



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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NEWSLETTER OF THE INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

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News Reports

International Mushroom Days, China 2024, Grandly Held with Enthusiastic Feedback

From April 22nd to 24th, the International Mushroom Days, China 2024 was grandly held at Xiamen Fliport Hotel C&E Center, Fujian Province, China. The total exhibition area was 17,000 square meters, equivalent to 550 international standard booths, of which more than 80% were special booths, increased by 28% compared to last year. Totally 271 exhibitors and enterprises participated in the exhibition, more than 2,000 people from Russia, Japan, India, France and other parts of the world registered and attended the event, a significant increase compared to last year.

This exhibition consists of two themed exhibition areas: the Intelligent Manufacturing Innovation Hall and Mushroom Industry Promotion Hall. The exhibits cover 11 categories of products and services, including mushroom cultivation, raw material supply, intelligent equipment, environmental control, energy management, cold chain logistics, as well as product processing and terminal channels, all of which reflect the technological innovation and industrial integration of Chinese mushroom industry. By clearly defining functional zones, achieved the integration of expertise and exhibition sales, creating a comprehensive exhibition feast that combined traditional and innovative elements.



The opening ceremony of the International Mushroom Days, China 2024

This event was hosted by China Chamber of Commerce of 1/E of Foodstuffs, Native Produce and Animal By-products (CFNA), International Joint Research Center for Creating New Germplasm Resources of Edible Fungi, Fujian Edible Fungi Society, Fujian Edible Fungi Industry Association, and Fujian Edible Fungi Industry Technology Innovation Alliance. It is jointly organized by Xiamen Vissea Exhibition Service Co., Ltd., Shenzhen Jiuneng Brand Management Co.,

Ltd., National and Local Joint Engineering Research Center for Economic Microbial Research and Utilization, and the Edible Fungi Research Institute of Fujian Academy of Agricultural Sciences. This was a large-scale mushroom industry chain special event following the 2023 Chinese Mushroom Day.

The opening ceremony was compered by Mr. Liu Ziqiang, secretary general of Edible Fungi Chamber of CFNA. More than 700 representatives including 18 local government leaders, 271 leading mushroom production enterprises, authoritative experts and scholars, professionals from supermarkets and catering industry, as well as representatives from upstream and downstream enterprises of mushroom industry chain, witnessed the opening of the conference. The "2023 China Edible Mushroom Industry Regional Brand Value Evaluation Ranking" was released at the opening ceremony.



This event also received strong support from professional associations such as National Edible Mushroom Industry Technology System, International Society for Medicinal Mushrooms (ISMM), International Society for Mushroom Science (ISMS), World Society for Mushroom Biology and Mushroom Products (WSMBMP), National and Local Joint Engineering Research Center for Characteristic Edible Mushroom Breeding and Cultivation, as well as the media such as the Food Headlines, Emushroom.net, Edible and Medicinal Mushrooms journal, and Brand Agriculture and Market.

The first Xiamen International Specialty Mushrooms Industry Conference and the first "Three Creatures Cycling Production" Edible Mushrooms Industry High-quality Development Conference were held in the same period, the multiple events created a new interactive platform of "government, industry, academic research, application and retail", strengthening the linkage and cooperation between the government, enterprises, universities, research institutes and the retail industry, and promoting the sharing and efficient utilization of information, technology, talent, products and sales channels. The successful holding of this expo not only provided a platform for enterprises and research institutions in the edible mushroom industry chain to showcase and exchange ideas, but also injects new vitality into promoting the innovative development of the edible mushroom industry. At the same time, it brings China's edible mushroom industry to a more prosperous and greener trend towards the future.

A Proposal on Establishment of World Mushroom Day

Edible macro fungi, also known as mushrooms, are a precious gift from nature. Historical records and archaeological evidence from various parts of the world indicate that humans have been consuming mushrooms since ancient times.

In recent times, driven by the development of modern biology and modern industrialization, the consumption of edible mushrooms by humans has reached an unprecedented high and extensive level, forming an innovative industry completely different from traditional planting.

The development of the edible mushroom industry increasingly affects ecological production of agriculture and citizen health, showing promising potential in a wide range of application scenarios.

Edible mushrooms ulteriorly integrate into the agricultural production system as a nonnegligible source of high-quality food, providing new approaches to meet the consumers' needs for diversified, nutritious, and healthy diets. Nowadays, *Agaricus bisporus* and *Pleurotus ostreatus* are broadly cultivated agricultural varieties worldwide. Edible mushrooms such as *Lentinula edodes*, *Flammulina velutipes*, *Auricularia heimuer*, *Hypsizygus marmoreus* are popular vegetables in East Asia, while healthy benefits of medicinal mushrooms such as *Ganoderma lucidum* are widely accepted. The production methods of edible mushrooms show an impact on human society equivalent to the "green revolution" in the history of crop production. The developing industry of edible mushrooms will provide more healthy food for global consumers, and mushrooms will gradually serve as indispensable new sources of human food. Promoting global development of the industry via popularizing cultivation technologies may become an effective strategy to solve food crisis, which enhances supply of edible mushrooms in areas with food shortage as well as helps supplementing dietary nutrients such as protein and vitamins among populations affected by hunger.

The production of edible mushrooms does not require a large amount of farmland or water consumption, allowing their cultivation particularly feasible in areas with limited water and land. Moreover, cultivation of edible mushrooms adopts a wide range of substrates, and has short production cycles while yielding high profits. Farmers, after short-term training or self-learning, can quickly master cultivation techniques and carry out production using surrounding resources and family environments. In addition, the production of edible mushrooms does not require strong labor and hence is convenient for women to participate. The scientific literacy of farmers is also improved while learning the cultivation technology. The production of edible mushrooms plays an important role in improving the natural and social environment in rural areas, as well as promoting a smooth and rapid transition from traditional to modern agriculture. During the rural reform in China, edible mushroom production is a major access to alleviating poverty and promoting prosperity, which is particularly applicable to remote, mountainous and underdeveloped areas.

Many agricultural wastes such as rice or wheat straws, cottonseed husk, corn cob, and sawdust are used as substrates for mushroom cultivation, largely reducing environmental burden caused by burning and discarding of agronomic residue. Meanwhile, a large amount of edible fruiting bodies (mushrooms) and

residues rich in organics are produced during the process. The remaining substrate residue after harvesting edible mushrooms contains many nutrients such as mycoprotein and vitamins, which could be applied as animal feed additives and plant fertilizers, as well as extracted for fungal active compounds. In an agrarian system dominated by agriculture, forestry, and aquaculture, edible mushroom production plays a crucial role in balancing by-product (such as straw) degradation and organic recycling, becoming an indispensable part of circular agriculture. The expansion of production scale of edible mushrooms guides the transformation of agricultural mode from resource consumption to resource recycling, making significant contributions to promoting the sustainable agriculture. The global promotion and application of this production manner helps establish a new mode for green agriculture development, hence contributing to reduction of greenhouse gas emissions.

Based on the continuous expansion of edible mushroom industry in modern society, which provides new and scalable solutions to poverty, uneven development, malnutrition, and environmental deterioration, I propose to establish a global "Mushroom Day" to attract more public attention, governmental support, and peer participation! Edible mushrooms will make greater contributions to humans!

TAN, Qi

Chair

World Society for Mushroom Biology and Mushroom Products

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Nammex Files Citizen Petition Requesting FDA Actions on Mushroom Product Labeling

Nammex, the premier North American supplier of Certified Organic Functional Mushroom Extracts, has filed a Citizen Petition with FDA requesting the Agency to address the mislabeling of dietary supplements and functional foods as “mushroom” or containing “mushrooms” when they contain other fungal parts, and do not contain “mushrooms” as claimed, or fail to disclose added grain ingredients.

For many years, Nammex has been advocating for full transparency in product labeling and urging companies in the industry to identify ingredients from fungi according to the part of the fungal organism from which they are derived, consistent with FDA’s labeling requirement for botanicals. While there has been some, although limited progress, in light of ambiguity in FDA’s labeling regulations and compliance policies, Nammex Founder Jeff Chilton decided that it was time to raise public awareness and request guidance as well as increased attention from FDA to ensure industry compliance.

Given the explosive growth the mushroom category is undergoing and entry of new companies marketing products with fungal ingredients that may not be aware of the regulatory requirements, it made sense to undertake this action now. We hope to raise awareness of the mislabeling problem that exists today in the US, and obtain FDA regulatory guidance on the labeling of mushrooms and other fungal ingredients to ensure truth-in-labeling,” Jeff said. “When consumers buy a product labeled as “mushroom”, they should feel confident that they are getting a genuine mushroom product.”

According to Nammex’s regulatory counsel, Holly Bayne of the Law Office of Bayne & Associates, “Citizen Petitions provide a public forum through which interested parties can request FDA to issue or amend a regulation or take other administrative action. As the petition has made clear, remedial action from FDA is warranted, including revisions to the Agency’s compliance policies to ensure foods and dietary supplements containing fungal ingredients are accurately labeled and not misbranded. We look forward to engaging with FDA on this important issue.”

The petition asks FDA to correct ambiguity in the dietary supplement labeling regulations to clarify that proper listing of ingredients from fungi on product labels includes identification of the part of the fungal organism from which the ingredient is derived. Nammex also requests that FDA issue industry guidance regarding the proper labeling of fungal ingredients, including a Glossary of Mycological terms. Further, Nammex requests that FDA increase regulatory enforcement to ensure foods and dietary supplements containing fungal ingredients are accurately labeled, and take appropriate action against products labeled as “mushroom” when they do not contain mushrooms as claimed, but contain other fungal parts, such as mycelium, and fail to identify the presence of grain in product.

The Agency has 180 days to respond to the petition. Nammex intends to keep the industry informed throughout the process.

Source: <https://www.nammex.com>

Death Cap Mushrooms are Extremely Deadly—and They're Spreading

By Emily Martin

The death cap is the world's deadliest fungus, responsible for 90 percent of the world's mushroom-related poisonings every year. Native to Europe, death caps have spread around the world over the past century.

The name itself is both alarming and self-explanatory: the death cap mushroom.

Scientifically known as *Amanita phalloides*, death caps are responsible for 90 percent of the mushroom-related fatalities that occur every year, making them the world's most lethal mushroom. The infamous fungus was recently in the news after three people in Australia died after ingesting what investigators suspect were death caps.

The mushroom originates from the U.K. and parts of Ireland, but over the past century, it has hijacked trips around the world, spreading to Australia and North America.

Since arriving on the West Coast, the invasive mushroom has spread rapidly throughout California and has even appeared as far north as British Columbia, but much about its arrival remains a mystery. Why the mushroom spread so quickly, when exactly it arrived, and how it will impact the environment it grows in are the topics of ongoing research.

Here's what you need to know about this deadly mushroom—and how to spot one—in case it emerges in a forest near you.

How the mushroom earned its name

The unassuming mushroom can grow up to six inches tall with a similarly sized domed cap, sometimes tinged yellow or green. Under its cap are white gills and an off-white stem—characteristics that make it difficult to distinguish from an edible mushroom.

Yet unlike an edible mushroom, it can cause extreme damage to the liver and kidneys, or in some cases, death.

That's because the mushrooms contain a unique set of toxins, says U.S. Department of Agriculture plant pathologist Milton Drott. Though it is safe to the touch, a death cap contains amatoxins, which prevent cells from creating proteins, ultimately causing cell death and organ failure.

