholesterol-lowering, antiviral, antibacterial, antiparasitic, antifungal, detoxification, hepatoprotective, antidiabetic, antiobesity, neuroprotective, neuroregenerative, and other effects. Substances derived from medicinal mushrooms can also be used as pain relievers or analgesics. The best implementation of medicinal mushroom drugs and medicinal mushroom dietary supplements has been in preventing immune disorders and maintaining a good quality of life, especially in immunodeficient and immunodepressed patients, individuals undergoing chemotherapy or radiotherapy, and patients with different types of cancers or other illnesses, including chronic bloodborne viral infections from hepatitis (B, C, and D), anemia, HIV/AIDS, herpes simplex virus (HSV), Epstein Bar virus, influenza viruses A and B, HSN1,[11] COVID-19,[12] West Nile virus, chronic fatigue syndrome, chronic gastritis and gastric ulcers caused by *Helicobacter*

pylori, and dementia (especially Alzheimer's disease).

New classes of drugs were developed from medicinal mushrooms called "mushroom pharmaceuti- cals or mushroom drugs" or biological response modifiers (like krestin [PSK] and polysaccharide peptide [PSP]) from *Trametes versicolor*, lentinan isolated from *Lentinus edodes*, schizophyllan (sonifilan, sizofiran) from *Schizophyllum commune*, befungin from *I. obliquus*, D-fraction from *Grifola frondosa*, polysaccharide fraction from *Ganoderma lucidum*, active hexose correlated compound, and others.[8-10]

Many, if not all, mushrooms contain biologically active compounds in fruit bodies, cultured mycelium, and cultured broth. Medicinal mushrooms present an unlimited source of polysaccharides (especially B-glucans) and polysaccharide-protein complexes with anticancer and immunomodulating properties and different types of low-molecular-weight compounds (triterpenes, lectins, steroids, phenols, polyphenols, lactones, statins, alkaloids, and antibiotics).[8-10,13-15]

Special attention is paid to mushroom polysaccharides. The data on mushroom polysaccharides and different secondary metabolites are summarized for > 700 species. Numerous bioactive polysaccharides or polysaccharide-protein complexes described from medicinal mushrooms appear to enhance innate and cell-mediated immune responses, and exhibit antitumor activities in animals and humans. Particularly, and most importantly for modern medicine, are polysaccharides and low-molecular-weight secondary metabo- lites with antitumor and immunostimulating properties.

Medicinal mushrooms represent an unlimited source of polysaccharides with antitumor properties and immunomodulatory properties. The first drugs derived from mushrooms were polysaccharides: krestin, lentinan, schizophyllan, ganoderan, grifolan, and pleuran.[16-20]

Several mushroom compounds have proceeded through Phase I, II, III, and IV clinical trials and are used extensively and successfully in Asia to treat various cancers and other diseases. Clinical studies on the effects of various medicinal mushroom preparations on humans were published in > 1000 papers and reports. Approximately 300 clinical studies were conducted only on *G. lucidum* and some other species of genus *Ganoderma.* The largest number of clinical trials were performed mainly using *G. lucidum*, *L. edodes*, *G. frondosa*, *T. versicolor*, *Sch. commune*, *Phellinus linteus*, and *Agaricus brasiliensis* (= *A. blazei* sensu Heinem.) for treatment of cancers and oncoimmunological and immunological diseases and in immune-adjuvant therapy. Fruiting bodies of mushrooms and/or their biomass from submerged cultivated mycelia, different types of extracts, rare spores (from *G. lucidum*), and pure B-glucans, proteoglucan (PSK), or PSP have been used in clinical trials for cancer treatment.[20] In many cases, mushrooms were used as adjuvant treatment with conventional chemo- or radiotherapy in different kinds of cancer.[21-24]

However, no clinical trials have been performed to confirm antiviral studies, which should be done before using these compounds for prevention and treatment of CoVs in the future, especially regarding SARS-CoV-2.[25] It is anticipated that not only antitumor properties but also antiviral activity will be found in medicinal mushrooms in the future.[26-29]

IV. ANTIVIRAL PROPERTIES OF MEDICINAL MUSHROOMS

Much information on biologically active substances of medicinal mushrooms possessing antiviral activity has been accumulated. Fungi-derived compounds producing an inhibitory effect on influenza virus are known. A protein substance, which prevents the replication of influenza A virus, was isolated from the aqueous extract of the fungus *Cortinarius caperatus* (= *Rozites caperatus*).[30]

Analysis of the antiviral activity of *Ganoderma pfeifferi* extract against influenza A virus and HSV-1 revealed that triterpenoids such as ganodermadiol, lucidodiol, and aplanoxinic acid G were the main anti- viral components of the extract.[31]

