ISMM

INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

国际药用菌学会

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

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

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

国际药用菌学会名誉主席：张树庭教授 S.P. Wasser教授
主席：李玉院士
执行主席：陈惠先生
秘书长：刘自强先生

Address: Room D-1216, Jun Feng Hua Ting, No. 69 West Beichen Road, Chaoyang District, Beijing 100029, China.
Tel: +86-10-58772596, 87109859 Fax: +86-10-58772190 Website: www.ismm2013.com E-mail: ismm.org@gmail.com

NEWSLETTER OF THE INTERNATIONAL SOCIETY FOR MEDICINAL MUSHROOMS

Volume 1, Issue 8

Date-released: December 18, 2017

Issue Editor- Mr. Ziqiang Liu
lzqynkm@vip.163.com
Department of Edible Mushrooms, CFNA,
4/F, Talent International Building
No. 80 Guangqumennei Street,
Dongcheng District, Beijing 10062, China

News Reports

The 9th International Medicinal Mushrooms Conference (IMMC9), September 24-28, 2017, Palermo, Italy

Maria Letizia Gargano[1]& Giuseppe Venturella[2]

[1]Department of Earth and Maine Science, University of Palermo, Bld. 16, I-90128 Palermo (Italy); [2]Department of Agricultural, Food and Forest Sciences, University of Palermo, Bld. 5, I-90128 Palermo (Italy)

In September 2017 over 200 delegates from 49 different countries (Fig. 1) gathered in Splendid Hotel La Torre, Mondello (Palermo, Italy), for the 9th International Medicinal Mushrooms Conference. IMMC9 in Palermo was the first to be held in Italy. The theme to the Conference was "Advances in Medicinal Mushroom Science: Building Bridges between Western and Eastern Medicine". IMMC9 participants had the opportunity to discuss and share scientific innovations in the medicinal mushroom sector and to become aware of current research results.

Fig. 1.Group of participants during the plenary session in Room Tancredi.

The 9th International Medicinal Mushrooms Conference was organized by one of the author (G. Venturella), full professor of Forest Botany and Mycology at the Department of Agricultural, Food and Forest Sciences (University of Palermo). IMMC9 was sponsored by DXN Malaysia, Jangsu Alphay Biological Technology Co. LTD, Funghi Energia e Salute di Funghi Meravigliao Sas, AVD Mico, Aloha Medicinals Inc., Freeland, Società Agricola IoBoscoVivo, Consiglio Nazionale delle Ricerche, Lickson s.r.l., Associazione Planthology, Gourmet Mushrooms Inc., Mycology Research Laboratories ed Energ-Etica Pharm. A number of donors supported the Conference: Gheos, Frantoio D'Orazio, Fondazione Internazionale pro Herbario Mediterraneo, Libera Accademia di Medicina Biologica, Italmiko, Azienda Agraria Castelluccio, Gruppo Micologico Siciliano, Erboristeria Galenus, Natural 1, Impresa Leone s.r.l., Autoscuole Ragona e Fata Assicurazioni. IMMC9 was organized under the patronage of Università degli Studi di Palermo, Ministero delle Politiche Agricole, Alimentari e Forestali, Città di Palermo, Unione Micologica Italiana, European Mycological Association, Società Botanica Italiana onlus, Project FUNGUS, Organization for the Phyto-Taxonomic Investigation in the Mediterranean Area (OPTIMA) and Istituto Euro-Mediterraneo di Scienza e Tecnologia.

6 keynote speeches, 64 oral presentations, included in 5 symposia, and 61 e-posters were presented during IMMC9.

On September 25, 2017, the keynote speeches were performed by S.P. Wasser (Israel/Ukraine) "Medicinal mushroom science and mushrooms in human clinical studies on anticancer, oncoimmunological, and immunomodulatory activities", P.C.K. Cheung (Hong Kong/People's Republica of China) "Mushroom non-digestible carbohydrates as novel prebiotics" and, L. van Griensven (the Netherlands) "Mushroom extracts suppress pain: a critical approach".

In the plenary session of Tuesday 26 September 2017 U. Lindequist (Germany) "Antiallergic activities of medicinal mushrooms", P. Stamets (USA) "Mycelial extracts from polypore mushrooms reduce viruses and extend lifespans of the European Honey Bee (*Apis mellifera*)", and O. Isikhuemhen (USA) "Advances in the application of medicinal mushrooms in animal health and production" has held the keynote speeches.

David Hibbett, Professor of Biology at Clark University (USA), offered a lecture by the title "The changing shape of mushrooms: toward the new science of fungal evo-devo" in the frame of Symposium 1 (Chairperson G.I. Zervakis, Greece). The molecular systematics and phylogeny of *Ganoderma*, *Fomitopsis*, *Schizophyllum* and other medicinal mushrooms were the topics of oral presentations performed by V. Papp (Hungary), V. Fryssouli (Greece), A. Shnyreva (Russia), N. Purtseva (Russia), and E. Bošković (Serbia). In the end, S. Redhead (Canada) reported a brief note on Mycological Changes in the New Shenzhen Code (International Code of Nomenclature for algae, fungi, and plants) relevant to mushrooms.

The Symposium 2 "Cultivation of medicinal mushrooms" [Chairpersons L. van Griensven, A. Amazonas (Brazil), J. Holliday (USA), and M. Berović (Slovenia)] is started with the lectures of J. Holliday (USA) "Simplified and lower cost methods for mushroom cultivation using cold sterilization techniques" and M. Berović " Cultivation of medicinal fungi biomass and pharmaceutical compounds in bioreactors". Other oral presentation were offered by C. Jaramillo (Colombia) on the use of coffee pulp as substrate of cultivation of some edible and medicinal fungi and S. Montoya (Colombia) on the effect of blue led-light on the production of *Ganoderma lucidum* using agricultural residues as substrate. I. Bandura (Ukraine) reported the effect of pretreatment of wheat straw and solid-state fermentation on the yield and biological efficiency in *Pleurotus ostreatus* while S. Montoya offered a second oral presentation on production of *Grifola frondosa* in tropical weathers. A. Jasińska (Poland) presented results on the influence of cultivation substrate on the zinc content of medicinal mushroom *Agaricus subrufescens*. The contribution made by African researchers (Fig. 2) was greatly appreciated. J. Okhuoya (Nigeria) reported preliminary studies on the growth and cultivation of edible *Marasmius* from Nigeria and a novel method of cultivation of *Volvariella volvacea* using customized oil palm fiber blocks while C. Adenipekun (Nigeria) showed results on the growth, yield and nutritional quality of *Pleurotus pulmonarius* and *P. ostreatus* on different substrates supplemented with wheat bran. ML. Gargano (Italy) illustrated a research project based on culture collections of strains of potential nutraceutical interest.

The Symposium III [Chaipersons V. Varshney (India) and M. Berović (Slovenia)] was devoted to "Biochemistry of Medicinal Mushrooms". V. Varshney offered a lecture by the title "Understanding diversity and potential of mushrooms derived low molecular weight aroma and biologically active metabolites", F. Cateni (Italy) reported results

Fig. 2.Prof. G. Venturella with a delegation of African researchers:
U.K. Sandabe, J.A. Okhuoya, O.S.Isikhuemhen (from left to right).

of a mycochemical investigation of *P. eryngii* var. *eryngii*, T. Reid (Zimbabwe) illustrated compounds with activity against *Salmonella typhi* from selected Zimbabwean mushrooms extracts. V. Varshney reported results on nutritional composition, bioactive compounds and antioxidant potential of *Astraeus hygrometricus* while S. Zhou (People's Republic of China) illustrated changes in triterpene and polysaccharide content in *Ganoderma lucidum* during fruiting growth. The molecular properties and biological activities of *Cordyceps sinensis* (J-Y Wu, People's Republic of China), the effect of pH and sodium chloride on vegetative growth and polysaccharide secretion in *Lentinus squarrulosus* (O. Isikuehmen) and the respirometric analysis by sequential mass flux for quantifying the growth rate and biomass in solid substrate fermentations (A. Taylor, USA) were discussed during the symposium. The programme was completed by oral presentations on the enhancement of bioactive compounds in *Pleurotus* mushrooms produced on substrates containing olive or wineries by-products (G. Koutrotsios, Greece) and the biopotential and phosphate metabolism of *Coprinuscomatus* and *Coprinellus truncorum* (K. Tešanović, Serbia).

The Symposium IV, "Science, Technology and Potential Value of Medicinal Mushrooms", coordinated by Hui-Chen Lo (Taiwan), Omon S. Isikhuemhen (USA) and John Holliday (USA), began with the lecture of Angel Trigos (Mexico) on the antiparasitic activity of ergosterol peroxide isolated from *Pleurotus ostreatus* f. sp. *florida*. Then Ha Won Kim (South Korea) offered a oral presentation on the anti-hypertensive mechanisms activated by β-glucans of mycelial extracts. Qi Wang (China) presented a short communication on biologically active compounds derived from edible fungi and Antonella Marino Gammazza (Italy) illustrated the anti-carcinogenic effects of *Pleurotus eryngii* var. *eryngii* and the role of Heat Shock Proteins on *in vivo* and *in vitro* models. O. Isikhuemhen (USA) and M. Nikšić (Serbia) have highlighted the antiallergic activity and the antioxidant potential of some medicinal fungi in their oral presentations. Maria Grazia Cusimano (Italy) illustrated the presence of new antimicrobial peptides from desert truffles (*Tirmania pinoyi* and *Terfezia boudieri*) and their role in limiting resistance to antibiotics. Adriano Bonanno (Italy) reported the results of a research on the beneficial effects of fungal extracts on sheep and Janelle Robinson (USA) illustrated the results of a trial on broilers fed with mycelial extracts. Bioactivity in the genus *Morchella* was the subject of Segula Masaphy's (Israel) report, while Carsten Gründemann (Germany), Boris Jakopovic (Croatia) and Hui Chen Lo (Chinese Taipei) have highlighted the action of extracts of *Inonotus hispidus*, *Trametes* sp. and other medicinal mushrooms on the mechanisms of activation of the immune response. Antioxidant activity and polyphenol content in *Pleurotus* species extracts from the Amazon rainforest has been highlighted in Ceci Sales-Campos (Brazil) report. Japanese researchers Masashi Mizuno and Ken-Ichiro Minato focused on the effects of Lentinan and extracts from *Pleurotus citrinopileatus* on anti-inflammatory and immunostimulant activity. The medicinal, nutritional, antioxidant, inhibitory capacity of acetylcholinesterase activity of *Amanita strobiliformis*, *Hydnum repandum*, *Pleurocybella porrigens*, *Sterum hirsutum*, *S. subtomentosum*, *Bjerkandera adusta*, *Pleurotus tuber-regium*, and *Hericium erinaceus* were the subject of reports by Maja Karaman (Serbia), Ljiljana Janjušević (Serbia), John Okhuoya (Nigeria), and Elena Savino (Italy). Xiatong Yang (China) has highlighted the role of *Trametes versicolor* in trans-epithelial transport and in the activation of dendritic cells. Umar Sandabe (Nigeria) presented the results of the oral administration of *Ganoderma*'s methanolic extracts of Nigerian fungi species on the organs and body weight of albino rats. *Lentinula edodes*, *Pleurotus ostreatus* and *Fomitopsis pinicola* as functional foods with pharmacological, antioxidant, antimicrobial and medicinal properties have been the subject of reports by Italian researchers Simone Parola and Paola Angelini. Finally, John Okhuoya (Nigeria) informed the participants about the establishment of a Center for Research and Technological Innovation in Africa.