Drott notes that these toxins may have allowed the populations spreading through the U.S. to thrive, serving up a defense against any new predators the fungus encounters in its environment.

But studying the death cap mushroom can be difficult. It's challenging to replicate ideal environmental conditions for a mushroom in a lab, and studying plucked mushrooms requires complex DNA sequencing.

Some fungi can damage the environment, like the fungus that wiped out American Chestnut trees, but so far, there's no strong evidence that death caps are a threat to their new environments. In fact, trees and other plants benefit from their presence.

Death caps are a mycorrhizal fungi, which means they form a relationship with plants that's mutually beneficial for both plant and fungus. The plant receives nutrients from the soil that the fungus extracts, while the fungus receives sugars from the plant.

A mysterious move around the world

It's nearly impossible to pinpoint the actual moment the deadly mushroom made its way to the western U.S. and why exactly it's continued to spread since then, says Anne Pringle, a mycologist at the University of Wisconsin-Madison and a leading expert on death caps.

The earliest record of the mushroom in California is from the 1930s. Some researchers theorize that death caps immigrated in the soil of a cork tree transported from Europe to California to make corks for a then burgeoning wine industry. Others say the mushroom may have hitched a ride on a mystery plant imported to beautify college campuses.

Regardless, both Pringle and Drott say the only thing they're certain of is that the fungus was likely dormant—and thus hidden from human eyes—in an imported plant's soil.

"When they planted that tree in the ground, they also effectively planted the fungus. So, what exactly is the smoking gun, who did it, and when—that's the thing I think we'll never truly know," Pringle says.

Pringle can't say for sure what makes the state such a friendly habitat for the invasive species, but she does note that the fungus can tolerate different environments throughout Europe, growing as far north as Sweden and as far south as southern France.

Since arriving, Pringle says its geographic extent has grown larger and spread to other states; most recently it appeared in Idaho.

Retracing their steps

When scientists first spotted death caps in the U.S., they thought they may be native to the region because of how widespread they are. In 2009, Pringle was the first to label the population in California as invasive, a discovery she made by inspecting the mushrooms' DNA. And when scientists did realize the death cap had newly spread into the U.S., there wasn't any preexisting data to provide clues about where exactly it entered North America and how quickly it multiplied.

"There's so many ideas to test, it's hard to even know where to get started," Pringle says.

Research on invasive fungi in the environment is quite new, Pringle says, so answers to questions of why death caps are spreading and its impact on local ecosystems may still be years away.

Drott thinks the mushroom may be proliferating because it thrives in its new soil and with its adoptive plants, or there may be a lack of predators in these new habitats to keep death cap populations in check.

His research has revealed at least one clue: the genes responsible for producing toxins in American death caps are extremely unique, distinct from their genetic cousins in Europe, and may be the key to understanding how the



Scientifically known as *Amanita phalloides*—death caps were first spotted in California in the 1930s.

invasive plant has thrived in North America.

Earlier this year, scientists published preliminary research suggesting the death cap can reproduce both with and without a mate, and that a single fungus can live a long, reproductive life.

Encountering a death cap

Spotting a death cap requires vigilance. "It's scary that these [pass for] delicious mushrooms," Drott says.

He adds that, in addition to an unalarming physical appearance, the death caps' toxins don't smell or provide any other obvious giveaways. Its toxins are also extremely stable when heated and don't break down when cooked, unlike other edible fungi that are only dangerous to eat raw.

That's why scientists suggest erring on the side of caution and steering clear of foraging mushrooms. Pringle also emphasizes the importance of learning the plants in your local environment.

"If you can tell the difference between Swiss chard and spinach, you can learn difference between edible and poisonous mushrooms," Pringle says, emphasizing the small but recognizable differences between the two greens. "People want a magic rule, but there's nothing I can hand you in a sentence or paragraph."

Rather, she says identifying physical differences between death caps and a safe mushroom can become easier with exposure.

Spreading awareness

Many death caps have been found in National Parks, including Point Reyes National Seashore in California, where Pringle assisted with a study on the invasion in 2010.

National Park Service (NPS) science advisor Ben Becker notes that parks are constantly seeing new invasive species with the frequent movement of people and equipment, and the death cap is a good example of how humans can transport tiny fungal invaders around the world.

Becker says NPS works with local mushroom science groups like the Bay Area Mycological Society to spread public awareness about the dangers of foraging mushrooms.

If you're concerned about something you have eaten, go to the emergency room and if possible, take pieces of the mushroom you ate for identification.

And as many foragers and scientists say, don't munch on a hunch.

Source: <https://www.nationalgeographic.com/>

Up-coming Events

Second Circular of the 12th International Medicinal Mushrooms Conference (IMMC12)



The purpose of this Second Circular is to invite you to attend the IMMC12 and to let us know if you plan to attend, and also to request that you submit your abstracts to the conference. Please complete the registration form and abstract template available on the web (www.immc12.com).

We would appreciate your early response if you plan to attend.

The third circular and final program will be distributed only to registered participants and will be posted on the IMMC12 website.

BARI, AN UNEXPECTED MEETING POINT BETWEEN EAST AND WEST

Bari is a very charming city, the third-largest city in Southern Italy, in order of the population.

It's incredible the contrast between the folkloristic old town and the cozy city center, full of branded shops and polished aristocratic buildings. Bari is highly multifaceted city, and you really need to discover every single aspect to understand its true core. Known as the "Gateway to the East" due to its long tradition of trade, this capital of Apulia is rich in history: see with your own eyes in the town of Bari Vecchia and surrounding area.

Exploring the historic centre allows us to discover its most authentic character, with signs of its past scattered through the local alleyways and endless examples of age-old traditions passed from generation to generation. Then there is the famous Bari promenade, one of the most beautiful in Italy, overlooking the clear sea and the unique

charm of Bari.

Today, this dynamic city, nestled in the heart of the countryside punctuated by white dry-stone walls, is an important university hub.

But it still holds dear the memory of its seafaring exploits of the Middle Ages, as well as its precious monuments and striking churches.

The history of Bari is fascinating and turbulent. The ancient settlement dates back to the Bronze Age, passing from rule by the Peucetians to the Goths, before being fought over by the Byzantines and Lombards. Repeatedly ransacked and destroyed, medieval Bari was conquered by the Saracens and became a small independent Muslim state. It was then taken over by the Franks, before returning to the hands of the Romans, who made it the major Italian political, military and commercial centre of the Eastern Roman Empire. In 1087, with the arrival of the relics of St Nicholas of Myra, commonly known as Santa Clause, Bari became a thriving religious centre uniting the East and West.



Norman rule in Apulia ensured a long period of prosperity for Bari, though it was still subject to conflict. Rebuilt by the Swabians, it experienced a new peak of splendour, until it declined again under the Angevins, torn apart by struggles between local squires and foreign bankers.

After going to the Aragonese and then the Dukes of Milan in 1464, it was restored to its former glory by Isabella of Aragon in 1500. In 1558, it fell into Spanish hands, experiencing numerous bloody rebellions, and in 1657 it was hit hard by plague. It then passed from Austrian to Bourbon rule, being renewed under French rule in the early 1800s with the construction of the new city.

After being returned to the Bourbons in 1815, it joined the Kingdom of Italy in 1860. This tumultuous history of dominations has left Bari with a unique artistic heritage for all to admire.

Bari is not only art, history, and ancient culture. In fact, a great social life awaits you.

WARNINGS

Bari is a relatively safe city for foreigners. Even though there are some areas to avoid (the main ones are the Libertà, Japigia, San Paolo, and Madonnelle neighborhoods), tourists should not face safety problems other than petty crime, the kind of crime you find in many cities. Use common sense and apply all usual safety precautions.

AVERAGES FOR BARI IN SEPTEMBER

This month is known as a warm month. The average maximum daytime temperature in Bari in September lies at 26.2°C (79.16°F). The average minimum temperature goes down to around 17.1°C (62.78°F) (often the minimum temperature is noted at night). Rainfall during September is moderate with an average of 66mm (2.6 inches). There are generally around 8 rainy days.

DATE AND VENUE

The conference will take place in Bari, Italy, 24-27 September 2024 at the **The Nicolaus Hotel Bari - HO Collection**. The conference will be organized in parallel sessions and poster exhibitions. The official language of the conference is English.

THEME OF THE CONFERENCE:

MEDICINAL MUSHROOMS: THE BET FOR THE FUTURE OF HUMANITY

ORGANIZED BY:

University of Bari, Department of Soil, Plant, and Food Sciences (Di.S.S.P.A.) Italian Society for Medicinal Mushrooms (SIFM)

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SCIENTIFIC PROGRAM OF CONFERENCE WILL INCLUDE:

- Keynote speeches
- Plenary lectures of invited speakers

Different symposia dedicated to:

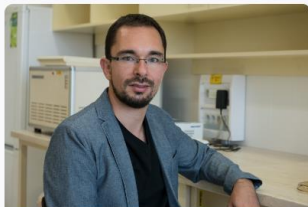
- Biodiversity, taxonomy and ecology of medicinal mushrooms;
- Medicinal mushrooms culture collections, cultivation technology and circular economy;
- Biochemistry, biotechnology and pharmacology of medicinal mushrooms;
- Use of medicinal mushrooms in animal husbandry and veterinary medicine;
- Medicinal mushrooms in human pre-clinical and clinical studies;
- Legislation, certification and safety of mushroom-based supplements;
- Medicinal mushrooms as a source of novel functional food and health benefits; Ethnomycology and the therapeutic potential of psychedelic mushrooms

KEYNOTE SPEAKERS



Dr Christoph Keßler
(Germany)

Clinical experiences from the use of medicinal mushrooms in outpatient hospital settings in Germany



Dr. László Nagy
(Hungary)

Basidiomycete fruiting body development: an exciting morphogenetic process and source of bioactive compounds



Prof. Robert Bruce Beelman (USA)

ERGO: A Potential Answer in Mushrooms for Healthy Aging



Dr. Tomáš Páleníček
(Czech Republic)

Does the phenomenology of psilocybin experience predict long-term outcomes on mood and well-being?

ROUND TABLE

USES OF PSLOCYBIN IN VARIOUS DISEASES AND IN END-OF-LIFE CARE

FRIDAY 27 SEPTEMBER 2024 H: 15:00-17:00

A panel discussion on the topic organized by the Luca Coscioni Association, an association founded in 2002 by Luca Coscioni, an economist with amyotrophic lateral sclerosis who died in 2006. among its priorities are the affirmation of civil liberties and human rights, particularly the right to science, self-directed personal care, the removal of architectural barriers, end-of-life choices, embryo research, access to medically assisted procreation, legalization of euthanasia, access to medical cannabinoids, and worldwide monitoring of laws and policies on science and self-determination.

CALL FOR PAPERS

We would be pleased to receive contributions from interested authors that follow the conference themes. Abstracts should focus on current issues relevant to progress in research and/or to industry and should be scientific and/or of technical content.

Your abstracts should clearly define the objectives of the presentation or the topics covered, key conclusions reached, and potential benefits for scientific developments and industry. Abstracts should not be more than 500 words but not less than 300.

Abstracts should be sent to IMMC12 (abstract@immc12.com) before the 15th of **February 2024**. Text documents must be in Word or PDF format and written according to the template included in the conference web site.