The substances hispidin and hispolon, which have an isoprenoid nature and are found in the ethanol extract of the fungus *I. hispidus*, showed antiviral activity against influenza A and B viruses. Both fruit body extracts and mycelial extracts exhibited antiviral activity.[32,33]

Animal studies have shown that α-glucans isolated from *L. edodes* can increase the body's resistance to pathogens as shown in experiments with influenza virus.[34,35] Sterols and triterpenes with antiviral ac- tivity were isolated from the fungus *G. pfeifferi* and other species of the genus *Ganoderma*. *In vitro*, they showed activity against influenza A virus in MOCK cells at concentrations > 0.22, 0.22, and 0.19 mmol/L, respectively (IC_{50}). Ganodermadiol, lucidadiol and applanoxidic acid have shown antiviral activity against both influenza type A virus and HSV-1.[36,37] Interest in the results on antiviral activity of fungi, especially in connection with the latest pandemic, continues to grow, as evidenced by new publications.[38] The authors believe that genetic methods should be applied to strains to improve them and increase their production in order to produce compounds with antiviral activity.

The SRC VB Vector of Rospotrebnadzor created a scientific collection comprising 132 strains of 60 species of basidial fungi isolated for the first time from natural habitats of Southwestern Siberia. To guarantee the use of true producers of Basidiomycetes in biotechnology, a standard operating procedure titled "Control of Basidial Fungi Cultures for the Presence of Mycophiles at Different Stages (Storage, Seeding, Biomass Cultivation)" was developed.

Water extracts, total polysaccharides, and melanins from fungi isolated for the first time in Siberia were screened for several pathogenic viruses available in the collection of SRC VB Vector of Rospotrebnadzor. It was shown that water extracts from fruit bodies of *Phallus impudicus* suppressed the replication of influenza virus HSN1 in cells by a mean ±SD of 5.20 ±1.50 lg and 4.45 ±1.60 lg of that from cultured mycelium.[39]

Among other fungi, the most active against influenza viruses were samples from fruit bodies of artist's bracket *G. applanatum* (neutralization index for subtype H5N1=5.00 ±0.15lg), sulphur polypore *Laetiporus sulphureus* (H5N1=5.00 ±1.67 lg and H3N2=6.16 ±0.14 lg), sclerotia of *I. obliquus* (neutralization index for subtype H5N1=4.7 ±1.2 lg), and *Pleurotus pulmonarius* (H5N1=6.06 ±0.18 lg and H3N2 =5.73 ±0.14 lg).[40-43] Antiviral activity of extracts of the same species, such as *L. sulphureus*, *P. pulmonarius*, *G. applanatum*, and *I. obliquus*, was shown for the pandemic influenza virus on MOCK cell culture and Balb/c mice. All mushroom extracts examined had low toxicity to MOCK cell culture and laboratory animals. Extracts of Basidiomycetes were found to inhibit the reproduction of the pandemic influenza A virus/Moscow/226/2009 (H1N1)v in MOCK cell culture by 2.6 3.2 lg, which was comparable in these experiments to the effect of the reference drug, Tamiflu (suppression of virus reproduction was 2.9 lg).

Extracts from *G. applanatum*, *L. sulphureus*, and *I. obliquus* were tested against the pandemic influenza virus A/Moscow/226/2009 (H1N1)v on MOCK cell culture and then on laboratory mice. Four days after infection, the virus titer in the lung homogenates of control mice was 3.83 lg. In the lungs of mice treated with extracts of *I. obliquus* and *L. sulphureus*, the virus titer was 1.83 and 2.00 lg, respectively. In the lungs of mice treated with Tamiflu, the virus titer was 1.67 lg.[44]

An aqueous extract from mycelium of *Fomitopsis officinalis* was active against different subtypes of influenza virus (H5N1 IN = 3.00 ±0.11 lg and H3N2 IN = 1.50 ±0.25 lg). The antiviral activity of *Daeda- leopsis confragosa* 2266 against H5N1 and H3N2 subtypes was demonstrated.[40,45,46] Later, two strains of *D. confragosa* were studied on the H1N1 pdm09 strain. They showed the advantages of the new strain of *D. confragosa* F-1368 such as antiviral activity and the presence of antitumor properties as well.[47]

The results of screening some samples from West Siberian mushroom cultures against influenza viruses and other viruses are summarized in reviews and monographs.[11,29,48 51]

Due to the current global situation with coronavirus, studies of biologically active compounds from fungi that are most effective against influenza viruses will be particularly relevant.