Symposium 5, dated 27 October 2017, entitled "Medicinal Mushrooms: The Importance of Randomized Clinical Trials and Evidence-Based Medicine", coordinated by Solomon P. Wasser (Israel/Ukraine) and Ulrike Lindequist (Germany), opened with an interesting report on "mycomedicine" in China by Prof. Hai-Ying Bao (China). Japanese researcher Daisuke Yamanaka reported the results of a study on *Agaricus brasiliensis* used as an oral vaccine to increase antibodies in the human body while Francesco Oliviero (Italy) focused on the antioxidant and anti-inflammatory properties of a Shiitake-Maitake-Reishi-*Cordyceps* preparation used in the prevention of oxidative stress and autoimmune diseases. Werner Brand (Germany) has highlighted the greatest bioavailability of water-poor elements in fungal extracts. Marco Tutone (Italy) presented a clinical trial on HPV patients, while Walter Ardigò (Italy) reported a case study on arterial hypertension control after administration of medicinal mushrooms such as *Auricularia auricula-judae* and *Polyporus umbellatus*. Stefania Cazzavillan (Italy) has highlighted the effects of *Hericium erinaceus* on the management of fecal calprotectin. Sandra Duque Henao (Colombia) reported a case study on children in disadvantaged areas of Medellin. In particular, Dr Henao highlighted the benefits to the patient's body after administering yogurt enriched with β-glucans. Paola Rossi (Italy) reported on a pilot study on overweight women and the beneficial effects of administering medicinal mushrooms to reduce mood and sleep disorders. Finally, Nicoletta Salviato (Italy) has highlighted the antioxidant, antimicrobial and anti-inflammatory properties of *Pleurotus eryngii* in the prevention of metabolic syndrome.

New to IMMC9 was e-poster session, an innovation never adopted in the previous editions of the Conference. The e-poster session has provided more immediate visualization of the contents, the opportunity to download the poster on a mobile device, also contributing to the environment in terms of paper savings.

During the closing ceremony, Prof. Werner Greuter, who has been Director of the Berlin Botanical Garden for years, has been present, on behalf of the Organization for the Phyto- Taxonomic Investigation in the Mediterranean Area (OPTIMA) and the International Foundation for Herbarium Mediterranean. Then Prof. Venturella and Prof. Wasser declared IMMC9 closed.

Subsequently, a prize money was awarded to two young participants, whose oral presentations were guided by high scientific content. Dr. Viktor Papp (Hungary) received the prize for his oral presentation “Which names should be used in medicinal mushroom science for the pharmacologically important *Ganoderma lucidum* complex? The impact of DNA sequence-data on taxonomy and nomenclature” and Dr. Vassiliki Fryssouli (Greece) for her oral presentation on “Phylogenetic study of European species of the genus *Ganoderma* (Basidiomycota) through the use of a multigene analysis combined with morphological characters”.

Award plates were distributed to the invited speakers David Hibbett and Paul Stamets and to IMMC9 Scientific Committee members. Prof. Venturella, on behalf of the IMMC9 Local Organizing Committee, also in the conviction of interpreting the feelings of the scientific community of medicinal mushrooms, took the opportunity in recognizing the scientific activity of Prof. Solomon Wasser, IMMC9 Honorary Chairman and Editor in Chief of the International Journal of Medicinal Mushrooms, for 20 years or more with the motivation: *For a lifetime dedication to Medicinal Mushroom research and their use as healthy food*.

At the end a video was presented for Nantong's candidacy in 2019, the next edition of the International Medicinal Mushrooms Conference (IMMC10). Professor Yu Li (Fig. 3), as the next organizer, invited attendees to participate in two years at the new event.

Fig. 3. Professor Yu Li (left) invited attendees to participate the IMMC10 in China

On September 28, 2017, the participants of the conference visited the medieval villages of Castelbuono and Cefalù and were received by the Mayors of the two towns that addressed them by the respective Administrations.

Fig.4. Participants of the IMMC9.

The 11th Chinese Mushroom Festival held in Zhangzhou

On the morning of November 17, the opening ceremony of the 11th China Mushroom Festival was held in Zhangzhou, Fujian. More than 2,000 guests from 22 countries, such as the US, Russia, Australia, Canada, Italy, the Netherlands, France, the United Kingdom, Ukraine, Japan and others, all attended the ceremony.

This year's Mushroom Festival was organized by China's Chamber of commerce, the Zhangzhou People's Government, the International Society for Medicinal Mushrooms (ISMM), the National Edible and Medical Mushroom Industry Technology and Innovation Strategic Alliance, the Fujian Edible Fungi Society and the Fujian Edible Fungi Industry Association.

Zhangzhou is very export-oriented, has a large agricultural output and a large number of brands. Since 2007, the Chinese Mushroom Festival has been successfully held in Zhangzhou ten times. The Festival was intended to be a platform for the domestic and foreign edible fungi industry representatives. Today it is the largest mushroom industry event in Asia.

Source: fj.chinanews.com

Up-coming Events

First Circular of the First Chinese (Gutian) Rare Mushroom Conference

The edible mushroom industry in Gutian Fujian has its special status in China and all over the world. Consider on the current situation and trend of domestic and foreign industrial development, Gutian plans to build and promote a top brand of edible mushroom industry by organizing marketing fairs in 3-5 years. The fair is aimed to improve the quality and increase efficiency of edible mushroom industry in Gutian, build the core competitiveness and promote a rise of the industry. It will enhance the influence of Gutian edible mushroom industry.

The conference will analysis the competitive advantage of Gutian edible mushroom industry objectively, highlight and create the brand of "Gutian", "*Tremella fuciformis*" and "Rare Mushrooms". With brand building, terminal channel construction, edible products trading and other means, Chinese (Gutian) Rare Mushroom Conference will be another beautiful scenery line of Chinese and world's edible mushroom industry convention.

The "Chinese Mushroom Days" is the brand held by the China Chamber of Commerce of Foodstuffs and Native Produce, which is the most successful and influential edible mushroom event in China and Asian-pacific region. "Chinese Mushroom Days" has become the platform of technology exchange for edible mushrooms by emphasizing technology introduction, communication and display.

More than 80% of the mushroom spawns (*Agaricus bisporus*, *Lentinula edodes, Flammulina velutipes*, *Hypsizygus marmoreus*) are imported from abroad for large-scale industrialized mushroom production in China. However, the spawns of *Tremella fuciformis, Auricularia auricular, Agrocybe cylindracea* and *Hericium erinaceus* are researched and well developed in China. These varieties have advanced world levels in production technology, equipment and industry development scale. The industry of the rare mushrooms in Gutian could dominate international market with core competitiveness! Therefore, the purpose of the conference is to create the "Chinese characteristic platform of display, trade and communication for valuable and rare edible mushrooms" that is totally different from "Chinese Mushroom Days".

Collaborated with China chamber of Commerce of Foodstuffs and Native Produce, the Gutian people's government will organize the first "Chinese (Gutian) Rare Mushroom Conference" from April 15th to 18th, 2018 in Gutian , Fujian province.

1 Event

The First Chinese (Gutian) Rare Mushroom Conference

2 Purpose of the Conference

To build Gutian as “the holy land Mecca”, and create platforms of “one belt and one road”, trading, display and communication for the Chinese rare mushroom industry.

3 Date

Apr. 16th-18th, 3 days conference. Registration on Apr. 15th.

(Visit is not included)

4 Theme

Session 1: Satellite meetings

(1) National purchaser conference for rare mushrooms (include production and marketing connection, trade promotion and investment promotion)

(2) Workshop on national regional brand and sales of channels building-up for rare mushroom industry

(3) Workshop on national investment and financing for rare mushroom industry

(4) Workshop on national sustainable development for rare mushroom industry

Main content: *Tremella fuciformis*, *Auricularia auricular*, *Agrocybe cylindracea* and *Hericium erinaceus* etc: factory cultivation and production technology, leisure and health food development, mushroom processing industry, mushroom leisure tourism industry and so on;

(5) Workshop on national bag-cultivation on automatic production and intelligent control for rare mushrooms

(6) The general election conference of China Chamber of Commerce of Foodstuffs and Native Produce Edible Mushroom Branch

Session 2: Exhibition

(1) Exhibition of the whole industrial chain of edible mushrooms in Gutian, around 40 standard booths

(2) Chinese edible mushrooms cultivation, production, processing, new technology, new equipment enterprises, around 60 labeled booths

(3) Set up special booth to display the image of Gutian County, including rural tourism, edible mushroom food, local culture, etc.

Session 3: Visit Gutian Rare Mushrooms Base

Include the base for *Tremella fuciformis*, *Auricularia auricular*, *Agrocybe cylindracea* and *Hericium erinaceus*, etc. (1 day)

5 Contact Information

Contacts: +86-13910657921 (Mr. Dongming Zhao) +86-13552827268(Mr. Yadong Huang)

+86-13311573135(Mr. Ziqiang Liu)

Tel: +86-10-87109859, 87109860, 67133450 Fax: +86-10-87109861

Email: zdmjordan@126.com (Mr. Dongming Zhao)

For more information about this conference, please refer to the second circular.

INTERNATIONAL MYCOLOGICAL CONGRESS July 16 - 21, 2018 | San Juan, PR "Mycological Discoveries for a Better World"

Welcome to International Mycological Congress (IMC) 11

The Mycological Society of America (MSA), the International Mycological Association, the Latin American Mycological Association (ALM), the Puerto Rican Mycological Society (SPM), Universidad del Turabo and Meet Puerto Rico are proud to sponsor the 11th International Mycological Congress in San Juan, Puerto Rico. This will be the first time IMC is celebrated in Latin America and the Caribbean region, one of the *circa* 30 biodiversity hotspots of the world. Puerto Rico is an ideal setting for a mycological congress because our long history in mycology and our location in the subtropical region offering a diversity of ecosystems (from dry to rain forests) harboring many tropical fungi.

San Juan, the capital city, possesses a state of the art convention center, excellent hotels, excellent cultural activities and an amazing culinary experience. The Luis Muñoz Marin International Airport is a main hub for different airlines receiving direct flights from major airports in the USA, Europe, Central and South America. Come and enjoy IMC 11 in San Juan, Puerto Rico in 2018.

Puerto Rico is ready for you!

Symposia

Applications Theme

- Food Mycology in the 21 century: impacts on food security and safety
- Home life: the mycobiomes of built environments
- Fungi and Fungal enzymes for a more sustainable world
- Challenges in the exploitation of beneficial fungal secondary metabolites
- Applications and molecular aspects of mycoparasitic fungi
- Fungi as biocontrol agents for sustainable agriculture

Cell Biology Theme

- Membrane dynamics in fungal cells
- Morphogenesis and invasion (Fungal-host interactions)
- Light sensing in fungi
- Fungal Sexual Development and Exploitation
- Biology of the fungal pigmentation: advances and perspectives of the study of melanin in fungi

Ecology Theme

- Bringing the dark taxa into the light – prospects and challenges
- Hot fungi in hot spots in a hot region
- Resolving uncharacterized symbiotic relationships: The delicate balance from mutualist to parasite
- A big puzzle to assemble: using taxonomy to unravel ecology and biogeography of ectomycorrhizal

symbiosis in the tropics

- Fungal-bacterial interactions and functions of the fungal metaorganism
- Fungal communities and the functioning of forest ecosystems
- Marine Mycology
- Experimental Approaches to the Conservation of Rare Fungi

Education Theme

- Teaching mycology around the world: examples from South America, North America, Europe, Japan and Australia
- Bringing awareness to fungi – for teachers and the general public
- Oral History for Mycology
- Boosting Diversity in Mycology

Environment Theme

- Rhizobiomes – their interactions with the hosts and function in a changing environment
- Fungi in a changing environment
- Polyextremotolerant fungi in natural and urban extreme environments
- Evolution and diversity of lichenization in the Basidiomycota
- Ethnomycology: Scientists and Shaman on Historic and Current Uses of Fungi

Evolution Theme

- Evolutionary genomics
- Gondwana reunited! Fungal biogeography in the Southern Hemisphere
- Early fungi that changed the world: Phylogenomic and fossil evidence.
- Lichens on Islands: Evolution, Endemism, and Conservation
- Species limits in the age of genomics.
- Integrative approaches to understanding the diversity and function of the Boletales