AT LEAST ONE OF THE AUTHORS NAMED IN THE ABSTRACT MUST REGISTER FOR THE CONGRESS. ONLY ABSTRACTS THAT ARE SUBMITTED BY THE AUTHORS WHO HAVE REGISTERED FOR THE CONGRESS SHALL BE INCLUDED IN THE PROGRAM.

HOW TO REGISTER

- 1) visit the conference web site (www.immc12.com)
- 2) click the menu button at the top to register (REGISTRATION) or directly go to <https://www.immc12.com/registration.html>
- 3) download file and fill in your details in the Conference Registration Form
- 4) edit the pdf file in each part
- 5) print and sign the pdf
- 6) pay the total registration fee due (registration+accommodations) through the bank account reported in the pdf file
- 7) send the pdf + the receipt of your bank payment to secretary@immc12.com

Registration form not accompanied by the registration fee will not be taken into consideration

For any question, please contact the conference organizers at secretary@immc12.com

IMPORTANT DATES AND DEADLINES

15 March 2024	Distribution of second circular
30 May 2024	Abstract submission deadline
15 June 2024	Notification to authors of abstract acceptance
30 June 2024	Early bird registration deadline
15 July 2024	Full paper submission deadline
31 July 2024	Closing date for registrations and accommodation
23 August 2024	Distribution of final scientific program
23 September 2024	Registration desk opens
24-27 September 2024	IMMC12-2024

For more information visit www.immc12.com

SPONSORSHIP

There are a number of sponsorship opportunities for this IMMC12 conference, where scientists from all over the world will meet in an atmosphere of excellence to discuss the most recent advances in medicinal mushroom researches. For more information on sponsorships, please contact secretary@immc12.com

We would like to extend our deep appreciation to all our partners and sponsors who will help make the IMMC12 Conference possible.

FULL PAPERS

Excellent papers of the IMMC12 will be published in the International Journal of Medicinal Mushrooms (IJMM). Please send the full paper according to journal format of the IJMM before **15 July 2024** if the IMMC12 secretary informs you of your abstract acceptance.

If you have any academic question, please send e-mail to secretary@immc12.com

Registration form is available starting **30 of May 2023** on the conference website www.immc12.com

Please print your registration form and send it to secretary@immc12.com

E-Poster

IN SUBSTITUTION OF THE TRADITIONAL POSTER SESSION (NOR PAPER POSTER NEITHER MOUNTING AREA WILL BE PROVIDED BY THE IMMC12 ORGANIZATION), IMMC12 ORGANIZE THE ELECTRONIC POSTER SESSION, OR E-POSTER SESSION.

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Failure to pay this fee will result in an incomplete registration.

If you have any question about payment, please send e-mail to secretary@immc12.com

REGISTRATION

Please note that individual registrations can be made ONLY using registration form available starting 30 of May 2023 on the conference website www.immc12.com.

All prices are in Euros and include VAT 22%.

REGISTRATION FEES

	EARLY BIRDS (until 30 May, 2024)	NORMAL (after 30 May, 2024)
REGULAR ATTENDEES	500,00 €	550,00 €
PHD STUDENTS, RESEARCH FELLOWS¹	300,00 €	350,00 €
ACCOMPANYING PERSON WITH LUNCHESES	350,00 €	380,00 €
ACCOMPANYING PERSON WITHOUT LUNCHESES	200,00 €	250,00 €
ONE-DAY REGISTRATION	150,00	180,00
LOWER INCOME COUNTRIES	350,00	350,00

¹PhD students and Research fellow registration forms must be accompanied by a signed letter from the head of Department attesting to student status.

The fee does not include accommodation costs.

REGISTRATION PACKAGE

The registration package for the participants includes:

Access to the conference and poster sessions, conference bag, final printed program, proceedings of the Conference, welcome cocktail reception, lunch on each conference day, coffee/tea/refreshment breaks, conference dinner, certificate of attendance.

Accompanying persons are entitled only to: welcome cocktail reception, lunch (only if required in the registration form) conference dinner.

TIMETABLE

Sept 23, 2024

09:00-22:00 Conference Registration

Sept 24, 2024

07:00-09:00 Breakfast

09:00-10:00 IMMC12 Opening Ceremony

10:00-10:30 Group Photo

10:30-12:30 IMMC12 Keynote Speeches

12:30-14:00 Lunch

15:00-18:00 Session 1

19:00-21:00 Welcome Reception

Sept 25, 2024

07:00-09:00 Breakfast

09:00-12:30 Session 2

12:30-14:00 Lunch

15:00-18:30 Session 3

Sept 26, 2024

07:00-09:00 Breakfast

09:00-12:30 Session 4

12:30-14:00 Lunch

15:00-18:30 Session 5

20:00 Congress Dinner

Sept 27, 2024

07:00-09:00 Breakfast

09:00-12:30 Session 6

12:30-14:00 Lunch

15:00-16:30 Closing Ceremony

INSURANCE

The registration fees do not include insurance of participants against accidents, sickness, cancellation, theft, property damage or loss. Participants are advised to arrange adequate personal insurance.

CONFIRMATION

Upon receipt of the registration form(s) with the appropriate fees, confirmation will be sent. Once registered, registrations cannot be changed to another fee category.

CANCELLATION OF REGISTRATION AND REIMBURSEMENT POLICY

Cancellations received before 30th June 2024 will be subject to a 40% surcharge on all monies paid. From this date onward, until 31st July 2024, cancellations will incur a 60% surcharge on all monies paid. From that date onward, no repayments will be made in the event of cancellation. Please note that refunds will be issued only after the end of the meeting.

ACCOMMODATION

To make room reservations, participants should use the link on the IMMC12 website at www.immc12.com/accommodation.html

Rooms are being held at the IMMC12 venue hotel at special rates. Accommodation at **The Nicolaus Hotel Bari - HO Collection (4 stars)** includes breakfast. **THE ACCOMMODATIONS WILL BE ARRANGED ON THE BASIS OF FIRST COME, FIRST SERVED. SINCE THE AREA OF BARI ATTRACTS A SIGNIFICANT NUMBER OF TOURISTS EACH YEAR, WE STRONGLY RECOMMEND TO BOOK YOUR ROOM IN ADVANCE.**

Once the availability of rooms at the Hotel Nicolaus has ended, participants will be arranged at the HI Hotel Bari, which is part of the same chain Ho Collection and is located 15-minute walk from the conference venue.

Alternatively, participants can independently decide to stay in one of the city's many hotels and B&Bs.

Since all activities of the IMMC12 will take place within the space of **The Nicolaus Hotel Bari - HO Collection** (conferences, meetings, display of posters and lunches), accommodation in this hotel is very advantageous and convenient.

All hotel rates are in Euros, per room/night, including service, breakfast and 22% VAT. The city of Bari does not currently have a city tax for accommodation.



The Nicolaus Hotel Bari - HO Collection

<https://www.thenicolaushotel.com/>

Via C.A. Ciasca 27, 70124 - Bari Phone - +39 080 5682111

Fax - +39 080 5042058

Email - info@nicolaushotel.com

ON SITE REGISTRATION HOURS

Visit the Registration Desk in the Congress Venue to register on site, should you check-in, or for assistance.

The Congress Hub will be located in the **The Nicolaus Hotel Bari - HO Collection, Via C.A. Ciasca 27, Bari.**

The hours of operation will be:

Monday 23 September 2024 – **09:00 to 22:00**

Tuesday 24 September 2024 to 26 Thursday 2024 – **09:00 to 19:00**

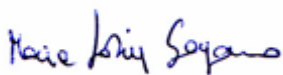
Friday 27 September 2024 – **08:00 to 17:00**

For more information: www.immc12.com

I Presidenti del Comitato Organizzatore / The Presidents of Organizing Committee

Prof. Maria Letizia Gargano

Prof. Giuseppe Venturella



India Mushroom Days

4th, 5th, 6th October the India Mushroom Days will be organized for the first time in New Delhi, India

WHY ATTEND?

Networking Opportunities

Whether you're looking to expand your business, share knowledge, or simply build valuable relationships, this event provides an unparalleled opportunity to network with like-minded individuals. Engage in discussions, exchange ideas, and forge partnerships that can drive your mushroom-related ventures to new heights.

Stay at the Forefront of Industry Trends

Stay at the forefront of the mushroom industry in the event. Engage with the latest trends, technologies, and market dynamics. Connect with peers, gain valuable insights and unlock new opportunities for success. Elevate your business and stay ahead of the curve in this dynamic and growing sector.

WHAT TO EXPECT?

Get a glimpse of the exciting lineup of workshops, seminars, networking opportunities, and more that await you at India Mushroom Days.



EXHIBITOR REGISTRATION

Exhibition booths are offered in multiples of 12 square meters at the India Mushroom Day'24. Minimum size for a booth is 12 square meters. Each booth will be equipped with prefabricated standard panels, lighting, a front table, a round table, four chairs, and a brochure display shelf. One complimentary conference registration and food coupons

for one person.

CONFERENCE REGISTRATION

Registration Information:

Conference registration provides delegates access to all three days of the IMD'24 event. The registration fee is for one participant & includes the registration kit, refreshments (morning tea, evening tea, lunch and entry to NETWORK DINNER) entry to the Exhibition Hall. This registration and fee does not include cost of stay in Delhi during the event days.

Registration Fee: FOREIGN PARTICIPANTS

Early Bird Registration (Till 31st May' 2024) : US\$490

General Registration (from 1st June' 2024 – 31st August' 2024): US\$590

Late Registration (After 1st September' 2024): US\$790

Registration Fee: INDIAN PARTICIPANTS

Early Bird Registration (Till 31/05/2024): 3995/-

General Registration (from 1/06/24 – 31/08/24): 5995/- + (18%GST)

Late Registration (After 1/09/2014): 7995/- + (18%GST)

Registration Fee: STUDENTS

GENERAL REGISTRATION: Rs. 2600/- (DOES NOT INCLUDE DINNERS)

** Registration is VOID if appropriate fee is not paid in prescribed deadlines.*

** This fee is refundable ONLY within Three Days of payment.*

** Fee is applicable for each participant please fill separate form for every candidate.*

CONTACT US

Info@Indiamushroomdays.com

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<https://www.cognitoforms.com/>

Research progress

Food and human health applications of edible mushroom by-products

Pablo Navarro-Simarro¹, Lourdes Gómez-Gómez^{1,2}, Oussama Ahrazem^{1,3}, Ángela Rubio-Moraga^{1,3}

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³*Escuela Técnica Superior de Ingeniería Agronómica y de Montes y Biotecnología. Departamento de Ciencia y Tecnología Agroforestal y Genética. Universidad de Castilla-La Mancha, Spain*

Abstract: Mushroom waste can account for up to 50% of the total mushroom mass. Spent mushroom substrate, misshapen mushrooms, and mushroom stems are examples of mushroom byproducts. In ancient cultures, fungi were prized for their medicinal properties. Aqueous extracts containing high levels of β -glucans as functional components capable of providing prebiotic polysaccharides and improved texture to foods have been widely used and new methods have been tested to improve extraction yields. Similarly, the addition of insoluble polysaccharides controls the glycemic index, counteracting the effects of increasingly high-calorie diets. Numerous studies support these benefits *in vitro*, but evidence *in vivo* is scarce. Nonetheless, many authors have created a variety of functional foods, ranging from yogurt to noodles. In this review, we focus on the pharmacological properties of edible mushroom by-products, and the possible risks derived from its consumption. By incorporating these by-products into human or animal feed formulations, mushroom producers will be able to fully optimize crop use and pave the way for the industry to move toward a zero-waste paradigm.