V. ANTIVIRAL PROPERTIES OF *I. OBLIQUUS*

The main biologically active substances of *I. obliquus* are water-soluble, intensely colored chromogens formed from a complex of chemically active phenolic aldehydes, polyphenols, oxyphenol carboxylic acids, and their quinones. Humin-like substances are also isolated from the chromogenic complex. All compounds are genetically related to oxyaromatic precursors of biosynthesis of birch bark tannins and birch wood lignin.[52 55]

In other countries, various compounds of *I. obliquus* are also actively studied for anticancer, antioxidant, antiallergic, anti-inflammatory, immunomodulatory, and antimicrobial activities.[56 58]

More than 4000 health products are produced from *I. obliquus* globally, and the scale of commercial exploitation of natural raw materials of *I. obliquus* is enormous.[59] Natural resources of this valuable medicinal mushroom are being depleted. Therefore, the production of bioactive compounds based on cultured strains of *I. obliquus* is one of the main tasks of medicinal mushroom biotechnology.

As noted earlier, according to the results of research launched by the SRC VB Vector in 2008, water extracts and melanins of *I. obliquus* exhibited the widest range of antiviral activity by suppressing the reproduction of all the studied viruses in cell cultures, including influenza virus, West Nile virus, HIV-1, HSV-2, variola virus, and vaccinia virus.[50,60]

The results obtained by other scientists demonstrate the effectiveness of *I. obliquus* extracts against hepatitis C virus, herpes virus, and HIV.[61 64] The range of viral pathogens on which water extracts, polysaccharides, and other components of *I. obliquus* are studied is constantly expanding.[65,66]

Melanins are of great interest for pharmaceutics. Melanins is a collective name for a group of high-molecular-weight black and brown pigmented, polymeric compounds formed during the oxidative polymerization of phenols, mainly pyrocatechin and tyrosine.[67] Melanins are found in animals, plants, bacteria, and fungi, giving them a dark color. They

are involved in DNA repair and in the processes of functioning of the respiratory chain as an electron acceptor; they present a modulator of important systems of cellular metabolism such as photo- and radioprotection, neutralize the products of lipid peroxidation, and participate in neurotransmitter processes in numerous pathological disorders of the functional structures of neurons.[68] Among tinder mushrooms, *I. obliquus* contains the greatest amount of melanin, up to 30% of weight. This is evidenced by literature data and our own research results.[29,69]

Table 1 shows the antiviral activity of water extract and melanin derived from natural *I. obliquus* and melanin from a submerged culture of the *I. obliquus* strain F-1244 against various viruses.[70]

Table 2 presents data on antiviral activity of melanin derived from the *I. obliquus* strain F-1244 and natural raw materials against the H1N1 pdm09 strain on MOCK cells.[70] The study was performed within the framework of the state task (SRC VB Vector of Rospotrebnadzor). Table 2 shows that *I. obliquus* strain F-1244 produces melanin, which exhibits a higher antiviral effect than melanin from natural raw materials of *I. obliquus*. It was shown that the IC_{50} (inhibiting virus reproduction by 50%) of melanin obtained from a submerged culture of *I. obliquus* strain F-1244 was four times lower than that of natural *I. obliquus* melanin (10 μg/mL and 40 μg/mL, respectively). The highest therapeutic index equal to 160 was shown for melanin of cultured *I. obliquus*, which was 2.5 times higher than for melanins from natural *I. obliquus*. Therefore, it is important to search for effective strains of *I. obliquus* for obtaining melanin by biotechnological methods. Electron microscopy studies conducted by us previously showed that there were no signs of reproduction of HSV-2 in the nucleus after treating Vero cells with *I. obliquus* extract, which contains melanin, whereas numerous nucleocapsids of herpes virus in the cell nucleus and disturbed structure of the nucleus were observed in the control.[71]

To conduct a similar study on influenza virus, melanin obtained from a submerged *I. obliquus* culture was used. MOCK cells were grown in culture vials, and the antiviral effect against H1N1 pdm09 was estimated. The results obtained on a series of sections demonstrated the influence of melanin on the morphogenesis of H1N1 pdm09 virus in MOCK cell culture. Virus reproduction decreased under the influence of melanin. In the experimental sample, in the presence of melanin, mainly globular small viral particles were observed in the intercellular space (Fig. 1). In control cells (without melanin), filamentous forms of the virus prevailed on the cell surface (Fig. 2), which correlates with a higher cytopathic effect of influenza virus. The most likely mechanism of antiviral activity may be the direct interaction of melanin with virions in the intercellular space.[72]

TABLE 1: Manifestation of antiviral activity of water extract and melanin of *Inonotus obliquus*

Sample	HSV-2	WNV	HIV-1	Influenza virus, subtypes			Orthopoxviruses	
				H5N1	H3N2	H1N1	VARV	VACV
Water extract from natural raw materials of chaga	•	•	•	•	•	•	•	•
Melanin from submerged culture of chaga strain F-1244	•	•	•	NP	NP	•	NP	NP
Melanin from natural chaga material	•	•	•	•	•	•	NP	•

NP, studies not performed; WNV, West Nile virus; VACV, vaccinia virus; VARV, variola virus.