Genomics Theme

- Integrative approaches to understand the ecology and evolution of fungi
- Fungal pan-genomes
- Metagenomics: whole fungal genomes from complex samples
- Fusarium: The genomics of functional and ecological diversity
- Expanding the taxonomic context of genome sampled fungi

Pathology Theme

- Threatening fungal plant pathogens for tropical countries – Acting before the foes arrive
- Deciphering fungi-archaea/bacteria interactions for biocontrol of soil-borne pathogens
- Fungal extracellular vesicles
- Molecular mechanisms of human fungal pathogenesis

- Breeding for resistance to fungal pathogens of crops
- IMC/ISHAM Symposium: Human pathogenic fungi, taxonomy and global emergence

Program at a glance

Saturday, July 14 2018

8:00 am – 5:00 pm Workshops

Sunday, July 15 2018

8:00 am – 5:00 pm Workshops, Field Trips and Tours

Monday, July 16 2018

8:00 am – 4:00 pm Workshops, Field Trips and Tours

12:00 pm – 4:30 pm Registration

5:00 pm – 5:30 pm Welcome Ceremony

5:30 pm – 6:30 pm Keynote Speaker

6:30 pm – 7:30 pm Enchanted sounds of Puerto Rico

7:30 pm – 9:30 pm A taste of Puerto Rico

Tuesday, July 17 2018

7:30 am – 8:30 am Continental Breakfast

8:00 am – 5:00 pm Registration and Exhibitors

8:30 am – 10:30 am Symposia

11:00 am – 12:00 pm Young Mycologist Award and Plenary Speaker

12:00 pm – 2:00 pm Lunch

2:00 pm – 4:00 pm Symposia

4:00 pm – 4:30 pm Coffee Break

4:30 pm – 5:30 pm Young Mycologist Award and Plenary Speaker

5:30 pm – 7:30 pm Poster Session by Theme and Reception

7:30 pm – 9:00 pm Special Interest Group Meetings

Wednesday, July 18 2018

7:30 am – 8:30 am Continental Breakfast

8:00 am – 5:00 pm Registration and Exhibitors

8:30 am – 10:30 am Symposia

11:00 am – 12:00 pm Young Mycologist Award and Plenary Speaker

12:00 pm – 2:00 pm Lunch

2:00 pm – 4:00 pm Symposia

4:00 pm – 4:30 pm Coffee Break

4:30 pm – 5:30 pm Young Mycologist Award and Plenary Speaker

5:30 pm – 7:30 pm Poster Session by Theme and Reception

7:30 pm – 9:00 pm Special Interest Group Meetings

Thursday, July 19 2018

8:00 am – 5:00 pm Registration, Nomenclature Session, Workshops, Field Trips and Tours.

6:00-7:00 pm MSA Presidential Address

7:00-10:00 pm MSA Awards and Banquet

Friday, July 20 2018

7:30 am – 8:30 am Continental Breakfast

8:00 am – 5:00 pm Registration and Exhibitors

8:30 am – 10:30 am Symposia

11:00 am – 12:00 pm Young Mycologist Award and Plenary Speaker

12:00 pm – 2:00 pm Lunch

2:00 pm – 4:00 pm Symposia

4:00 pm – 4:30 pm Coffee Break

4:30 pm – 5:30 pm Young Mycologist Award and Plenary Speaker

5:30 pm – 7:30 pm Poster Session by Theme and Reception

7:30 pm – 9:00 pm Special Interest Group Meetings

Saturday, July 21 2018

7:30 am – 8:30 am Continental Breakfast

8:00 am – 12:00 pm Registration and Exhibitors

8:30 am – 10:30 am Symposia

11:00 am – 12:00 pm Plenary Speaker

12:00 pm – 2:00 pm Lunch

2:00 pm – 4:00 pm Symposia

5:00 pm – 6:30 pm Closing Ceremony and Awards Presentation

7:00 pm – 12:00 pm Banquet and Celebration

http://imc11.com/ for more information

Research progress

Immunomodulatory Properties of Plants and Mushrooms

By Jan Martel, Yun-Fei Ko, David M. Ojcius, Chia-Chen Lu, Chih-Jung Chang, Chuan-Sheng Lin, Hsin-Chih Lai, John D. Young

Abstract: Plants and mushrooms are used for medicinal purposes and the screening of molecules possessing biological activities. A single plant or mushroom may produce both stimulatory and inhibitory effects on immune cells, depending on experimental conditions, but the reason behind this dichotomy remains obscure. We present here a large body of experimental data showing that water extracts of plants and mushrooms usually activate immune cells, whereas ethanol extracts inhibit immune cells. The mode of extraction of plants and mushrooms may thus determine the effects produced on immune cells, possibly due to differential solubility and potency of stimulatory and inhibitory compounds. We also examine the possibility of using such plant and mushroom extracts to treat immune system disorders.

Keywords: herbal medicine, hydrophilicity, hydrophobicity, medicinal mushrooms, traditional Chinese medicine

Trends in Pharmacological Sciences, Volume 38, Issue 11, November 2017,Pages 967-981

The inhibitory effects of polysaccharide peptides (PsP) of *Ganoderma lucidum* against atherosclerosis in rats with dyslipidemia

By Titin Andri Wihastuti, Teuku Heriansyah

Abstract: Atherosclerosis occurs as a result of low-density lipoprotein (LDL) deposits oxidation. Endothelial dysfunction is an early process of atherosclerosis. Restoring endothelial lining back to normal by endothelial progenitor cells (EPCs) is critical for slowing or reversing vascular disease progression. Oxidative stress from hydrogen peroxide (H_2O_2) is increased in dyslipidemia so that antioxidant agent is required to prevent destruction of blood vessels.

This study aims to report *Ganoderma lucidum* polysaccharide peptide (PsP) effects in atherogenic process by measuring H_2O_2 level, IL-10 level, and EPC number in blood serum, and also intima-media thickness of aorta in dyslipidemia Wistar rat model by giving them a hypercholesterol diet (HCD).

The study was an experimental in vivo post-test with control group design. Thirty-five Wistar rats (Rattus norwegicus) were divided into five groups (normal diet group, HCD group, and hypercholesterol groups that received 50 mg/kg, 150 mg/kg, and 300 mg/kg bodyweight PsP).

Each treatment group showed significant results for the administration of PsP using the one-way analysis of variance test ($p<0.050$) for the reduction of H_2O_2 ($p = 0.003$), levels of IL-10 ($p = 0.027$), number of EPC in the blood serum (p =

0.011), and the intima-media thickness of the aorta (p = 0.000). PsP from *G. lucidum* is a potent antioxidant and may prevent atherogenesis process in patients with dyslipidemia.

The optimum doses of PsP in this study is 300 mg/kg bodyweight. Further studies are required to determine the antioxidant effects of PsP *G. lucidum* and its benefits in the management of dyslipidemia.

Heart International, 2017, 12 (1) :e1-e7

Identification and Evaluation of Bioactivity of Compounds from the Mushroom *Pleurotus nebrodensis* (Agaricomycetes) against Breast Cancer

By Jingfeng Hao, Xueya Zhang, Wancong Yu, Ru Wang, Zhaohui Xue, Xiaohong Kou

Abstract: Breast cancer affects millions of women annually worldwide and is the leading cause of cancer death in women. Various bioactive phytochemicals based on natural products are considered to be an important source of chemopreventive agents. In this study we report−to our knowledge for the first time−9 phytochemicals isolated by nuclear magnetic resonance spectroscopy and mass spectrometry from the acetic ether extract of *Pleurotus nebrodensis* and identified as (1) ergosterol, (2) uracil, (3) ergosterol-3-O-β-D-glucopyranoside, (4) cerevisterol, (5) cerebroside B, (6) 5'-methylthioadenosine, (7) adenosine, (8) hypoxanthine, and (9) uridine. Their bioactivities were screened with an MTT assay using breast cancer MCF-7 cells *in vitro*. As a result, about half of the isolated compounds demonstrated moderate or strong inhibitory activity in a concentration-dependent manner. Among them, compound 1 (ergosterol) exhibited superior activity and the lowest half-maximal inhibitory concentration (112.65 μmol/L). Further mechanistic study elucidated that compound 1 led to significant S-phase cell cycle arrest and induced apoptosis in MCF-7 cells. Our study shows the mycochemical composition of the *P. nebrodensis* mushroom and provides guidance for use of compound 1 as a promising lead in cancer therapy.

Keywords: bioactivity, breast cancer, medicinal mushrooms, mycochemical, *Pleurotus nebrodensis*, structure

International Journal of Medicinal Mushrooms, Volume 19, 2017 Issue 9, pages 839-848

Mushrooms: A rich source of the antioxidants ergothioneine and glutathione

By Michael D. Kalaras, John P. Richie, Ana Calcagnotto, Robert B. Beelman

Abstract: While mushrooms are the highest dietary source for the unique sulfur-containing antioxidant ergothioneine, little is known regarding levels of the major biological antioxidant glutathione. Thus, our objectives were to determine and compare levels of glutathione, as well as ergothioneine, in different species of mushrooms. Glutathione levels varied >20-fold (0.11–2.41 mg/g dw) with some varieties having higher levels than reported for other foods. Ergothioneine levels also varied widely (0.15–7.27 mg/g dw) and were highly correlated with those of glutathione ($r = 0.62$, $P < 0.001$). Both antioxidants were more concentrated in pileus than stipe tissues in selected mushrooms species. *Agaricus bisporus* harvested during the third cropping flush contained higher levels of ergothioneine and glutathione compared to the first flush, possibly as a response to increased oxidative stress. This study demonstrated that certain mushroom species are high in glutathione and ergothioneine and should be considered an excellent dietary source of these important antioxidants.

Keywords: Mushrooms, Glutathione, Ergothioneine, Antioxidants

Food Chemistry, Volume 233, 15 October 2017, Pages 429-433

UV-irradiated mushrooms as a source of vitamin D2: A review

By Oludemi Taofiq, Ângela Fernandes, Lillian Barros, Maria Filomena Barreiro, Isabel C.F.R. Ferreira

Abstract:

Background

The deficiency of vitamin D has been widely reported all over the world and linked to several chronic diseases. Mushrooms are valuable nutritional foods with recognized bioactive properties, leading the application of UV irradiation to the production of significant amounts of vitamin D_2. In this context, cultivated species such as *Agaricus bisporus*, *Lentinula edodes* and *Pleurotus ostreatus* have been widely studied.

Scope and approach

However, there is still gap considering the knowledge of the most appropriate irradiation procedures (dose, intensity, distance between source and sample, exposure time) in order to maximize the content of vitamin D_2 in the mushrooms. This strategy will enable vitamin D_2-enhanced mushrooms to be commercially available at affordable costs. Considering the interest and potential of application, this review mentioned some of the physiological roles and sources of vitamin D, while the major focus was on mushroom's UV irradiation as a source of vitamin D_2. Also, topics related to its bioavailability and clinical studies evidencing the health benefits reported so far were also addressed.

Key findings and conclusions

UV-irradiated mushrooms present a high rate of conversion from ergosterol to vitamin D_2 at short treatment time and have the potential to increase serum 25-hydroxyvitamin D levels. Even though irradiated mushrooms exhibit some promising advantages, there is still a huge knowledge gap to allow for extraction, separation, recovery and purification of vitamin D_2 from irradiated mushroom at minimal process cost and high purity percentage to be utilized as bio-based ingredient to reduce vitamin D deficiency as well as present other health promoting benefits.