Keywords: Mushroom, Byproducts, Food Health, Antioxidants, Prebiotics

New Biotechnology, Volume 81, 25 July 2024, Pages 43-56

<https://doi.org/10.1016/j.nbt.2024.03.003>

A review of the effects of mushrooms on mood and neurocognitive health across the lifespan

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Abstract: Mushrooms contain bioactive compounds with documented antioxidant and anti-inflammatory actions. Here, we present a systematic evaluation of epidemiological and clinical studies that investigate the role of mushrooms, either as a separate or integral dietary component, on neurocognition and mood. Following a search of four databases, a total of 34 human studies examining the effect of different mushrooms across varying age cohorts and health statuses were selected for inclusion. Epidemiological studies included in this review (n = 24) revealed a significant benefit of dietary patterns that included mushrooms of any species on cognition and mood in both healthy and compromised populations. However, the results obtained from intervention studies (n = 10) were mixed. Studies mainly investigated Lion's Mane (*Hericium erinaceus*), showing some enhancement of mood and cognitive function in middle-aged and older adults. Further acute and chronic human intervention studies are needed, using adequate sample sizes, employing appropriately sensitive neurocognitive tests, and investigating a range of dietary mushrooms, to confirm the effects of mushroom supplementation on neurocognition and mood in humans.

Keywords: Mushroom, Neurocognition, Mood, Human

Neuroscience & Biobehavioral Reviews, Volume 158, March 2024, 105548

<https://doi.org/10.1016/j.neubiorev.2024.105548>

Design and implementation of a cost-aware and smart oyster mushroom cultivation system

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⁴School of Engineering, Technology and Design, Canterbury Christ Church University (CCCU), Canterbury, United Kingdom

⁵Department of Chemical and Environmental Engineering, University of Nottingham, Nottingham NG7 2RD, United Kingdom

Abstract: Mushrooms are a nutritious food source, which can play a crucial role in providing affordable sources of proteins, vitamins and minerals for people worldwide, but their cultivation requires extensive training and considerable relevant expertise in order to fine-tune multiple environmental parameters.

Internally displaced people in the Northern regions of Syria rely on very small-scale traditional oyster mushroom production, which cannot meet their local demand. Many international and local non-governmental organizations (NGOs) working for Syrian refugees, work on mushroom cultivation projects. They have reported significant difficulties and challenges in mushroom cultivation amongst the targeted beneficiaries. Therefore, the two main questions driving this research are: (1) How can organic mushroom cultivation be promoted using a robust and affordable intelligent mushroom farming system? (2) How can organic mushroom farming practices be simplified to support internally displaced and refugee Syrians?

This research evaluates the process of automating mushroom cultivation by designing and implementing a smart oyster (*Pleurotus ostreatus*) mushroom farming system to remotely monitor and manage environmental parameters,

such as temperature, humidity, air quality and illumination, inside the farm. Furthermore, ready and dedicated user-friendly web interfaces were also implemented to enable farmers to remotely monitor and manage their farms through the Internet. As a result, a dependable and cost-effective intelligent oyster mushroom cultivation system was designed and implemented in this work. The system includes remote monitoring and management via user-friendly interfaces. This simplifies mushroom cultivation for not only refugees and displaced communities, but also for mushroom farmers in low-income countries. This work can contribute to the eradication of poverty and hunger, in line with the United Nations Sustainable Development Goals one and two.

Keywords: Mushroom cultivation, Smart farming, Smart agriculture, Remote monitoring and management (RMM), Internet of Things (IoT), ThingSpeak™

Smart Agricultural Technology, Volume 8, August 2024, 100439

<https://doi.org/10.1016/j.atech.2024.100439>

A Poisoning Case Involving *Gymnopus dryophiloides* (Agaricomycetes)

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³*The First People's Hospital of Kunming, Calmette Hospital, Kunming 650000, P.R. China*

Abstract: Recently, mushroom poisoning is becoming one of the most serious food safety problems in China, especially in Yunnan province. However, there is insufficient information on many poisoning incidents, including mushroom information, identification and poisoning symptoms etc. In October 2022, a female midwife in Yunnan province consumed a wild mushroom twice. Detailed epidemiological investigation and mushroom identification were performed in this report. Based on morphological and phylogenetic analysis, the suspected mushroom was identified as *Gymnopus dryophiloides* (Omphalotaceae, Agaricomycetes). The victim reported nausea, vomiting, diarrhea, stomachache, accompanied by dizziness, headache, drowsiness, chest tightness, shortness of breath, palpitation, and weakness. The incubation period was approximately 30 min. After the victim's own vomiting, the symptoms began to subside for about an hour. Up to date, there are no detailed reports of poisoning in *G. dryophiloides*. In conclusion, it is the first detailed poisoning report of *G. dryophiloides* in the world.

Keywords: *Gymnopus dryophiloides*, mushroom poisoning, wild mushroom, gastroenteritis

International Journal of Medicinal Mushrooms, Volume 26, Issue 3, 2024, pp. 77-82

DOI: 10.1615/IntJMedMushrooms.2024052509

Advances in metabolomics to optimize quality parameters of culinary mushrooms

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²Biotechnology Department, Faculty of Health Sciences, Esa Unggul University, Jakarta, 11510, Indonesia

³Food Technology Department, Faculty of Engineering, Bina Nusantara University, Jakarta, 11480, Indonesia

Abstract

Background

Mushroom is a well-known food valued for its pleasant taste and medicinal benefits. Commercialization of mushrooms is quite challenging due to their perishability; their chemical composition fluctuates in response to many factors such as genotype, geographical origin, pre- and postharvest handling, and processing, leading to inconsistencies in functionality. Understanding how these metabolites respond to such factors is a prerequisite to optimizing mushroom handling of mushrooms for consumer needs. This review discusses how metabolomics has enhanced our understanding of mushroom quality at the molecular level. Once translated, this basic information can address numerous challenges associated with mushroom commercialization.

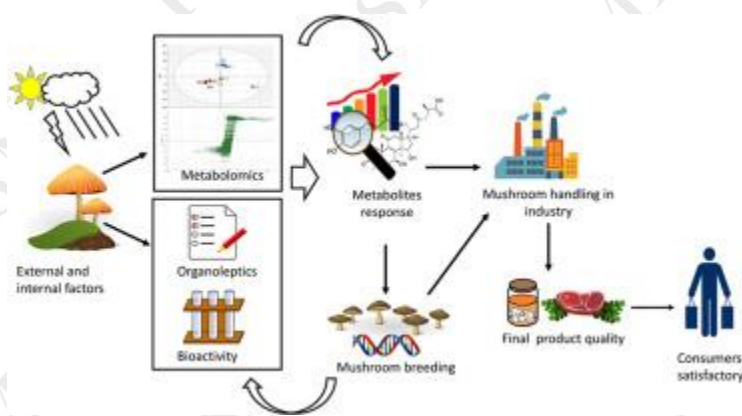
Scope and approach

This study comprehensively reviews and criticizes recent metabolomics-based research on culinary mushrooms.

Key findings and conclusions

Metabolomics is often used to explore how mushroom metabolites respond to various pre- and post-harvest handling conditions (genotype, storage condition, drying, and packaging). Using multivariate data analysis, the impact of metabolite changes on the physicochemical and organoleptic profiles (color, aroma, taste, and flavor) of various mushrooms can be clarified. Metabolomics has not yet been used optimally to link mushroom metabolite responses to their functionalities in various processed foods.

Graphical abstract



Trends in Food Science & Technology, Volume 145, March 2024, 104378

<https://doi.org/10.1016/j.tifs.2024.104378>

Chemical structure characterization of edible mushroom-extracted beta-glucan and its bioactivity

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¹Research Center for Applied Microbiology, National Research and Innovation Agency, Kawasan Sains dan Teknologi (KST) Ir. Soekarno, Cibinong, 16911, Indonesia

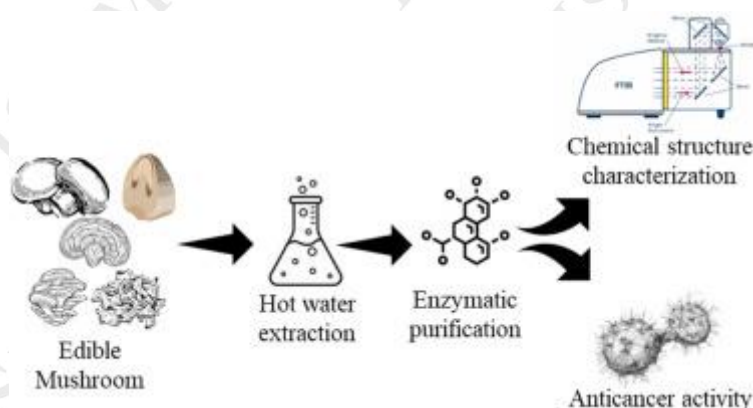
²Research Center for Biomass and Bioproducts, National Research and Innovation Agency, Kawasan Sains dan Teknologi (KST) Ir. Soekarno, Cibinong, 16911, Indonesia

³Research Center for Chemistry, National Research and Innovation Agency, Building 452, Kawasan Sains dan Teknologi (KST) BJ Habibie, Serpong, 15314, Indonesia

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Abstract: Beta-glucan has been known for its bioactivity such as for anticancer, antioxidant and antimicrobial agent. Naturally, beta-glucan is chemical structurally diverse in various beta-glucan sources such as edible mushroom. The chemical structure diversity of edible mushroom-origin beta-glucan has not yet been studied for its correlation with their bioactivity. Hence, this study observed the chemical structure and the bioactivity of beta-glucan extracted from five different edible mushrooms, which are *Pleurotus ostreatus*, *Ganoderma lucidum*, *Volvariella volvacea*, *Agaricus bisporus*, and *Auricularia auricula*. *A. auricula* contained the highest beta-glucan among the other edible mushroom (26.47 ± 3.45 g/100g). While *V. volvacea* beta-glucan extract possessed the highest cytotoxicity against breast cancer cells which enabled to inhibit 126.42% of cancer cells growth. It is shown that each edible mushroom has a different content of beta-glucan and bioactivity.

Graphical abstract



Bioactive Carbohydrates and Dietary Fibre, Volume 31, May 2024, 100411

<https://doi.org/10.1016/j.bcdf.2024.100411>

Comprehensive review on oyster mushroom species (Agaricomycetes): Morphology, nutrition, cultivation and future aspects

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²Department of Plant Pathology, Dr. Yashwant Singh Parmar University of Horticulture and Forestry, Nauni-173230, Solan, Himachal Pradesh, India

³Department of Plant Pathology, Chaudhary Charan Singh Haryana Agricultural University, Hisar-125004, (CCS HAU), Haryana, India

Abstract: Huge volumes of organic matter are produced on earth via photosynthesis and their disposal is a serious threat to the environment and public health all over the world. Nevertheless, these agricultural wastes possess a chemical composition conducive to mushroom cultivation. Lignocellulosic wastes, comprising cellulose, hemicellulose and lignin, offer vital nutrients for mushroom growth. Oyster mushrooms are well known for their unique ability to degrade lignocellulosic materials, making them valuable contributors to the process of organic waste decomposition and nutrient cycling in ecosystems. Employing agricultural by-products as a substrate for mushroom cultivation presents a sustainable approach to waste reduction and the production of nutritionally enriched food. Cultivating oyster mushrooms, presents an economically feasible and environment friendly method of transforming waste materials into highly nutritious food. These edible mushrooms are widely grown worldwide, comprising around 27 percent of the total global production. Oyster cultivation has rapidly increased in Asia due to its low production technology, easy availability of substrates, temperature tolerance and high yield capacity. Oyster mushrooms are sought after as a functional food due to their appealing taste, aroma, flavor, nutritional benefits and medicinal properties. They contain high levels of protein, fiber, vitamins B complex, C and D₂, as well as minerals like potassium, phosphorus, selenium, zinc and essential amino acids. These mushrooms are versatile, as they thrive in both tropical and temperate regions without requiring complex controlled environmental conditions for growth. This review article provides insights into the cultivation aspects of important oyster species including a novel species called *Hypsizygus ulmarius*. Oyster mushroom cultivation is rapidly growing in developing countries, where it can contribute to food security for the world's growing population, which is expected to reach 9.7 billion by 2050.