TABLE 2: Antiviral activity of melanin from naturally occurring *Inonotus obliquus* and a cultured strain against the pandemic A/California/07/09 virus strain (H1N1 pdm09)

Sample	Toxic dose (TC_{50}), µg/mL	Effective dose (IC_{50}), µg/mL	Therapeutic index (IS)
Melanin from *I. obliquus* F-1244 culture	1600 ± 188	10.0 ± 2.0	160 ± 30
Melanin from natural raw materials of *I. obliquus*	2500 ± 240	40.0 ± 4.4	62.5 ± 21

Values are presented as the mean ± SD.

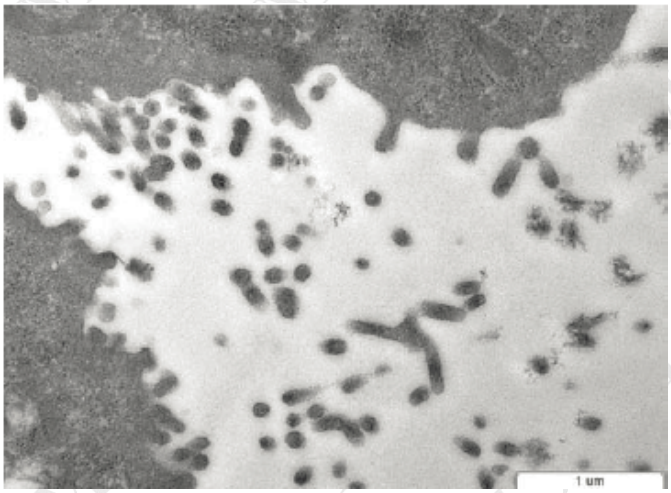

FIG. 1: *The effect of melanin on influenza virus. In the intercellular space, mainly spherical, small viral particles were observed. The reproduction of the influenza virus was reduced.*

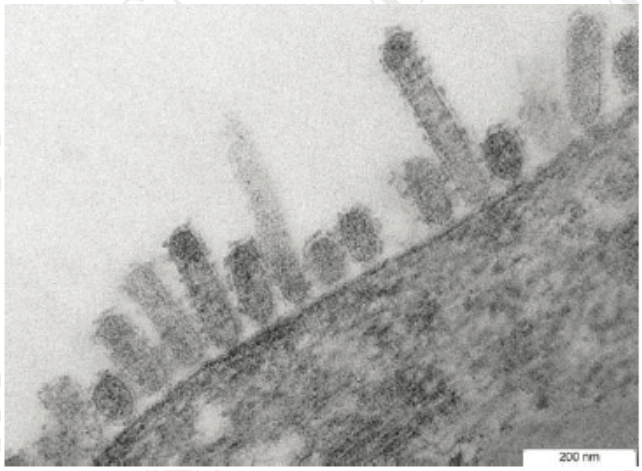

FIG. 2: *Influenza virus A/California/07/09 (HlNl pdm09). Control. In control cells (without melanin), fllamentous forms of the virus prevailed on the cell surface, and this correlated with a higher cytopathic effect of the influenza virus.*

VI. DISCUSSION AND CONCLUSIONS

The search for new antiviral drugs in connection with new influenza viruses that threaten the population and lead to pandemics are currently very relevant. The number of new publications on this topic continues to increase.[73]

Based on the data presented, it can be observed that many species of medicinal mushroom have antiviral activity, including that against influenza viruses. The development of preventive and medicinal products based on

polysaccharides and their complexes with proteins as well as terpenes and melanins is necessary to protect the population from new influenza pandemics, since the development of vaccines requires time.

Many medicinal compounds can be derived from fruit bodies of cultured mushrooms. However, promising species such as *I. obliquus* should be protected from predatory extermination, since mainly natural raw materials are used to produce many drugs. At the same time, the production of melanin based on strains isolated in culture demonstrates its higher antiviral effect against pandemic H1N1 pdm09 in MDCK cell culture. The highest therapeutic index (equal to 160) was shown for melanins of cultured *I. obliquus*, which was 2.5 times higher than for melanins from natural *I. obliquus*. It is advisable to use genetic methods for strains producing medicinal compounds in order to increase the productivity of active substances and to improve drugs. Thus, the search for new effective strains of medicinal mushrooms that produce antiviral compounds and obtaining them by biotechnological methods is a promising and relevant direction for the development of preventive and curative medicinal products against influenza viruses, including SARS-CoV-2.

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