Keywords: Vitamin D, Mushrooms, Irradiation, Bioavailability

Trends in Food Science & Technology, Volume 70, December 2017, Pages 82-94

The use of Basidiomycota mushrooms in poultry nutrition—A review

By D. Bederska-Łojewska, S. Świątkiewicz, B. Muszyńska

Abstract: Recently, there has been a noticeable growth in interest in the potential of edible mushrooms and their application in prevention and therapy. The numerous health-promoting properties of edible mushrooms include:

antioxidant, immunostimulatory, anti-inflammatory, antibacterial, antiviral and *hypocholesterolemic properties.* Considering such a broad spectrum of action, and based on the recent literature data, the use of mushrooms is justified in the feeding of farm animals, including poultry. The aim of this review paper is to present the current state of knowledge concerning the use of edible mushrooms as a feed additive with dietary and health-promoting activities in the nutrition of broiler chickens and laying hens. Based on the results of studies presented in this article, it can be concluded that many mushroom species e.g. *Lentinula edodes*, *Agaricus bisporus*, *Agaricus blazei*, Hericium caput-medusae, *Pleurotus ostreatus*, *Pleurotus eryngii*, *Fomitella fraxinea*, *Flammulina velutipes*, *Ganoderma lucidum*, *Cordyceps* inensis and *Cordyceps militaris* can be the source of active substances that might positively affect poultry performance and health status.

Keywords: Broiler chickens,Laying hens, Egg production, Edible mushrooms, Antioxidative properties, Immunomodulatory properties

Animal Feed Science and Technology, Volume 230, August 2017, Pages 59-69

The Efficacy and Toxicity of Using the Lingzhi or Reishi Medicinal Mushroom, *Ganoderma lucidum* (Agaricomycetes), and Its Products in Chemotherapy (Review)

By Martina Cizmarikova

Abstract: Around the world, cancer patients often combine conventional anticancer treatment with complementary alternative medicines derived from natural sources such as fungi and mushrooms, including the popular lingzhi or reishi medicinal mushroom *Ganoderma lucidum*. Many studies to date have described the anticancer properties of *G. lucidum*, which are attributed to its major pharmacologically bioactive compounds, such as terpenoids and polysaccharides. Moreover, several scientific observations have suggested a potential beneficial therapeutic strategy using *G. lucidum* in combination with chemotherapeutic agents to improve therapeutic outcome. However, to my knowledge, no systematic review has been conducted in this area. Therefore, this review summarizes the current knowledge on *G. lucidum* or its individual components in relation to chemotherapeutic efficacy, ability to reverse multidrug resistance, and chemotherapeutic toxicity.

Keywords: efficacy, *Ganoderma lucidum*, medicinal mushrooms, multidrug resistance, polysaccharides, terpenoids, toxicity

International Journal of Medicinal Mushrooms, Volume 19, 2017 Issue 10, pages 861-877

A Primary Study of the Antioxidant, Hypoglycemic, Hypolipidemic, and Antitumor Activities of Ethanol Extract of Brown Slimecap Mushroom, *Chroogomphus rutilus* (Agaricomycetes)

By Jinxiu Zhang, Xiaojing Zhao, Li Qiang Zhao, Junxia Zhao, Zhiguang Qi, Li-An Wang

Abstract: *In vivo* and *in vitro* treatments were carried out to investigate the effects of a 95% ethanol extract of *Chroogomphus rutilus* (CRE) on antioxidant, hypoglycemic, hypolipidemic, and antitumor properties. CRE showed potent radical scavenging activity against DPPH *in vitro*. It could increase antioxidant enzymatic activities (superoxide dismutase and glutathione peroxidase) and could reduce malondialdehyde content *in vivo* in mice in which aging was induced by D-galactose. CRE had hypoglycemic activity and could significantly inhibit α-glucosidase activity *in vitro* and decrease blood glucose concentration *in vivo*. CRE could decrease the serum total cholesterol, triglyceride, and low-density lipoprotein cholesterol levels and increase the high-density lipoprotein cholesterol level in diabetic mice. The MTT assay showed that CRE also had a certain inhibitory effect on the tumor cells. These results suggest that CRE may be beneficial for human health and could be useful for applications in medicine, the food industry, and agriculture.

Keywords: antioxidant enzymes, biological activity, cytotoxicity, *Chroogomphus rutilus*, medicinal mushrooms

International Journal of Medicinal Mushrooms, Volume 19, 2017 Issue 10, pages 905-913

Fungal communities in a Korean red pine stand, Gwangneung Forest, Korea

By Chang Sun Kim, Sang-Kuk Han, Jong Woo Nam, Jong Won Jo, Seunghwan Oh

Abstract: For the seasonal changes of fungi (Ascomycota and Basidiomycota) diversity, we performed a biweekly survey of macrofungi on defined plot in a Korean red pine (*Pinus densiflora*) stand (Gwangneung Forest, Pochen-si, Korea) from April 2014 to December 2014. The plot was surveyed 18 times. We also investigated the diversity of the soil fungi community during four seasons using pyrosequencing method. The collected macrofungi (25 specimens) were classified into one phylum, one class, four orders, 10 families, 13 genera, and 17 species; the soil fungal communities were classified into two phyla, 15 classes, 43 orders, 91 families, and 124 genera (49,937 sequence reads), designated as 124 genus-level operational taxonomic units. Using macrofungal collection data, environmental factor data (n = 10), and pyrosequencing data, we evaluated changes in fungal diversity with seasons and soil layers. Nonmetric multidimensional scaling ordination revealed distinct clusters of genus-level operational taxonomic units assemblage with season. Two environmental factors (exchangeable K and C/N ratio) were found to be significantly associated with soil fungi communities in the Korean red pine stand. This study will lead to a better understanding of relationships between Korean red pine stand stands and soil fungal communities.

Keywords: diversity, environmental factors, macrofungi, pyrosequencing, soil layers

Journal of Asia-Pacific Biodiversity, Volume 10, Issue 4, 1 December 2017, Pages 559-572

International Journal of
Medicinal Mushrooms

2017, Vol. 19, Issue no. 11

International Journal of

Medicinal Mushrooms

2017, Vol. 19, Issue no. 12

International Journal of

Medicinal Mushrooms

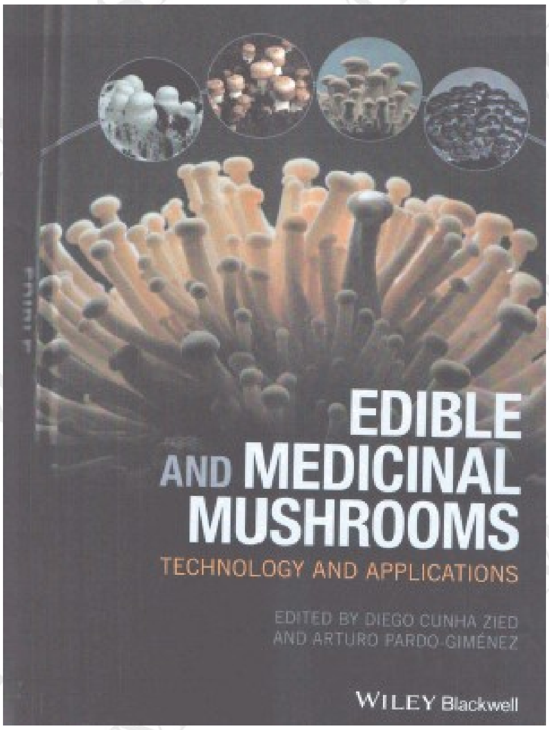
2018, Vol. 20, Issue no. 1

Recommendation of Book--

Edible and Medicinal Mushrooms

Technology and Applications

Edited by Diego Cunha Zied and Arturo Pardo-Gimenez



Comprehensive and timely, Edible and Medicinal Mushrooms: Technology and Applications provides the most up to date information on the various edible mushrooms on the market.

Compiling knowledge on their production, application and nutritional effects, chapters are dedicated to the cultivation of major species such as *Agaricus bisporus*, *Pleurotus ostreatus*, *Agaricus subrufescens*, *Lentinula edodes*, *Ganoderma lucidum* and others.

With contributions from top researchers from around the world, topics covered include:

- Biodiversity and biotechnological applications
- Cultivation technologies
- Control of pests and diseases
- Current market overview
- Bioactive mechanisms of mushrooms
- Medicinal and nutritional properties

Extensively illustrated with over 200 images, this is the perfect resource for researchers and professionals in the mushroom industry, food scientists and nutritionists, as well as academics and students of biology, agronomy, nutrition and medicine.

Edited by Professor Dr Diego Cunha Zied of Universidade Estadual Paulista (UNESP), Brazil and Researcher Dr Arturo Pardo-Gimenez of Centro de Investigacion, Experimentacion y Servicios del Champinon (CIES), Spain.

www.wiley.com/wiley-blackwell

Points and Reviews

Medicinal Mushrooms （Part III）

By Jure Pohleven, Tamara Korošec, Andrej Gregori

Published by MycoMedica, d. o. o., Podkoren 72, 4280 Kranjska Gora, Slovenia www.goba.eu

Continued from previous issue:

Piptoporus betulinus (Birch Polypore)

Therapeutic Application: Antimicrobial, Antiparasitic, Anti-Inflammatory

Piptoporus betulinus is a polypore mushroom that has been used for medicinal purposes since prehistoric times. It was found with a 5300-year-old mummy, Otzi the Iceman, who was presumably using *Piptoporus betulinus* fruiting bodies for their antibiotic properties and against parasites (Capasso 1998). In traditional medicine, tea prepared from young fruiting bodies of the fungus has been used to reduce fatigue, soothe, strengthen the immune system, and for the treatment of different types of cancer in humans as well as in domestic animals. *Piptoporus betulinus* has also been used as antiseptic, pain reliever, and externally as styptic (Grienke et al. 2014).

Despite the lack of clinical evidence, scientists have demonstrated antimicrobial activity of *Piptoporus betulinus* against several pathogenic bacteria and fungi with active compound piptamine (Schlegel et al. 2000). Potential antitumour activity (Lemieszek et al. 2009) and anti-inflammatory properties of triterpene acids (Kamo et al. 2003) have also been shown for the fungus.

***Pleurotus ostreatus* (Oyster Mushroom)**

Therapeutic Application: Cholesterol Control,

Cardiovascular Protective, Overall Health

Pleurotus ostreatus is one of the most popular and widespread cultivated edible mushrooms, which has, in addition to good taste, relatively high nutritional value and is easy to grow. The mushroom is a healthy food, low in fat, containing mainly unsaturated fatty acids and ergosterol (provitamin D2), and has a high content of dietary fibre and good quality proteins with most of the essential amino acids, which makes it suitable for vegetarians and vegans. Moreover, *Pleurotus ostreatus* contains pharmacologically active compounds with therapeutic properties known in traditional medicine of Asia, as well as Europe, South America and Africa. *Pleurotus ostreatus* is therefore not only a tasty edible mushroom easy to grow, but could be on the basis of traditional knowledge and increasing scientific evidence also viewed as a medicinal mushroom with therapeutic potential (Gunde-Cimerman 1999).

Pleurotus ostreatus is recognised as a natural regulator of cholesterol and other lipids, and in addition lowers blood pressure and sugar levels, prevents the formation of blood clots (antithrombotic activity), and has anti-inflammatory properties. Thus, it protects against arterial wall thickening (atherosclerosis), cardiovascular disease and diabetes. The mushroom also strengthens the immune system, has antitumour properties, beneficial effects on the liver (hepatoprotective activity), and improves antioxidant status. Taken together, *Pleurotus ostreatus* helps prevent age-associated diseases, therefore is considered to have anti-ageing properties, and moreover, exhibits antimicrobial and antiviral activities (Gunde-Cimerman 1999; Gunde-Cimerman & Plemenitaš 2001; Patel et al. 2012).

Clinical studies have shown that *Pleurotus ostreatus* reduces cholesterol and triglyceride levels, without any deleterious effect on the liver and kidney (Khatun et al. 2007). The hypocholesterolaemic activity is due to the combined action of dietary fibre and primarily of a natural statin lovastatin or mevinolin, the most important pharmacologically active compound in *Pleurotus ostreatus*, which inhibits cholesterol synthesis. Lovastatin reduces blood levels of total cholesterol, triglycerides, and LDL (bad) cholesterol, whereas increases HDL (good) cholesterol. It has been proposed that the addition of 5% dried *Pleurotus ostreatus* to a high-cholesterol diet could effectively improve blood lipid profile (Gunde-Cimerman & Plemenitaš 2001). The mushroom also reduced blood sugar levels, as well as systolic and diastolic blood pressure in patients with type 2 diabetes and high blood pressure (hypertension) (Khatun et al. 2007; Choudhury et al. 2013).