Keywords: Edible oyster mushrooms, Food security, Health benefits, Mycelium, Spawn, Waste management

Heliyon, Volume 10, Issue 5, 15 March 2024, e26539

<https://doi.org/10.1016/j.heliyon.2024.e26539>

Strategy on rapid discrimination of different varieties based on the combination of HS-GC-IMS and DNA Mini-barcode, spore powder of *Ganoderma* as a case study

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¹State Key Laboratory of Component-based Chinese Medicine, Tianjin Key Laboratory of TCM Chemistry and Analysis, Tianjin University of Traditional Chinese Medicine, Tianjin 301617, China

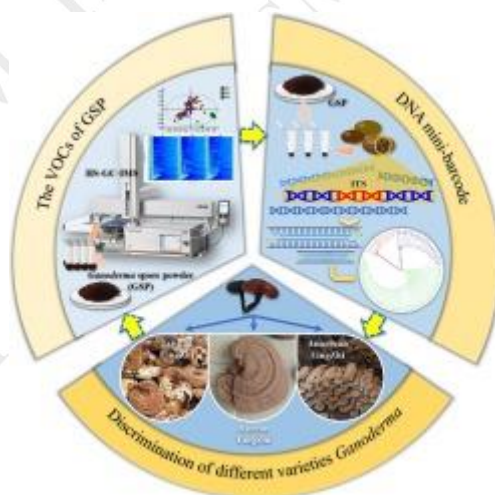
²Haihe Laboratory of Modern Chinese Medicine, Tianjin 301617, China

³School of Pharmaceutical Sciences, Guizhou Medical University, Guiyang, Guizhou, China

Abstract: The demand for the consumption of *Ganoderma* (LingZhi) is increasing significantly nowadays. While the wild resources of *Ganoderma lucidum* and *Ganoderma sinense* have been reduced severely, and artificially cultivated products are gradually occupying the market. However, it is usually difficult to distinguish the different species of *Ganoderma* spore powder (GSP). In this research, a rapid and accurate identification method which combined headspace-gas chromatography-ion mobility spectrometry (HS-GC-IMS) with the DNA mini-barcode was successfully

developed to discriminate different GSP. The feasibility of the method was evaluated by both GSP and its Chinese patent medicines. HS-GC-IMS was used to characterize GSP volatile organic compounds (VOCs) and a total of seventy-one VOCs were identified. Principal component analysis could be utilized to show the significantly difference between Korean LingZhi (KL) and American LingZhi (AL) or Taishan LingZhi (TL). Then, we clarified the species information of all samples based on the internal transcribed spacer (ITS) regions. The identification results showed that TL and KL were *Ganoderma lucidum*, and the AL was *Ganoderma resinaceum*. Furthermore, according to the mutation sites of the above ITS sequences, the specialized DNA mini-barcode was successfully developed and applied. The artificial mixtures of the three types of GSP and Chinese patent medicines containing GSP were used to authenticate the barcode capability. The mixing experiment found that there was a linear relationship between the sequence numbers and the mixed biomass, indicating that the qualitative and quantitative ability of DNA mini-barcode performed well. The investigation of the ingredients of commercially available GSP products found that the commercial products maybe contain *Ganoderma resinaceum*, *Ganoderma applanatum* and *Daedaleopsis confragosa*, except for *Ganoderma lucidum*. Therefore, the results suggested that the available GSP products might be adulterated according to Chinese Pharmacopoeia. In this paper, we established a novel approach to distinguish the different GSP samples based on HS-GC-IMS and DNA mini-barcode, and the results indicated that our strategy could not only discriminate different GSP samples, but also identify the origins in their related products.

Graphical abstract



Microchemical Journal, Volume 200, May 2024, 110212

<https://doi.org/10.1016/j.microc.2024.110212>

International Journal of Medicinal Mushrooms Call for Papers

We would like to invite you to submit an article to the [International Journal of Medicinal Mushrooms](https://www.begellhouse.com/journals/medicinal-mushrooms.html) (IJM), published by Begell House Publishers. As a leader in this field, we feel you would be an excellent fit as a contributor to this journal.

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The mission of [IJM](https://www.begellhouse.com/journals/medicinal-mushrooms.html) is to be a source of information that draws together all aspects of the exciting and expanding field of medicinal mushrooms - a source that will keep you up to date with the latest issues and practice.

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

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

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

Sincerely,

Solomon P. Wasser

Editor-in-Chief, International Journal of Medicinal Mushrooms

International Centre for Biotechnology and Biodiversity of Fungi

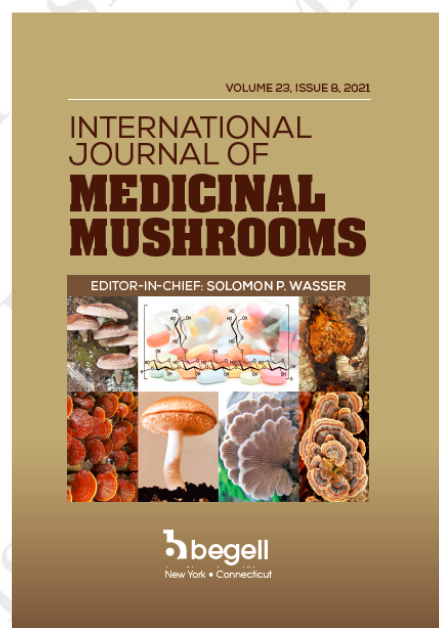
Institute of Evolution and Faculty of Natural Sciences

University of Haifa, Mt. Carmel, Haifa 31905, Israel

E-mail: spwasser@research.haifa.ac.il

For More Information and Submission

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



International Journal of Medicinal Mushrooms

2024, Vol. 26, Issue no.4

POTENTIAL ANTIVIRAL EFFECT OF KOREAN FOREST WILD MUSHROOMS AGAINST FELINE CORONAVIRUS (FCOV)

Rhim Ryoo, Hyorim Lee, Youngki Park

COMPARATIVE ANALYSIS OF AGRONOMIC TRAITS, YIELD, AND EFFECTIVE COMPONENTS OF MAIN CULTIVATED GANODERMA MUSHROOMS (AGARICOMYCETES) IN CHINA

Lei Sun, Yin Li, Lei Wang, Xiumin Pu, Wei-Huan Li, Xian-Hao Cheng

INSIGHTS ON STRAIN-SUBSTRATE INTERACTIONS AND ANTIOXIDANT AND ANTI-BACTERIAL PROPERTIES OF THE VELVET FOOT MEDICINAL MUSHROOM FLAMMULINA VELUTIPES (AGARICOMYCETES)

Rajnish Kumar, Dharmesh Gupta, Anupam Barh, Manoj Nath, Ved Parkash Sharma, Neerja Rana, Pawan Kumar Sharma, Chidembra Bhardwaj

THE LIQUID FERMENTATION PROCESS FOR MYCELIA OF PORIA COCOS (AGARICOMYCETES) BY SINGLE-FACTOR EXPERIMENTATION AND RESPONSE SURFACE METHODOLOGY

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ANTIOXIDANT DEFENSES AGAINST AIR HUMIDITY STRESS IN FRUIT BODIES OF AURICULARIA HEIMUER (AGARICOMYCETES)

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Points and Reviews

Ganoderic Acid A: A Potential Natural Neuroprotective Agent for Neurological Disorders: A Review

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ABSTRACT: Ganoderic acid A (GAA) is one of the major triterpenoids in *Ganoderma lucidum* (GL). Accumulating evidence has indicated that GAA demonstrates multiple pharmacological effects and exhibits treatment potential for various neurological disorders. Here, the effects and mechanisms of GAA in the treatment of neurological disorders were evaluated and discussed through previous research results. By summarizing previous research results, we found that GAA may play a neuroprotective role through various mechanisms: anti-inflammatory, anti-oxidative stress, anti-apoptosis, protection of nerve cells, and regulation of nerve growth factor. Therefore, GAA is a promising natural neuroprotective agent and this review would contribute to the future development of GAA as a novel clinical candidate drug for treating neurological diseases.

KEY WORDS: *Ganoderma lucidum*, ganoderic acid A, neuroprotection, neurological disorders, anti-inflammatory, medicinal mushrooms

ABBREVIATIONS: AD, Alzheimer's disease; AP, β -amyloid; CaSR, calcium-sensing receptor; CSDS, chronic social defeat stress; CPZ, cuprizone; CUMS, chronic unpredictable mild stress stimulations; EAE, experimental autoimmune encephalomy- elitis; EP, epilepsy; FST, forced swim test; FXR, farnesoid-X-receptor; GAA, ganoderic acid A; GAB, ganoderic acid B; GL, *Ganoderma lucidum*; HNs, hippocampal neurons; LSP, lipopolysaccharide; MBP, myelin basic protein; MCAO, middle cerebral artery occlusion; MOG, myelin oligodendrocyte glycoprotein; MS, multiple sclerosis; NDs, neurological disorders; NFTs, neuro- fibrillary tangles; PSD, post-stroke depression; PTZ, pentylenetetrazole; TST, tail suspension test

I. INTRODUCTION

At present, neurological disorders (NDs) have been the major threat to our health besides cardiovascular diseases and cancer. Common NDs include Alzheimer's disease (AD), epilepsy (EP), and depression. Given the relevance of aging and NDs,¹ it is urgent to find effective therapies with the coming of an aging society. Disappointingly, many clinical medicines are unable to achieve satisfactory effects and only delay the progress of NDs due to the complex symptoms and pathophysiology of NDs. Compared with chemical drugs, natural products have fewer adverse reactions and multiple targets. Thus, researchers pay attention to natural products to find effective therapies.

Ganoderma lucidum (Curt.:Fr.) P. Karst. (GL) (Ganodermataceae, Agaricomycetes) a famous medical mushroom (lingzhi or reishi), has been used in Oriental medicine for thousands of years and seems to be a great source of natural active ingredients. Because of its comprehensive applications in curing kinds of diseases, it was described as "herb of spiritual potency" in ancient China and "magic mushroom" in the West. GL has been commonly served as a tranquilizing agent to cure insomnia in China, which means GL could have some effects related to the nervous system. Modern studies showed that the compounds of GL mainly contain polysaccharides and triterpenes have a good effect on the treatment of NDs.²

TABLE 1: The pharmacological activity and mechanism of GAA in NDs

Pharmacological effects	Mechanisms	Ref.
Anti-Alzheimer's disease	p-Tau, A β peptides, APOE, TREM2, CD33, TNF- α and NF- κ B p65 \downarrow LC3A/B \uparrow Regulates sphingolipid metabolism	20
	Conversion of LC3B-I to LC3BII, Atg5, Becn1, Map1lc3b, Axl and Pak1 phosphorylation \uparrow p62 expression \downarrow	22
	LDH leakage \downarrow , Prevents Ca ²⁺ overload caspase-3 activity and Bax expression \downarrow tau protein phosphorylation at sites S199 and T231 \downarrow	24
	LC3B expression \uparrow Inhibits microglia activation Promotes autophagy in an Axl-dependent manner	30
	Bcl-2, LC3B I / II, PADI4 expression \uparrow P16, P21, Hmgal, ATG5, Beclin 1, p-Akt, p-mTOR \downarrow	32
	The percentages of IL-17A, IL-17F, IL-21, and IL-22 \downarrow The percentage of CD4 ⁺ CD25 ⁺ Foxp3 ⁺ \uparrow	
	IL-17A, IL-6, P-JAK2, P-STAT3, and ROR- γ t \downarrow IL-10, IL-35, TGF- β 1, and Foxp3 \uparrow	
	Enhances oxidative phosphorylation by regulating Tregs	
Antiepilepsy	SOD activity \uparrow Stabilizes the mitochondrial membrane potential	3
	calcium-sensing receptor, p-P38, p-JNK, cleaved caspase-3, and Bax \downarrow p-ERK and Bcl-2 \uparrow	39
	IL-1 β , IL-6 and TNF- α , p-I κ B α and NF- κ B (p65) \downarrow	41
	Iba1, iNOS, IL-1 β , IL-6 and TNF- α \downarrow	42
	Arg-1, BDNF, FXR \uparrow	47
Anti-multiple sclerosis	Myelin content, MBP, IL-4, BDNF, FXR \uparrow IL-1 β , IL-17 and IL-6 \downarrow	
Antidepressant-like effects	p-GluA1 (S845), GluA1, GluA2 and FXR \uparrow NLRP3, pro-caspase-1, caspase-1, pro-IL-1 β , and IL-1 β expression levels \downarrow	55
	BDNF, NGF, IL-10, Arg-1 and CD206 \uparrow TNF- α , IL-1 β , IL-6, iNOS and CD86 \downarrow Activates the ERK/CREB pathway	56

Ganoderic acid A (GAA), one of the major triterpenes of GL, is commonly used as one of the quality evaluation indicators of GL. Most GAA research focuses on the anti-tumor aspect. Recently, some studies indicated that GAA may have a great potential to treat NDs. For example, it was found that GAA protected neurons from apoptosis by improving the antioxidant effect and stabilizing the mitochondrial membrane potential.³ In addition, GAA also protected neural cells against NO stress injury via stimulating β adrenergic receptors.⁴ Moreover, GAA was found to be able to through blood-brain barrier,⁵ which also directly proved the treatment potential of GAA on NDs.

In this paper, we reviewed and summarized the effects and related mechanisms of GAA on the treatment of NDs such as AD and multiple sclerosis (MS) (Table 1 and Fig. 1), to serve for the further exploration of the interaction between them.

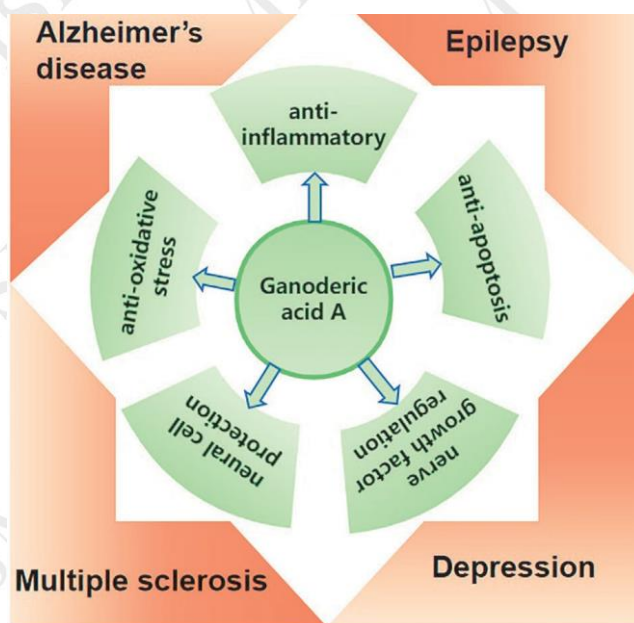


FIG. 1: Overview of the effects of GAA on neurological disorders. GAA is effective in treating neurological disorders, mainly including Alzheimer's disease, epilepsy, depression, and multiple sclerosis, through various mechanisms: anti-inflammatory, anti-oxidative stress, anti-apoptosis, neural cell protection, and nerve growth factor regulation.

II. GAA

In 1982, Kubota et al.⁶ first isolated GAA from *Ganoderma lucidum*. GAA has the chemical formula, $C_{30}H_{44}O_7$, and a molecular weight of 514.65. It is a white crystal that is soluble in trichloromethane, ethyl acetate, and other organic solvents. The structure of GAA is shown in Fig. 2. It was primarily distributed in the pileus and stipe regions. In addition, the shape of the fruit body and the growth stage of GL affect the content of GAA.⁷ Compared to normal shape (kidney), ginkgo leaf-shaped GL has higher GAA content owing to the large area of the outer layer and stout outer context. Different metabolites are produced during different growth stages, especially when a mushroom is in its growth phase.⁸ The study showed that the fruit bodies at an early growth stage had a higher content of GAA than those at a later growth stage. These results led us to select a more suitable growth phase and region for harvesting to obtain extracts with higher contents of GAA.

GAA has a tetracyclic ring with one internal double bond and a terminal carboxyl group on the branch (Fig. 2). Analyzing the binding modes of GAA and its isoforms with STAT3, the $-COOH$ group was seen to play a crucial role, leading to differences in bioactivity and binding affinities.⁹ In addition, the free carboxyl group of GAA is similar to that of many aldose reductase inhibitors such as tolrestat and zopolrestat, and this head can bind to aldose reductase in the form $(COO)^-$. It can be concluded that GAA has therapeutic potential for diabetic complications, which contain

neuropathy and are caused by the accumulation of sorbitol, based on their inhibition of aldose reductase.^{10,11} Additionally, GAA has an α , β -unsaturated ketone in its structure. Most anti-inflammatory steroids have the α , β -unsaturated ketone in their structures.¹² Therefore, we could suppose that the α , β -unsaturated ketone may be the reason for anti-inflammatory of GAA. The relationship of both needs to be explored.

Docking studies were performed for the interaction investigation between ganoderic acids and AChE protein.¹³ The results showed that the C-17 side chain of ganoderic acid, especially 25-COOH group may play a key role for the inhibition activity of acetylcholinesterase. All of these related research provide the foundation for GAA eventually playing an important role in the treatment of NDs.

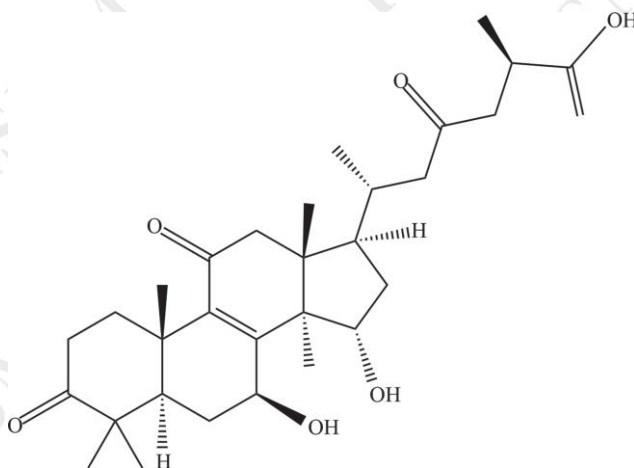


FIG. 2: Chemical structural formula of GAA

III. EFFECTS OF GAA IN NERVOUS SYSTEM DISEASES

A. Protective Effects Against Alzheimer's Disease (AD)

AD, characterized by progressive cognitive dysfunction and memory impairment, is one most common form (60–80%) of dementia and brings great burdens to the life and health of elderly.¹⁴ It is reported that about 6.7 million Americans over the age of 65 are now living with AD and by 2060, that terrible number could increase to 13.8 million.¹⁵ Between 2000 and 2019, the number of deaths due to AD increased by more than 145%, and AD is still the fifth cause leading to death in America. The main neuropathological profiles of AD are abnormal deposition of β -amyloid ($A\beta$) in the brain leading to senile plaques and neurofibrillary tangles (NFTs) formed by hyperphosphorylation of tau protein.¹⁶ Although it has been 100 years since AD was discovered, the complex mechanisms that bring about the pathological characteristics of AD have been not clear. Therefore, existing drugs can only relieve symptoms rather than cure the disease and have kinds of adverse actions. Thus, seeking help from nature productions may be a choice due to its safety and rich biological activities.

One molecular docking experiment was designed to find neuroprotective agents in GL extract for the treatment of AD and GAA was selected as one promising agent against microtubule affinity regulation kinase 4, which is recognized as a potential cure target for AD.¹⁷ Oxidative stress plays a pivotal role in the pathogenesis of AD and may even serve as a fundamental factor.¹⁸ GAA has been found to have a positive effect in reducing the oxidative damage caused by H_2O_2 in neurons.¹⁹ Thus, there are many *in vitro* and *in vivo* experiments that have been performed to explore the effects of GAA on AD (Fig. 3). $3 \times Tg-AD$ mice model was used by Zeng et al.²⁰ to study the effect of GAA on improving brain function in AD. After the treatment of GAA, the expression of AD biomarkers p-tau, $A\beta$ peptides, APOE, TREM2, and CD33 in brain tissues were reduced, and the level of the autophagy-associated gene LC3A/B was upregulated in AD mice.

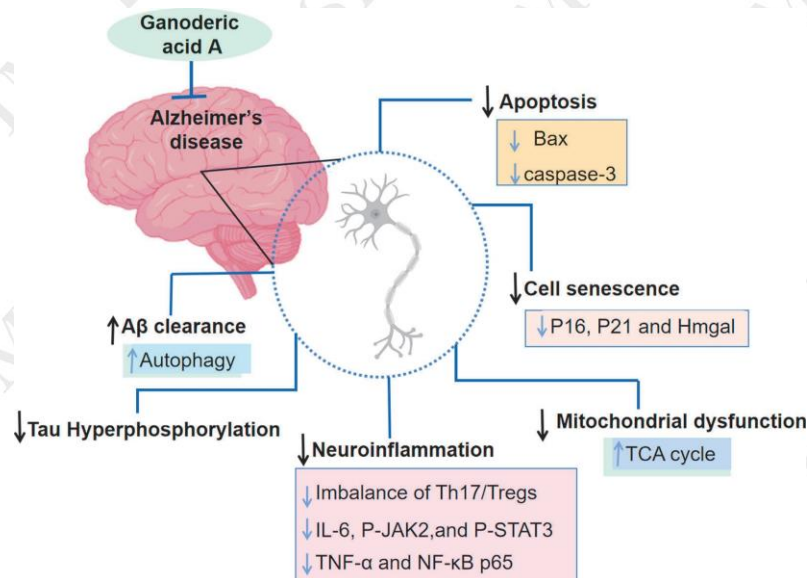


FIG. 3: The main mechanisms of GAA affecting Alzheimer's disease. GAA can treat Alzheimer's disease by enhancing autophagy to induce A β clearance, inhibiting tau hyperphosphorylation, lessening neuroinflammation, reducing neuronal apoptosis and neuronal cell senescence, and improving the mitochondrial dysfunction of the neuron. \uparrow , upregulating; \downarrow , downregulating.