In addition, β-glucans, including pleuran and related polysaccharides from *Pleurotus ostreatus*, have been shown to possess antitumour and antiviral properties, which are the result of the activation of the cellular immune response against tumour cells and viral infections. A clinical trial involving athletes has demonstrated that pleuran protects against respiratory tract infections (Majtan 2012), therefore *Pleurotus ostreatu*s β-glucans represent promising natural compounds for strengthening the immune system. The mushroom also contains terpenes, lectin proteins, and other compounds with potential antitumour properties, as well as antibiotic and fungicidal activities (Gunde-Cimerman 1999).

***Polyporus umbellatus* (Umbrella Polypore)**

Therapeutic Application: Diuretic, Urinary Tract, Anticancer

Polyporus umbellatus is a fungus with edible fruiting bodies, while its underground structures, called sclerotia, have been used for thousands of years in traditional medicine in China, Japan and India. Sclerotia of the fungus are commonly used as an ingredient in various traditional Asian herbal preparations, mainly as a diuretic for the treatment of oedema or swelling, kidney or urinary tract infections and disorders, scanty and painful urination, jaundice, leucorrhoea (vaginal discharge), and diarrhoea (Hobbs 1986; Zhao 2013).

Recent scientific research on therapeutic properties of *Polyporus umbellatus* supports the findings of traditional medicine and has demonstrated a potent diuretic effect of the fungus showing 62% increase in urine output (Powel 2010). In addition, the fungus has been shown to have a stimulatory effect on the immune system, potential antitumour properties, beneficial effects on the kidney and liver (nephroprotective and hepatoprotective activities), as well as anti-inflammatory and antioxidant activities (Zhao 2013).

Two main groups of pharmacologically active compounds have been identified in *Polyporus umbellatus*, i.e. polysaccharides and phytosterols, including ergosterol and ergone, which is the main compound responsible for diuretic and nephroprotective properties of the fungus. Other compounds have also been identified in the fungus and contribute to its diuretic activity, such as triterpenoids, mannitol etc (Zhao 2013).

Clinical studies using polysaccharides from *Polyporus umbellatus* as an adjunct to chemotherapy have shown that they enhanced the immune system and improved the treatment outcomes in patients with leukaemia, lung, liver, oesophageal, throat and nasal cancer. Furthermore, the polysaccharides improved the quality of life of the patients by reducing chemotherapy-related side effects (Hobbs 1986; Powel 2010). Clinical symptoms were also improved in patients with hepatitis who were administered *Polyporus umbellatus* polysaccharides. No negative reactions to *Polyporus umbellatus* have, however, been reported in clinical trials (Hobbs 1986).

***Poria cocos* (Hoelen, Poria Mushroom)**

Therapeutic Application: Overall Health

Poria cocos or *Wolfiporia extensa* has been in traditional Chinese and Japanese medicine used as a diuretic, sedative, and tonic for overall health and vitality. For therapeutic purposes, powdered underground fungal sclerotia have been used, which resemble a coconut, hence the scientific name of the fungus. These have been rarely used alone, but rather as a component of many traditional Asian herbal formulae (Ríos 2011).

Scientists have identified several pharmacologically active compounds in *Poria cocos*, including triterpenes, which are in addition to polysaccharides the main compounds of the fungus with a broader spectrum of activity. There is a lack of clinical studies on the fungus; nevertheless, its medicinal properties have been demonstrated in different experimental models (Ríos 2011).

Triterpenes of *Poria cocos* have been shown to exhibit potent anti-inflammatory activity by suppressing dermatitis and oedema, as well as have potential antitumour properties (Powell 2010; Ríos 2011). Antitumour activity has also been shown for polysaccharides from the fungus, such as PCS3-II, which exhibited the effects by potentiating the immune response (Chen et al. 2010b; Ríos 2011). Furthermore, an immunomodulatory protein PCP has been isolated from *Poria cocos* (Chang et al. 2009).

Poria cocos has also been shown to have therapeutic potential in diabetes by reducing blood glucose levels (antihyperglycaemic activity), as well as in nephritis and hepatitis B. The fungus also exhibited activity against parasites, including *Trypanosoma cruzi* and several nematode species (Ríos 2011).

Trametes versicolor (Turkey Tail)

Therapeutic Application: Anticancer, Antiviral, Immunity

Trametes versicolor or *Coriolus versicolor* is one of the most studied and clinically important medicinal mushrooms used for the treatment of a variety of cancers. The research has focused primarily on the antitumour properties of the two pharmacologically active polysaccharide-protein complexes or proteoglycans, called PSK (Polysaccharide-K or Krestin) and PSP (Polysaccharide-Peptide), which have been evaluated in large-scale clinical trials. The compounds have been shown to be very effective immunotherapeutics in cancer management, especially when combined with conventional treatment, without exhibiting toxicity or serious adverse side effects (Kidd 2000).

PSK is the first approved medicine derived from a mushroom and is one of the most widely accepted for the treatment of certain types of cancer, particularly in Japan. In numerous clinical studies, PSK has shown impressive results in patients with gastric, as well as colorectal, oesophageal, nasopharyngeal, uterine, lung and breast cancer, and leukaemia. In conjunction with conventional treatment, PSK significantly (up to several times) extended the survival, enhanced the immune system by increasing immune cell count, reduced side effects of radiation and chemotherapy, and improved the quality of lives of the patients. In addition, PSK also possesses antioxidant properties (Kidd 2000). Similarly, clinical studies have shown that PSP prolonged the survival of patients with oesophageal cancer and potentiated the immune response in 70–97% of patients with gastric, oesophageal, lung, ovarian and endometrial cancer. Furthermore, PSP reduced side effects of chemotherapy and improved the quality of life in more than 70% of patients, while enhancing its therapeutic effects (Kidd 2000).

Trametes versicolor has also been shown to exhibit antiviral activity in patients with human immunodeficiency virus (HIV) and herpes simplex virus. Moreover, it has been shown to have beneficial effects on the liver (hepatoprotective activity), and in patients with fatigue (Powell 2010).

USES OF MEDICINAL MUSHROOMS IN ANIMALS

Throughout history, humans have been constantly observing animals, learning from them, and thus have discovered beneficial properties of certain mushroom species. Herders in the Himalayas, for example, noticed improved performance of their domestic animals, yaks, goats and sheep, after consuming *Cordyceps sinensis* (caterpillar fungus) during grazing, and thus began to explore the beneficial effects of the mushroom. They started to intentionally feed the animals with the mushroom to increase milk production, and improve reproductive capacity and vitality of their cattle. Eventually, the use of *Cordyceps* has expanded to traditional medicine (Panda & Swain 2011). Today, a number of medicinal mushrooms are used in animals for a variety of purposes presented below.

Curative Treatment of Domestic Animals Using Medicinal Mushrooms

Therapeutic properties of medicinal mushrooms on animals have been mainly investigated by *in vitro* studies and experiments on laboratory animals, or deduced from human clinical trials. Controlled scientific studies on the potential of medicinal mushrooms in the treatment of certain animal disease are scarce. There is a study on the activity of *Ganoderma lucidum* (reishi) against coccidiosis in broiler chickens. Coccidiosis is an animal disease caused by coccidian parasites, which represents a major problem in chicken and rabbit meat production. *Ganoderma lucidum* has been shown to be a promising new strategy to control chicken coccidiosis caused by *Eimeria tenella*, whereas an effective alternative for other coccidian parasites has not yet been discovered (Ogbe et al. 2009).

A number of individual case studies have been conducted on the treatment of domestic animals, which are largely limited to companion animals (pets), involving dogs, cats, and horses. These animals are predominantly administered medicinal mushrooms for the treatment of cancer, and such therapy is chosen by veterinarians familiar with alternative medicine, or by animal owners themselves (Robinson 2007).

Medicinal Mushrooms in Sport Animals

Certain medicinal mushroom species are, as by athletes, also used in animals involved in sports, since they improve their physical and mental performance, as well as overall health. Race horses and dogs, trotters, dressage horses, show jumpers, sledge dogs, agility dogs etc., can be supported by specific mushroom preparations when subjected to excessive physiological and psychological stress due to intensive training, competitions and transportation. However, the owners or persons responsible for animals that participate in professional sports competitions should consult an anti-doping organisation regarding the potentially prohibited substances contained in medicinal mushroom feed supplements before administering to animals.

A mixture of several mushroom species is usually used in such feed supplements, including the indispensable species of the genus *Cordyceps*, which increase the blood flow, oxygen utilisation and consumption by cells, and thus increase cellular energy (ATP) levels. Moreover, the invigorating properties of *Cordyceps* and neuroprotective effects of *Hericium erinaceus* (lion's mane) can help improve cognitive-behavioural function in animals. Mushroom blends usually also contain *Grifola frondosa* (maitake, hen of the woods) to increase the production of blood cells (haematopoietic effect), and *Ganoderma lucidum* to improve overall health (adaptogenic effect) and strengthen the immune system of animals.

Preventive Care and Improvement of Production Performance of Economically Important Animals

Most of the scientific research on the use of medicinal mushrooms in animals has been conducted in an effort to improve production performance and maintain health of economically important (farm) animals. Since 2006, when the European Union banned the use of nutritional antibiotics as growth promoters and production enhancers in production animals, the intensive search of natural feed supplements has begun, which would be as effective, or even more so, in maintaining health and high productivity of animals.

Numerous basic research studies have focused on the effects of medicinal mushrooms on the immune system of animals, since a potent immune response can protect them against diseases. In addition, the effects of medicinal mushrooms on production performance of farm animals have also been studied, mostly in broiler chickens, laying hens and pigs, which is measured or assessed by monitoring their growth performance, weight gain, as well as feed consumption and conversion.

The majority of studies on pigs have focused on weaning phase of piglets, when they are subjected to the highest physiological stress. During that time, they change the environment, are separated from their mothers, completely stop suckling, and switch exclusively to feed of plant origin. Accordingly, piglets lose the protection provided by their mother’s milk and are in a vulnerable period, when their immune system has not yet fully developed, therefore are more susceptible to infections. *Ganoderma lucidum* has been shown to be an effective feed supplement for weanling pigs, since it enhances their immune response to viruses and improves their growth performance (Chen et al. 2008b).

Mushroom species of the genus *Cordyceps* have been used in traditional medicine to enhance sexual function and fertility, and could also be applied in animal husbandry to improve reproductive function of animals. Scientists have shown that *Cordyceps militaris* can increase the production, motility and morphology of sperm in subfertile boars. The effect was observed for another two weeks after the end of the treatment with the mushroom (Lin et al. 2007). *Cordyceps* species have, therefore, further potential application in increasing the reproductive capacity also of other animal species.

Several studies have been conducted on the beneficial effects of mushrooms on broiler chickens. *Agaricus bisporus* (white button mushroom)-supplemented diet (20 g/kg of feed) has been shown to improve growth performance and feed conversion efficiency in broiler chickens, as well as antioxidant status in chicken tissue. The latter, provides protection for the animal itself and also prevents the oxidation of its meat (Giannenas et al. 2010a). Essentially the same results were obtained in the study with fermentation concentrate of *Hericium caput-medusae* (Shang et al. 2014a), whereas *Agaricus brasiliensis* has been demonstrated positive effects on the production performance and immune system of broiler chickens (Guimaraes et al. 2014). Furthermore, microbiological analysis has demonstrated a prebiotic effect of *Agaricus bisporus*, *Lentinula edodes* (shiitake), and *Hericium caput-medusae*, which were shown to promote probiotic bacteria in the intestine of chickens supplemented with the three mushroom species (Guo et al. 2004; Giannenas et al. 2010b; Shang et al. 2014b).