In addition, the results of the unsupervised metabolome analysis showed that sphingolipid metabolism was influenced by exposure to GAA, which is crucial to the normal function of brain.²¹ Together these results, GAA may play a role in improving brain function in AD by regulating the sphingolipid metabolism and enhancing autophagy to promote the removal of pathological metabolites. Especially, in this research, it was found that GAA could breach the blood-brain barrier, which provides an opportunity for GAA to play its neuropharmacological role. In addition, one *in vitro* study showed that GAA could promote the clearance of A β 42 in BV2 cells by activating autophagy through the Axl/Pak1 signaling pathway.²² Furthermore, the researchers also investigated the effect of GAA on the cognitive function of AD mice model and found that GAA ameliorated cognitive deficits and decreased the A β 42 accumulation by promoting autophagy in an Axl-dependent manner. Significantly, GAA may be more suitable in the treatment of early-stage AD because increasing autophagy can lead to lysosomal blockage in late-stage AD.²³ Additionally, Cui et al.²⁴ investigated the protective action of GAA on PC12 cells treated with okadaic acid (OA), which contributes to tau phosphorylation to induce NFTs formulating. The results showed that GAA prevented PC12 cells from apoptosis by downregulating Bax and markedly suppressed the hyperphosphorylation of tau.²⁴

Cellular senescence refers to a state of permanent cell growth arrest.²⁵ Numerous brain cells related to AD have shown a tendency to senescence.^{26–28} The studies also indicated the important role of cell senescence in the progress of AD and removing the senescent cells may improve the mitigation of the disease.²⁹ Shen et al.³⁰ explored the effect of GAA on HT22 cell senescence induced by A β 25–35, a neurotoxin sub-type of A β and transfected PADI4 into GAA-treated AD model cells to further explore the roles of PADI4 and GAA in the pathogenesis of AD. It is a common method of establishing an *in vitro* AD model that uses A β 25–35 to deal with normal neuronal cells.³¹ The results showed that GAA could significantly relieve the toxicity of A β 25–35. After GAA treatment, the viability of AD cells was increased, the generation of senescent cells and the apoptosis rate of AD cells were significantly decreased. The results were consistent with the detection of the related protein. Furthermore, siPADI4 transfection partially reversed the effects of GAA on AD model, but the result of which is contrary to the result induced by overexpression of PADI4. Thus, PADI4 takes part in the role of GAA on AD and the clear mechanism needs in-depth study.

As we all know, neuroinflammation is also involved in the progress of AD and plays a noticeable role. GAA was found to decrease the level of inflammatory cytokines including tumor necrosis factor alpha (TNF- α), as well as nuclear factor kappa B (NF- κ B) in the brain of 3 \times Tg-AD mice, which indicated that GAA inhibited the inflammation response occurring within the AD brains.²⁰ Zhang et al.³² found GAA mitigated neuroinflammation of AD mice by promoting

the balance of Th17/Tregs axis, and the potential mechanism was related to inhibiting the JAK/STAT signaling pathway induced by Th17 cells and enhancing mitochondrial oxidative phosphorylation by regulating Treg cells, thereby improving the mitochondrial dysfunction of AD mice. Furthermore, GAA also improved the injury of the abilities of learning and memory and hippocampus of AD mice.

B. Antiepilepsy Effect

Epilepsy (EP) is a common neurological disorder that can affect every age group.³³ The obvious character of this disease is its durable tendency to bring forth epileptic seizures spontaneously.³⁴ It causes a huge burden for low- and middle-income countries due to the difficulty of treatment.³⁵ Unfortunately, about 1/3 of patients with EP are resistant to therapeutic drugs for a variety of reasons such as neurological deficits, age of seizure and the present drugs have some severe side effects.^{36,37} Happily, existing experiments have confirmed the fact that GAA shows considerable promise as a new drug to treat EP.

Hippocampal neurons were cultured without magnesium conditions, which is a common method for establishing vitro epileptic cell model.³⁸ This model was performed to preliminarily explore the therapeutic effect of GAA and ganoderic acid B (GAB) on epilepsy.³ The results showed that GAA and GAB treatment for 24 h improved the decrease of cell viability of hippocampal neurons (HNs) cultured in Mg^{2+} -free medium, the effect of which is equal to sodium valproate (one first-line antiepileptic drug) treatment. Thus, GAA and GAB can play a role in protecting neurons to lessen HNs damage caused by Mg^{2+} -free condition. In addition, the neuroprotective effect of GAA in HNs was found to be related to its anti-oxidative stress effect. In this experiment, GAA enhanced the SOD activity of HNs with epileptic while GAB did not show a similar effect. Furthermore, GAA as well as GAB stabilized the mitochondrial membrane potential of damaged neurons, which has a strong relevance with apoptosis. Thus, GAA prevents HNs from apoptosis caused by seizure through the mitochondrial pathway.

Pang et al.³⁹ investigated the role of GAA in the treatment of seizure mice caused by pentylenetetrazole (PTZ) and the results showed the action of GAA was like that of sodium valproate in intervening seizure. After GAA was administrated for 7 d, the epileptic behaviors of seizure mice were attenuated, which was like the treatment of sodium valproate. However, the duration of administration of GAA was not enough, which limited it to play a more visible role. Thus, the reasonable dosing duration of GAA needs to be further explored for its great utilization. The fact that because of the treatment of GAA, the latency of seizure mice was reduced, accomplished with the duration of seizure decreasing proved the feasibility of GAA as an antiepileptic drug. Through pathological assessment, GAA protected the neurons of cortex and hippocampal tissues from damage by PTZ. GAA remarkably alleviated the neuron apoptosis in the cerebral cortex of epileptic mice and the effect was stronger than sodium valproate. As the further study of the mechanism, the results showed that GAA decreased calcium-sensing receptor (CaSR) expression and promoted the downregulation of p-p38 and p-JNK expression involved in the MAPK pathway, as well as the upregulation of p-ERK expression. Beyond that, GAA lessened the level of two proapoptotic proteins, Bax and cleaved caspase-3, and increased the level of Bcl-2 protein playing an anti-apoptosis effect. Consequently, the *in vivo* study greatly indicated the antiepileptic effect of GAA which is through lessening neuron apoptosis, inhibiting CaSR expression, and the stimulation of MAPK/ERK signal pathway.

Microglia was reported to take part in inducing epilepsy via the release of inflammatory mediators.⁴⁰ The inhibition of microglia-mediated inflammation may be a potential precaution and therapeutic for epilepsy. GAA could support the activated microglial cells in M1 status (secreting inflammatory factors) conversing to M2 status (secreting anti-inflammatory factor) to attenuate inflammatory response. In the effect of GAA on factors release, it could reduce interleukin-6 (IL-6), IL-1 β and TNF- α release, which are proinflammatory cytokines from microglial cells induced by lipopolysaccharide (LSP), partly through inhibiting the NF-KB signaling pathway. Researchers also observed that GAA suppressed the increased mitochondrial activity caused by LSP. Furthermore, the effect of GAA induced the upregulation of farnesoid-X-receptor (FXR) was found to be involved in the inhibition of proinflammatory cytokines release and the promotion of BDNF expression to exert anti-inflammatory action.^{41,42}

In addition, seizures can lead to brain neuron damage, dendritic spines abnormalities, neurodegeneration, resulting in cognitive, learning, memory dysfunction.⁴³ GAA could protect the hippocampal dendritic spines of epileptic rats and improve their learning and memory function, which is another advantage of GAA for the treatment of epilepsy and whose specific regulatory molecular mechanism still need to be further studied.⁴⁴

Together with the above findings, GAA is promising for development as an effective drug for the treatment of epilepsy because it possesses the effects of neuroprotective, anti-oxidative stress, anti-apoptosis, and anti-inflammatory (Fig. 4).

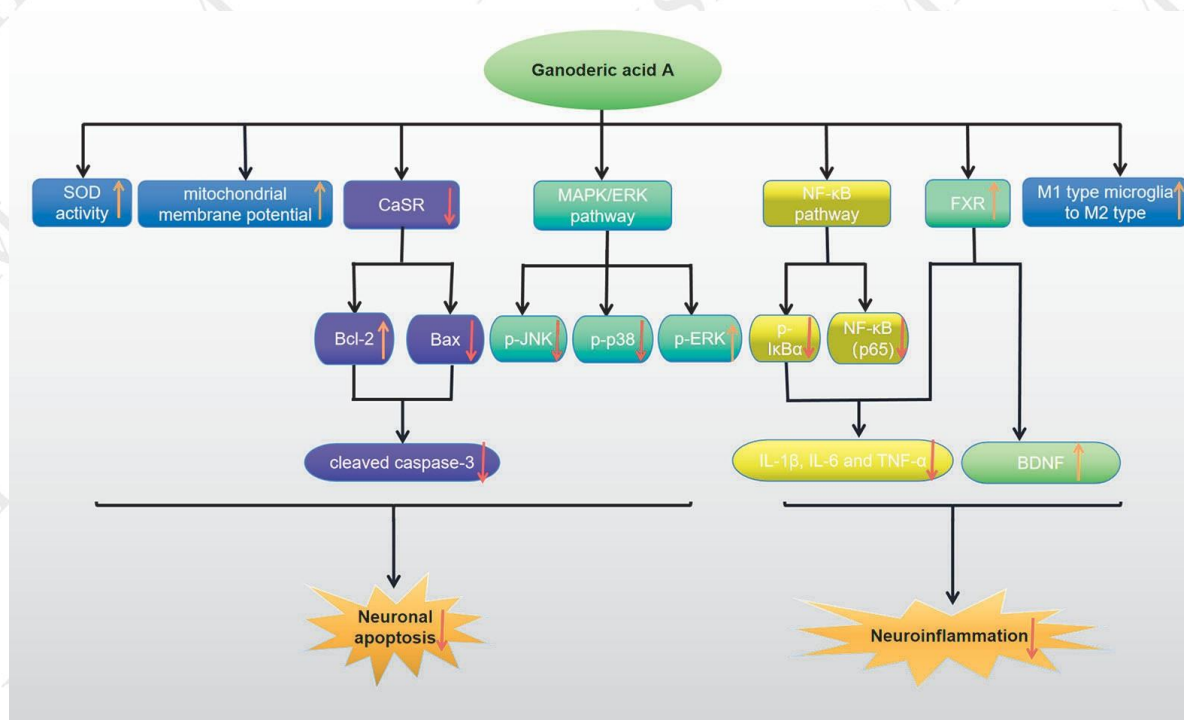


FIG. 4: Protective function of GAA in epilepsy. GAA can improve the SOD activity and mitochondrial membrane potential of hippocampal neurons, downregulate CaSR expression, and stimulate the MAPK/ERK pathway, all of which can preserve neurons by preventing apoptosis. Meanwhile, it can also reduce neuroinflammation by regulating the NF-KB pathway, upregulating FXR expression, and promoting the conversion of M1 type microglia to M2 type. CaSR, calcium-sensing receptor; FXR, farnesoid-X-receptor; ↑, upregulating; ↓, downregulating.

C. Therapeutic Effect on Multiple Sclerosis (MS)

MS is a kind of chronic immune-mediated neurodegenerative disease characterized by inflammatory demyelinating disease of the central nervous system.⁴⁵ In a cuprizone (CPZ)-induced demyelination model, GL was found to reduce demyelination and ameliorate motor impairment.⁴⁶ GAA is one of the pharmacodynamic material foundations for GL to be used in the treatment of MS. In terms of MS treatment, GAA was found to improve the remyelination as well as motor deficiency in two independent MS animal models, CPZ-induced demyelination model and myelin oligodendrocyte glycoprotein (MOG) 35-55-induced experimental autoimmune encephalomyelitis (EAE) model (Fig. 5).⁴⁷ CPZ was applied in the formation of acute demyelination. Then, the effect of GAA on the remyelination process was investigated. Compared to CPZ model group, the GAA-treated CPZ group showed an increase in locomotion time of the rotarod test, myelin content, and myelin basic protein (MBP) expression of corpus callosum. The results indicated that GAA improved the motor dysfunction and remyelination of demyelination mice. Especially, GAA at a dosage of 2.5 mg/kg resulted in the best therapeutic effect among the three dosages (1, 2.5, and 5 mg/kg). In addition, compared with control group, CPZ treatment increased the expression of the proinflammatory markers IL-1 and IL-6, and decreased the expression of regeneration markers IL-4 and BDNF. The effect of CPZ was significantly reversed by GAA. In addition, GAA inhibited the activation of microglia and astrocytes to act anti-inflammatory effect. Furthermore, GAA was found to play a useful effect on demyelination strongly related to interacting with FXR receptor.

Additionally, EAE model commonly serves as the demyelination model due to its pathophysiological characteristics related to clinic of MS. GAA treatment lessened clinical signs of EVE and reduced inflammatory infiltration and IL-17 in the spinal cord. GAA similarly enhanced remyelination in EAE mice and inhibited the activation of microglia and astrocytes induced by EAE. Together with the results, GAA may be a promising candidate against MS because of its properties of anti-inflammation, repairing myelin, and enhancing remyelination. It also could be combined with clinical MS therapeutics which mainly focus on the immune modulating.⁴⁸ However, successfully translating the findings to the application for treating MS clinical patients will be achieved by further research.

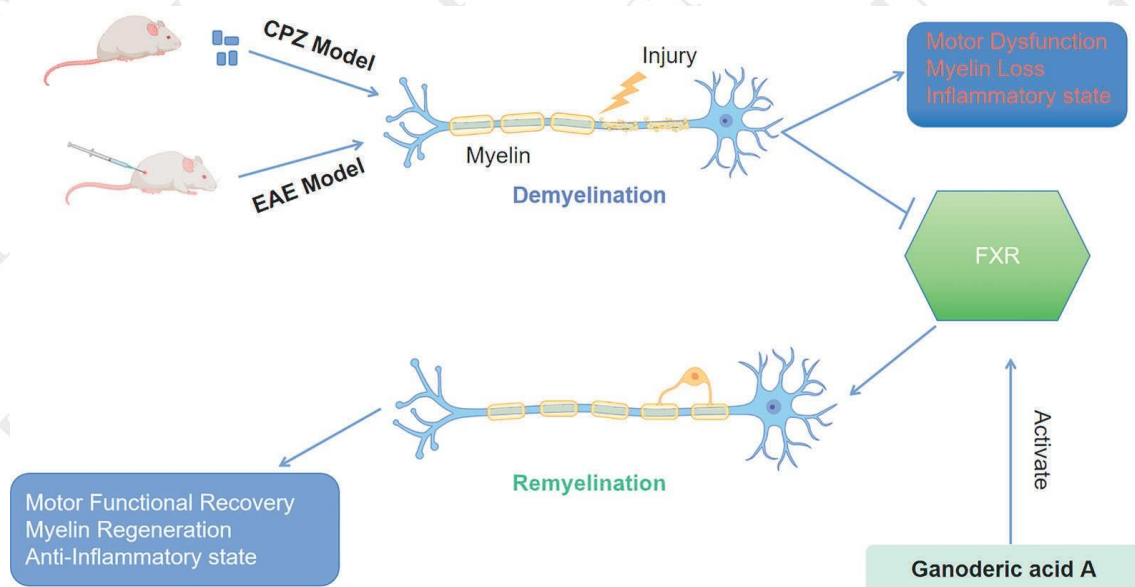


FIG. 5: Mechanism of GAA against multiple sclerosis. GAA can decrease disease severity of EAE or CPZ animal models by directly activating FXR to induce the anti-inflammatory and regeneration status, leading to enhanced remyelination and functional recovery.

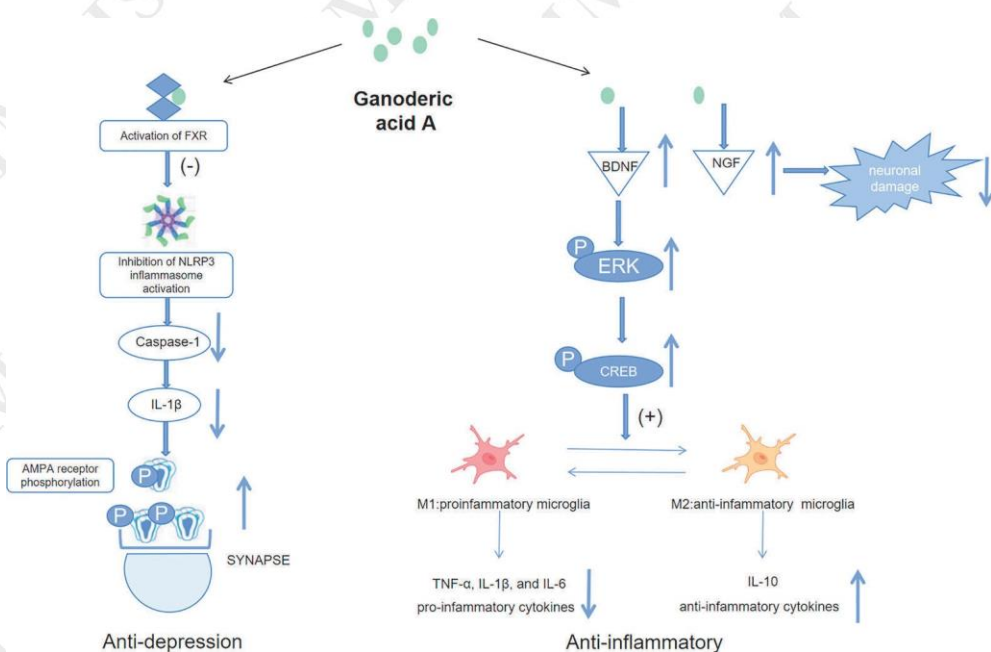


FIG. 6: Mechanism of GAA against depression. Anti-depression: The activation of FXR by GAA leads to the inhibition of NLRP3 inflammasome activity and a decrease in capase-1, which will subsequently reduce the production of inflammatory IL-1β and enhance the phosphorylation of AMPA receptors. Anti-inflammatory: GAA can increase the expression of BDNF and NGF to attenuate the neuronal damage and inhibited M1 microglial polarization and facilitated M2 microglial polarization by activating the ERK/CREB pathway. (), inhibition; (+), promotion; ↑, upregulating; ↓, downregulating.

D. Antidepressant-Like Effect

Depression is a common chronic neuropsychiatric disease seen in clinics, characterized by negative attitudes, sadness, and delayed cognitive function.⁴⁹ Depression may result in an increased incidence of diabetes, cardiopathy, and even mortality.^{50–52} At present, the prevalence rate of depression tends to increase as social pressure increases. It is still an important contributor to the global burden of disease. Synaptic abnormalities as well as inflammation are considered to cause brain function abnormal resulting in depression.⁵³ It was reported that GL triterpenoids extract could reduce the occurrence of depressive symptoms in adult mice that had previously been exposed to maternal separation and subacute stress by alleviating brain inflammation.⁵⁴

In present studies, GAA shows antidepressant and anti-inflammatory effects in animal models of depression (Fig. 6). To investigate the antidepressant effect of GAA, some tests, including tail suspension test (TST) and forced swim test (FST) were performed.⁵⁵ Researchers showed that GAA could significantly decrease immobility time in TST and FST, which was comparable to imipramine, one common antidepressant. Additionally, GAA did not influence the locomotor activity and weight of mice. On this basis, a depression model induced by chronic social defeat stress (CSDS) was established to further study the antidepressant effect of GAA. GAA was found to reduce depression-like behaviors and increase the FXR expression to inhibit the activity of NLRP3 inflammasome and promote the phosphorylation of AMPA receptors in CSDS mice. Especially, FXR knockout induced depression in mice, which indicated that FXR may be a potential target for treating depression. In addition, Zhang et al.⁵⁶ explored the impact of GAA on post-stroke depression (PSD) model which was established by middle cerebral artery occlusion (MCAO) combined with chronic unpredictable mild stress stimulations (CUMS). Results showed that GAA alleviated the depression-like behaviors and the hippocampal neuronal damage in PSD rats. In addition, GAA enhanced the expression of BDNF and NGF to protect neurons. GAA also lessened the inflammation in the hippocampus of PSD rats via the degradation of TNF- α , IL-1 β , and IL-6 and the increase of IL-10. GAA was found to suppress M1 microglial polarization and promote M2 microglial polarization, which was involved in the antidepressant therapy.^{57,58} The ERK/ CREB pathway is reported to be involved in preventing depression symptoms.⁵⁹ In this experiment, GAA could activate the ERK/CREB pathway by increasing the phosphorylation of ERK and CREB, and the effect of inducing M1/M2 microglial polarization was reversed when the pathway was inhibited. Thus, it could be concluded that GAA possessed its effect on PSD through the regulation of ERK/CREB pathway.

IV.. CONCLUSIONS

The potential therapeutic action of GAA on NDs mainly owing to its anti-inflammatory, antioxidant, and antiapoptotic activities. In many situations, GAA seems to have a promising alternative to treating NDs accompanied by fewer side effects than present drugs. In addition, GAA is quickly absorbed by the body, slowly eliminated, and permeates the brain, which is beneficial in the treatment of NDs.⁵ However, the low oral bioavailability of GAA may cause problems in its application against NDs.⁵ In this case, one liposome-gold nanorod vesicular system was designed for the improvement of bioavailability of GAA and showed great antibacterial and antitumor activities.⁶⁰ Additionally, many herbal ingredients such as quercetin naringin and genistein can serve as bioavailability enhancers,⁶¹ which provides a novel insight into dealing with bioavailability issues. In addition, the low index of brain penetration is another limitation and could be enhanced by modern pharmaceutical techniques. For example, fabricating nanocrystals was reported to help lipophilic bioactive substances gain a higher index of brain penetration as well as oral bioavailability.⁶²

Although existing reports have shown the great neuroprotective properties of GAA, further research is still requested for the use of clinical treatment. The evidence is formed from studies *in vitro* and *in vivo* animal models. Thus, we need human studies to further confirm the fact that GAA could be a neuroprotective agent. Beyond that, it is suggested that we should pay attention to exploring the other possible applications of GAA as a novel option compared with existing therapies of NDs.

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

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