Polysaccharides from *Ganoderma lucidum* have been shown to be a potential vaccine adjuvant against Newcastle disease, a viral infectious disease affecting many domestic (poultry) and wild avian species. Adjuvant is immunological agent, which is added to a vaccine to prolong and potentiate the immune responses by increasing antibody production or to direct the immune response to particular types of immune cells. *Ganoderma lucidum* polysaccharides promoted lymphocyte proliferation and increased antibody titre in the serum of chickens vaccinated with Newcastle disease vaccine (Zhang et al. 2014).

However, medicinal mushrooms are not only used in most common terrestrial domestic animals; their effects have also been studied in fish farming, especially in trouts. Lentinan, a β-glucan from *Lentinula edodes*, has been shown to inhibit the expression of genes involved in acute inflammatory reactions in rainbow trout (*Oncorhynchus mykiss*), while its immune response remained unchanged. Thus, lentinan has potential as an immunomodulator that enhances beneficial and reduces detrimental immune responses (Djordjevic et al. 2009).

Functional (Designer) Foods of Animal Origin

Functional foods are foods containing biologically active compounds, which promote health and prevent or control certain diseases. The most common functional foods of animal origin are foods rich in omega-3 unsaturated fatty acids or antioxidants (Se, vitamin E), with low cholesterol and saturated fatty acids contents, foods supplemented with probiotic bacteria, lactose-free foods etc. Research on medicinal mushrooms used in farm animal feed has shown that certain biologically active compounds can be transferred from mushrooms to animal products, thus altering the product composition and exerting indirect effects on the consumers of such functional foods.

Supplementation of laying hens with *Lentinula edodes* has been shown to increase their egg production, improve egg quality and fatty acid composition (increased linoleic acid, omega-6 and polyunsaturated fatty acids contents), and reduce the cholesterol content in egg yolk. Despite the change in the composition of the eggs, no adverse effects on their sensory properties (flavour, colour etc) have been observed (Hwang et al. 2012).

In addition, cordycepin, the main active compound in mushroom species of the genus *Cordyceps*, has been shown to be highly effective in transferring to animal products (Chen et al. 2014). Designer eggs obtained by standardized feeding of laying hens with mycelium of *Cordyceps*, and containing cordycepin and 30% less cholesterol, are already available on the Asian market. The effect of these eggs on a consumer is double. Since they contain less cholesterol, they are beneficial for people with high cholesterol levels (hypercholesterolaemia); moreover, cordycepin consumed with designer eggs has further favourable effects on cholesterol metabolism and other physiological functions in humans.

Mushroom species of the genus *Cordyceps* also show potential for reducing methane emissions from modern intensive cattle farming, which is often accused of being a major contributor to global warming. Methane is a potent greenhouse gas produced by microorganisms and protozoa in an anaerobic environment of the ruminant stomach (namely, in the rumen), and released to the atmosphere. A study has shown that *Cordyceps militaris* stimulated the mixed ruminal microorganism fermentation and was effective in reducing methane production in ruminal fluids from cattle (Kim et al. 2014).

The use of medicinal mushrooms in the prevention and treatment of animal diseases, as well as for improving the production performance of animals has only seen the light of day in the West. Since there is restricted use of certain pharmacological compounds and because of the increasing demand for natural forms of animal treatment, medicinal mushrooms with their therapeutic properties have potential for their application in veterinary practices as well as animal husbandry.

(The end)

REFERENCES

Capasso L. 1998. 5300 years ago, the Ice Man used natural laxatives and antibiotics. Lancet, 352, 9143: 1864.

Chang H.H., Yeh C.H., Sheu F. 2009. A novel immunomodulatory protein from *Poria cocos* induces Toll-like receptor 4-dependent activation within mouse peritoneal macrophages. Journal of Agricultural and Food Chemistry, 57, 14: 6129–6139.

Chen S.D., Hsieh M.C., Chiou M.T., Lai Y.S., Cheng Y.H. 2008b. Effects of fermentation products of *Ganoderma lucidum* on growth performance and immunocompetence in weanling pigs. Archives of Animal Nutrition, 62, 1: 22–32.

Chen X., Zhang L., Cheung P.C.K. 2010b. Immunopotentiation and anti-tumor activity of carboxymethylated-sulfated β-(1–>3)-D-glucan from *Poria cocos*. International Immunopharmacology, 10, 4: 398–405.

Chen Y.H., Lim C.W., Chan S.H. 2014. Evaluation of triple stage mass spectrometry as a robust and accurate diagnostic tool for determination of free cordycepin in designer egg. Food Chemistry, 150: 213–219.

Choudhury M.B.K., Rahman T., Kakon A.J., Hoque N., Akhtaruzzaman M., Begum M.M., Choudhuri M.S.K., Hossain M.S. 2013. Effects of *Pleurotus ostreatus* on blood pressure and glycemic status of hypertensive diabetic male volunteers. Bangladesh Journal of Medical Biochemistry, 6, 1: 5–10.

Djordjevic B., Škugor S., Jørgensen S.M., Øverland M., Mydland L.T., Krasnov A. 2009. Modulation of splenic immune responses to bacterial lipopolysaccharide in rainbow trout (*Oncorhynchus mykiss*) fed lentinan, a beta-glucan from mushroom *Lentinula edodes*. Fish & Shellfish Immunology, 26, 2: 201–209.

Giannenas I., Pappas I.S., Mavridis S., Kontopidis G., Skoufos J., Kyriazakis I. 2010a. Performance and antioxidant status of broiler chickens supplemented with dried mushrooms (*Agaricus bisporus*) in their diet. Poultry Science, 89, 2: 303–311.

Giannenas I., Tontis D., Tsalie E., Chronis E.F., Doukas D., Kyriazakis I. 2010b. Influence of dietary mushroom *Agaricus bisporus* on intestinal morphology and microflora composition in broiler chickens. Research in Veterinary Science, 89, 1: 78–84.

Grienke U., Zöll M., Peintner U., Rollinger J.M. 2014. European medicinal polypores – A modern view on traditional uses. Journal of Ethnopharmacology, 154, 3: 564–583.

Guimarães J.B., dos Santos E.C., Dias E.S., Bertechini A.G., da Silva Ávila C.L., Dias F.S. 2014. Performance and meat quality of broiler chickens that are fed diets supplemented with *Agaricus brasiliensis* mushrooms. Tropical Animal Health and Production, 46, 8: 1509–1514.

Gunde-Cimerman N. 1999. Medicinal value of the genus *Pleurotus* (Fr.) P.Karst. (Agaricales s.l., Basidiomycetes). International Journal of Medicinal Mushrooms, 1, 1: 69–80.

Gunde-Cimerman N., Plemenitaš A. 2001. Hypocholesterolemic activity of the genus *Pleurotus* (Jacq.: Fr.) P. Kumm. (Agaricales s. l., Basidiomycetes). International Journal of Medicinal Mushrooms, 3, 4: 395–397.

Guo F.C., Williams B.A., Kwakkel R.P., Li H.S., Li X.P., Luo J.Y., Li W.K., Verstegen M.W.A. 2004. Effects of mushroom and herb polysaccharides, as alternatives for an antibiotic, on the cecal microbial ecosystem in broiler chickens. Poultry Science, 83, 2: 175–182.

Han C., Yuan J., Wang Y., Li L. 2006. Hypoglycemic activity of fermented mushroom of *Coprinus comatus* rich in vanadium. Journal of Trace Elements in Medicine and Biology, 20, 3: 191–196.

Hobbs C. 1986. Medicinal mushrooms: An exploration of tradition, healing, & culture. Summertown, TN, Botanica Press.

Hwang J.A., Hossain M.E., Yun D.H., Moon S.T., Kim G.M., Yang C.J. 2012. Effect of shiitake [*Lentinula edodes* (Berk.) Pegler] mushroom on laying performance, egg quality, fatty acid composition and cholesterol concentration of eggs in layer chickens. Journal of Medicinal Plants Research, 6, 1: 146–153.

Kamo T., Asanoma M., Shibata H., Hirota M. 2003. Anti-inflammatory lanostane-type triterpene acids from *Piptoporus betulinus*. Journal of Natural Products, 66, 8: 1104–1106.

Khatun K., Mahtab H., Khanam P.A., Sayeed M.A., Khan K.A. 2007. Oyster mushroom reduced blood glucose and cholesterol in diabetic subjects. Mymensingh Medical Journal, 16, 1: 94–99.

Kidd P.M. 2000. The use of mushroom glucans and proteoglycans in cancer treatment. Alternative Medicine Review, 5, 1: 4–27.

Kim W.Y., Hanigan M.D., Lee S.J., Lee S.M., Kim D.H., Hyun J.H., Yeo J.M., Lee S.S. 2014. Effects of *Cordyceps militaris* on the growth of rumen microorganisms and *in vitro* rumen fermentation with respect to methane emissions. Journal of Dairy Science, 97, 11: 7065–7075.

Lemieszek M.K., Langner E., Kaczor J., Kandefer-Szerszen M., Sanecka B., Mazurkiewicz W., Rzeski W. 2009. Anticancer effect of fraction isolated from medicinal birch polypore mushroom, *Piptoporus betulinus* (Bull.: Fr.) P. Karst. (Aphyllophoromycetideae): *In vitro* studies. International Journal of Medicinal Mushrooms, 11, 4: 351–364.

Lin Z.B. 2005. Cellular and molecular mechanisms of immuno-modulation by *Ganoderma lucidum*. Journal of Pharmacological Sciences, 99, 2: 144–153.

Lin W.H., Tsai M.T., Chen Y.S., Hou R.C.W., Hung H.F., Li C.H., Wang H.K., Lai M.N., Jeng K.C.G. 2007. Improvement of sperm production in subfertile boars by *Cordyceps militaris* supplement. The American Journal of Chinese Medicine, 35, 4: 631–641.

Liu J., Zhang J., Shi Y., Grimsgaard S., Alraek T., Fonnebo V. 2006. Chinese red yeast rice (*Monascus purpureus*) for primary hyperlipidemia: A meta-analysis of randomized controlled trials. Chinese Medicine, 1, 4, doi: 10.1186/1749-8546-1-4.

Majtan J. 2012. Pleuran (β-glucan from *Pleurotus ostreatus*): An effective nutritional supplement against upper respiratory tract infections? Medicine and Sport Science, 59: 57–61.

Nanba H., Kodama N., Schar D., Turner D. 2000. Effects of maitake (*Grifola frondosa*) glucan in HIV-infected patients. Mycoscience, 41, 4: 293–295.

Ogbe A.O., Atawodi S.E., Abdu P.A., Sannusi A., Itodo A.E. 2009. Changes in weight gain, faecal oocyst count and packed cell volume of *Eimeria tenella*-infected broilers treated with a wild mushroom (*Ganoderma lucidum*) aqueous extract. Journal of the South African Veterinary Association, 80, 2: 97–102.

Panda A.K., Swain K.C. 2011. Traditional uses and medicinal potential of *Cordyceps sinensis* of Sikkim. Journal of Ayurveda and Integrative Medicine, 2, 1: 9–13.

Patel Y., Naraian R., Singh V.K. 2012. Medicinal properties of *Pleurotus* species (oyster mushroom): A review. World Journal of Fungal and Plant Biology, 3, 1: 1–12.

Powell M. 2010. Medicinal mushrooms: A clinical guide. East Sussex, Mycology Press.

Rios J.L. 2011. Chemical constituents and pharmacological properties of *Poria cocos*. Planta Medica, 77, 7: 681–691.

Robinson N.G. 2007. Complementary and alternative medicine for patients with cancer. In: Withrow & MacEwen's small animal clinical oncology. 4th edition. Withrow S.J., Vail D.M (editors). St. Louis, MO, Saunders: 347–371.

Robles-Hernandez L., Cecilia-Gonzalez-Franco A., Soto-Parra J.M., Montes-Dominguez F. 2008. Review of agricultural and medicinal applications of basidiomycete mushrooms. Tecnociencia Chihuahua, 2, 2: 95–107.

Schlegel B., Luhmann U., Hartl A., Grafe U. 2000. Piptamine, a new antibiotic produced by *Piptoporus betulinus* Lu 9-1. The Journal of Antibiotics, 53, 9: 973–974.

Seniuk O.F., Gorovoj L.F., Beketova G.V., Savichuk N.O., Rytik P.G., Kucherov I.I., Prilutskaya A.B., Prilutsky A.I. 2011. Anti-infective properties of the melanin-glucan complex obtained from medicinal tinder bracket mushroom, *Fomes fomentarius* (L.: Fr.) Fr. (Aphyllophoromycetideae). International Journal of Medicinal Mushrooms, 13, 1: 7–18.

Shang H.M., Song H., Jiang Y.Y., Ding G.D., Xing Y.L., Niu S.L., Wu B., Wang L.N. 2014a. Influence of fermentation concentrate of *Hericium caput-medusae* (Bull.:Fr.) Pers. on performance, antioxidant status, and meat quality in broilers. Animal Feed Science and Technology, 198: 166–175.

Shang H.M., Song H., Wang L.N., Wu B., Ding G.D., Jiang Y.Y., Yao X., Shen S.J. 2014b. Effects of dietary polysaccharides from the submerged fermentation concentrate of *Hericium caput-medusae* (Bull.:Fr.) Pers. on performance, gut microflora, and cholesterol metabolism in broiler chickens. Livestock Science, 167: 276–285.

Zhang P., Ding R., Jiang S., Ji L., Pan M., Liu L., Zhang W., Gao X., Huang W., Zhang G., Peng L., Ji H. 2014. The adjuvanticity of *Ganoderma lucidum* polysaccharide for Newcastle disease vaccine. International Journal of Biological Macromolecules, 65: 431–435.

Zhao Y.Y. 2013. Traditional uses, phytochemistry, pharmacology, pharmacokinetics and quality control of *Polyporus umbellatus* (Pers.) Fries: A review. Journal of Ethnopharmacology, 149, 1: 35–48.

Medicinal Mushrooms in Human Clinical Studies.

Part I. Anticancer, Oncoimmunological, and Immunomodulatory Activities: A Review (Part I)

Solomon P. Wasser

Institute of Evolution and Department of Evolutionary and Environmental Biology, Faculty of Natural Sciences, University of Haifa, 199 Aba Khoushy Ave., Mount Carmel, Haifa 3498838, Israel; N.G. Kholodny Institute of Botany, National Academy of Sciences of Ukraine, Kiev, Ukraine; Tel.: +972-4-8249218; Fax: +972-4-8288649; spwasser@research .haifa.ac.il

Published in the Int J Med Mushrooms.2017;19(4):279-317.

ABSTRACT: More than 130 medicinal functions are thought to be produced by medicinal mushrooms (MMs) and fungi, including antitumor, immunomodulating, antioxidant, radical scavenging, cardiovascular, antihypercholesterolemic, antiviral, antibacterial, antiparasitic, antifungal, detoxification, hepatoprotective, antidiabetic, and other effects. Many, if not all, higher Basidiomycetes mushrooms contain biologically active compounds in fruit bodies, cultured mycelia, and cultured broth. Special attention has been paid to mushroom polysaccharides. Numerous bioactive polysaccharides or polysaccharide-protein complexes from MMs seem to enhance innate and cell-mediated immune responses, and they exhibit antitumor activities in animals and humans. While the mechanism of their antitumor actions is still not completely understood, stimulation and modulation of key host immune responses by these mushroom compounds seems to be central. Most important for modern medicine are polysaccharides and low–molecular weight secondary metabolites with antitumor and immunostimulating properties. More than 600 studies have been conducted worldwide, and numerous human clinical trials on MMs have been published. Several of the mushroom compounds have proceeded through phase I, II, and III clinical studies and are used extensively and successfully in Asia to treat various cancers and other diseases. The aim of this review is to provide an overview of and analyze the literature on clinical trials using MMs with human anticancer, oncoimmunological, and immunomodulatory activities. High-quality, long-term, randomized, double-blind, placebo-controlled clinical studies of MMs, including well-sized population studies are definitely needed in order to yield statistical power showing their efficacy and safety. Clinical trials must obtain sufficient data on the efficacy and safety of MM-derived drugs and preparations. Discussion of results based on clinical studies of the anticancer, oncoimmunological, and immunomodulating activity of MMs are highlighted. Epidemiological studies with MMs are also discussed.

KEY WORDS: antioxidant activities, antitumor, β-glucans, biological response modifiers, cancer patients, clinical studies, clinical trials, epidemiological studies, immunomodulation, interferons, interleukins, medicinal mushrooms, natural killer cells, oncoimmunology, polysaccharides, quality of life, secondary metabolites

ABBREVIATIONS: AHCC, active hexose correlated compound; **AIDS**, acquired immunodeficiency syndrome; **ALL**, acute lymphocytic leukemia; **BRM**, biological response modifier; **CAPE**, caffeic acid phenethyl ester; **COX**, cyclooxygenase; **DC**, dendritic cell; **DS,** dietary supplement; **DSHEA**, Dietary Supplement Health and Education Act; **GXM**, glucuronoxilomannan; **HIV**, human immunodeficiency virus; **HSV**, herpes simplex virus; **IC50**, half-maximal inhibition concentration; **IFN**, human type I interferon; **IκBα**, nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor alpha; **IL**, interleukin; **iNOS**, inducible nitric oxide synthase; **MDS**, myelodysplastic syndromes; **MM**, medicinal mushroom; **NF-κB**, nuclear factor kappa B; **PAMP**, pathogenassociated molecular pattern; **NK**, natural killer; **PRR**, pattern-recognition receptor; **PSP**, polysaccharide peptide; **QOL**, quality of life; **RCT**, randomized controlled trial; **TCM**, traditional Chinese medicine; **TLR**, Toll-like receptor; **TNF-a**, tumor necrosis factor-a; **WHO**, World Health Organization

I. INTRODUCTION

The use of mushrooms in traditional ancient therapies dates back to at least the Neolithic Age. For millennia, mushrooms have been valued as edible and medical provisions for humans. Contemporary research has validated and documented much of the ancient knowledge on medicinal mushrooms (MMs). The interdisciplinary field of science that studies MMs has developed and increasingly demonstrates potent and unique properties of compounds extracted from a range of mushroom species, especially in the past 3 decades. Modern clinical practice in Japan, China, Korea, Russia, and several other countries relies on mushroom-derived preparations.[1–4]

The long history of mushroom use has been documented in Europe (e.g., the story of the mushrooms found in the Iceman Ötzi's girdle bag: *Piptoporus betulins* [birch polypore] and *Fomes fomentarius* [tinder conk],5,6 as well as *Amanita muscaria* [fly agarics mentioned in Celtic myths]) and in Asia (especially lingzhi or reishi mushrooms [*Ganoderma lucidum* in China], *A. muscaria* [fly agaric in Russia and in Tibetan shamanism and Buddhism], and *Lentinus edodes* [shiitake mushroom in Japan]). Other examples include the use of *Phellinus igniarius* by the Eskimos of Alaska, and some other species used in the African continent (e.g., mushrooms used by Yoruba populations in Nigeria and Benin, and used in Algeria and Egypt). Hallucinogenic species of the genus *Psilocybe* occupy a special place in cultures of Mesoamerica, Mexico, and Guatemala.[1–7]

Nowadays, MMs are used as (1) food (world mushroom production was 33 million tons in 2015); (2) dietary supplements (DSs) (the market for MM-derived DSs is rapidly growing and has a value of more than US$18 billion/year); (3) a new class of drugs called "mushroom pharmaceuticals" or "mushroom drugs"; (4) natural biocontrol agents in plant protection, demonstrating insecticidal, fungicidal, bactericidal, herbicidal, nematocidal, and antiphytoviral activities; and (5) cosmeceuticals, that is, different MM compounds, including polysaccharides (e.g., soluble β-glucans, glucuronoxilomannan, sacchachitin, tyrosinase, and other enzymes) used by cosmetic companies because of their film-forming capability; ability to activate epidermal growth factor; antioxidative, antiallergic, antibacterial, and anti-inflammatory activities; and ability to stimulate collagen activity, inhibit autoimmune vitiligo, and treat acne.[3,4,8]

MMs are comparable to "medicinal plants" and can be defined as macroscopic fungi, mostly higher Basidiomycetes and some Ascomycetes, that are used in the form of extracts or powder for preventing, alleviating, or healing multiple diseases and/or in balancing a healthy diet. According to the definition of "herbal drugs," dried fruit bodies, mycelia, and spores are considered mushroom drugs or "fungal drugs." Analogous to "phytopharmaceuticals" or "herbal preparations," the resulting mushroom preparations should be considered as "mushroom pharmaceuticals," mushroom drugs, or mushroom preparations.

The pharmacological properties of mushrooms are currently widely recognized. They make up a vast and yet largely untapped source of powerful new pharmaceutical products. In particular, and most important for modern medicine, MMs present an unlimited source of polysaccharides (especially β-glucans) and polysaccharide-protein complexes with anticancer and immunostimulating properties. Many, if not all, higher Basidiomycetes mushrooms contain different types of biologically active high– and low–molecular weight compounds (triterpenes, lectins, steroids, phenols, polyphenols, lactones, statins, alkaloids, and antibiotics) in fruit bodies, spores, cultured mycelia, and cultured broth.[3,4,9–12]

MMs and fungi have more than 130 medicinal functions. Recently studied medicinal actions of mushrooms include antitumor, immunomodulating, antioxidant, radical scavenging, cardiovascular, cholesterol-lowering, antiviral, antibacterial, antiparasitic, antifungal, detoxicative, hepatoprotective, antidiabetic**,** antiobesity, neuroprotective, and neuroregenerative effects, among others. Also, substances derived from MMs can be used as painkillers or analgesics. The best implementation of MM-derived drugs and DSs has been in preventing immune disorders and maintaining a good quality of life, especially in immunodeficient and immunodepressed patients; patients receiving chemotherapy or radiotherapy; patients with different types of cancers, chronic blood-borne viral infections (hepatitis B, C, and D), different types of anemia, human immunodeficiency virus/AIDS, herpes simplex virus, chronic fatigue syndrome, and Epstein-Barr virus; patients with chronic gastritis and gastric ulcers caused by *Helicobacter pylori*; and people suffering from dementia (especially Alzheimer's disease).[3,4,13–15]

Mushroom polysaccharides prevent oncogenesis, show direct antitumor activity against various synergetic tumors, and prevent tumor metastasis. Their activity is especially beneficial when used in conjunction with chemotherapy. The antitumor action of polysaccharides requires an intact T-cell component; their activity is mediated through a thymus-dependent immune mechanism. They activate cytotoxic macrophages, monocytes, neutrophils, natural killer (NK) cells, dendritic cells (DCs), and chemical messengers (cytokines, such as interleukins [ILs], interferons [IFNs], and colony-stimulating factors) that trigger complementary and acute phase responses. Also, mushroom polysaccharides can be considered as multicytokine inducers and are able to induce gene expression of various immunomodulating cytokines and cytokine receptors.[3,16–21]

A 2-stage model of the anticancer activity of β-glucans seems the most persuasive. The first stage is mediated by macrophages and DCs and the second by granulocytes and NK cells. The first stage is initiated when β-glucan binds dectin-1 and Toll-like receptors (TLRs) that are expressed by macrophages and DCs. β-Glucans are taken up by macrophages into endosomes, where they are fragmented and then transported to the spleen, lymph nodes, and bone marrow and released. The movement of cells containing β-glucan is traced using β-glucan labeled with fluorescein. The second stage is achieved by NK cells or granulocytes that express CR3 on their surface. The β-glucan fragments released by macrophages are recognized by CR3, which triggers signaling pathways that induce the eventual release of cytokines that stimulate adaptive immune cells (Fig. 1). Therefore, antitumor activities may be generated by the orchestrated cooperation of innate and adaptive immunity.[20]

However, the binding mechanism of b-glucan to the dectin-1/TLR complex is not fully recognized. β-Glucan does bind to dectin-1. It is dependent on CARD9, but not Myd88. Much research supports this concept. Not much research supports the binding of "purified" β-glucan to the dectin-1/TLR complex. It is, however, well known that zymosan, a crude particle of yeast β-glucan, binds to both dectin-1 and TLR (Professor N. Ohno, personal communication, December 2016).

A review published by Wu et al.[22] proposed a novel mechanism of action of polysaccharide peptide (PSP) from cultured mycelia of the highly PSP-expressing *Trametes versicolor* strain Cov-1. Figure 2 presents novel mechanistic aspects underlying the action of PSP. PSP, by virtue of its structural similarity to proteoglycans, may conceivably act directly as an agonist/antagonist of specific surface receptor ligands, thereby augmenting the trigger of the Janus kinase/signal transducer and activator of transcription signaling pathway while simultaneously dampening the events that culminate in the extracellular signal–regulated kinase signaling cascade.[22] PSP may also function as a sequestrant/decoy to trap the relevant growth factor/cytokine required for cancer cell function, or to bind the pertinent receptor in ways that block further engagement and interaction with their physiological, cognate ligands. Such a mechanism seems plausible in light of the structural resemblance between bioactive constituents present in PSP, with proteoglycans occurring in the extracellular matrix of cancer cells. Another possibility is that PSP exerts a modulatory effect targeting the intracellular signaling cascade via internalization, which may involve its binding with components present in the pertinent cellular microenvironment, forming a complex accessible for cellular uptake. The outcome of the internalized PSP is regulation of specific genes that effectively inhibit cell cycle checkpoint transition and increase the expression and/or release of apoptogenic factors and suppress levels of antiapoptotic factors.[22]This mechanism may be supported by drawing a parallel with lipid-mediated delivery of highly charged and heterogeneous plasmid DNA into cultured mammalian cells, as well as the intestinal absorption of the orally ingested, heterogeneous, charged mucopolysaccharide heparin or heparin sulfate (e.g., chondroitin sulfate). The structural homology PSP shares with proteoglycans and of the macrophages or dendritic cells (DCs) and engulfed. The intracellular b-glucans are translocated to the endosome, where they are digested and released. In the second stage, the released b-glucan fragments or low–molecular weight b-glucans are recognized by CR3 on the neutrophils, granulocytes, or natural killer (NK) cells. Tumor cells can be killed by activated macrophages and NK cells.[20]

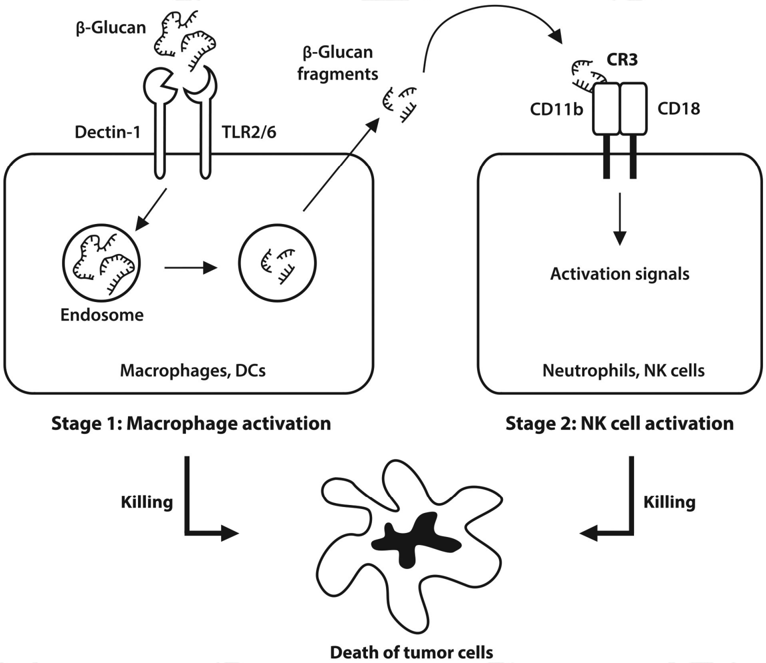


FIG. 1: The proposed 2-stage model for the anticancer activity of fungal b-glucans by dectin-1 and the CR3 receptor. In the first stage, high–molecular weight b-glucans are bound to dectin-1 and Toll-like receptor (TLR) 2/TLR6 glycosaminoglycans suggests that PSP elicits antiprostate cancer stem cell effects by inducing global changes in chromatin structure and transcriptional profile expression in cancer

stem cells via sitespecific histone modifications.[22]

II. MM PREPARATIONS

Immunoceuticals isolated from more than 30 MM species have demonstrated antitumor activity in different studies. Modern studies demonstrated that MM drugs and MM polysaccharide preparations from different species show positive results in treating cancers *in vitro* and *in vivo*. A new class of antitumor MM-derived DSs and drugs is called biological response modifiers (BRMs). BRMs help to treat cancers, with a focus on improving the patient's quality of life (QOL) because they significantly reduce side effects and help overcome cancer growth. Most BRMs activate the natural immune responses of the host and can be used as supportive treatment to prevent cancer and, in some cases, alone with conventional therapies. The incorporation of BRMs with conventional methods such as surgery, chemotherapy, and radiotherapy has become the new trend in modern cancer treatment.[3,4,8,16–20,22]

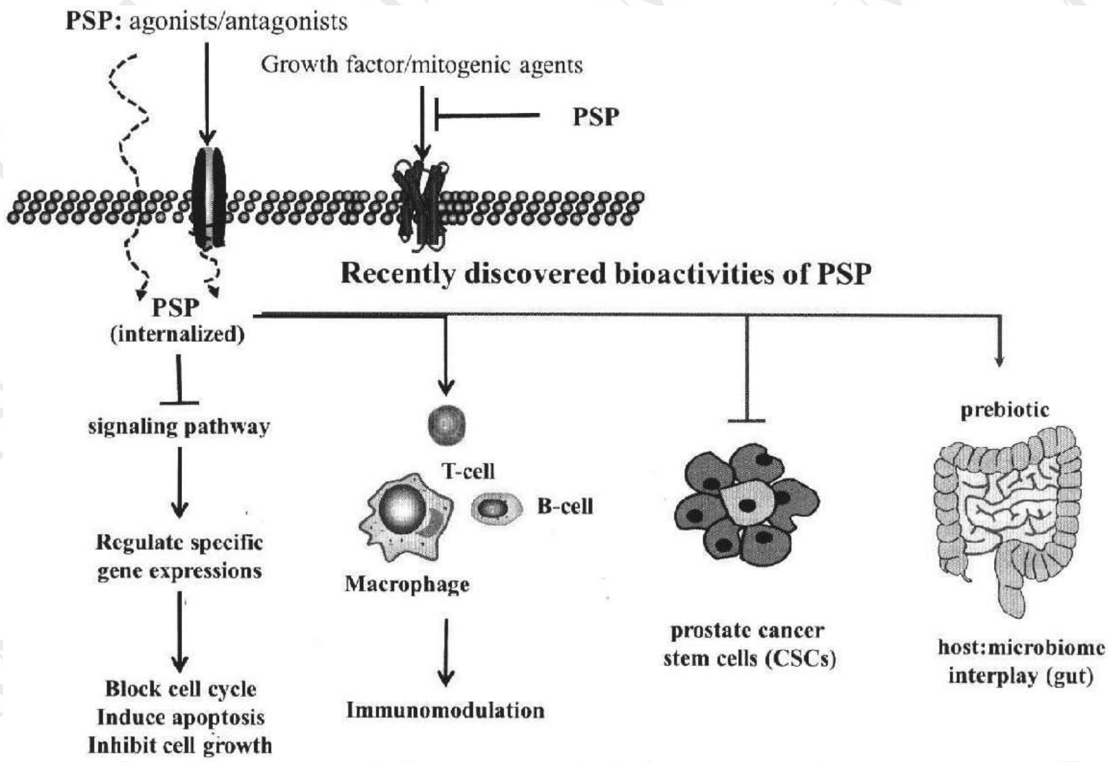


FIG. 2: Novel mechanism of action of polysaccharide peptide (PSP). In the model shown, PSP exerts effects on immunomodulation, the eradication of prostate cancer stem cells, the regulation of host-microbiome interplay, and the inhibition of cell proliferation. The multifaceted activities of PSP may be attributed to (1) the sequestration of growth factors/mitogens and/or action as their agonists/antagonists, thereby interfering with their binding to specific cell surface receptors; (2) its internalization to subsequently exert control of signaling events that further affect the expression of specific genes; (3) the disruption of cell cycle phase transition; and (4) the perturbation of the expression of apoptogenic/antiapoptotic regulatory proteins impinging on the induction of apoptosis.[22]

However, only a few BRMs have been tested for their anticancer potential in humans. Among the substances that have been tested, β-D-glucans or β-D-glucans are linked to proteins. Moreover, the latter have demonstrated greater immunopotentiation activity than free glucans. Numerous studies prove the cancer-inhibitory effects of *L. edodes*,[16,18] *Grifola frondosa* (Dicks.: Fr.) Gray,[23,24] *Schizophyllum commune* Fr.: Fr.,[19,25] *G. lucidum*,[26,27] *T. versicolor* (L.: Fr.) Lloyd,[28] *Inonotus obliquus*,[29,30] *Ph. linteus* (Berk. et M.A. Curt.) Teng,[31] *Flammulina velutipes* (W. Curt.: Fr.) Singer,[32] *Hypsizygus marmoreus* (Peck) Bigel.,[33] *Ophiocordyceps* (=*Cordyceps*) *sinensis* (Berk.) G.H. Sung et al.,[34] *Agaricus brasiliensis* S.

Wasser et al. (=*A. blazei* sensu Heinem.),[35,36] and *Tremella mesenterica* Retz.: Fr.[37] Mushroom immunoceuticals act mainly by enhancing the host immune system. Several MM products, mainly polysaccharides and especially b-glucans, were developed with clinical and commercial purposes: krestin (polysaccharide K) and PSP from *T. versicolor*; lentinan, isolated from *L. edodes*; schizophyllan (sonifilan, sizofiran) from *Sch. commune*; befungin from *Inonotus obliquus*; the D-fraction from *G. frondosa*, a polysaccharide fraction from *G. lucidum*; active hexose-correlated compound; and many others.

Other mushroom compounds of therapeutic interest are secondary metabolites and especially some low–molecular weight compounds, which are also important for the immune function of an organism. Small molecular sizes help these compounds contain a number of enzymes, such as laccase, superoxide dismutase, glucose oxidase, and peroxidase. Enzyme therapy plays an important role in treating cancer, preventing oxidative stress, and inhibiting cell growth.[3,11]

It has been documented that MMs produce a huge number of biologically active compounds that not only stimulate the immune system but also modulate specific cellular responses by interfering in particular transduction pathways. For instance, the caffeic acid phenethyl ester, which specifically inhibits the DNA binding of nuclear factor κB (NF- κB) and has shown some promising results against human breast cancer MCF-7 cells, was found to be produced by *A. bisporus* (J. Lge) Imbach, *Marasmius oreades* (Bolt.) Fr., *L. edodes*, and *Ph. linteus.* Also, a methanol extract of *F. fomentarius* was reported to inhibit inducible nitric oxide synthase and cyclooxygenase expression because of the downregulation of NF-κB binding activity to DNA. Panepoxydone, a compound isolated from *Panus* spp. and found in *Lentinus crinitus*, interferes with the NF-κB-mediated signal by inhibiting the phosphorylation of IκBα. These reports demonstrate that such substances can be used as molecular targets in malignant cells in order to combat cancer. Many mushroom species have been reported to produce various metabolites capable of modulating different intracellular pathways, thus playing an essential role in cancer treatment.[3,4,11,38,39]

III. CANCER AND IMMUNOMODULATING DISEASES

Cancer has undoubtedly always existed in humans and is probably as old as complex multicellular life itself. Signs of bone cancer were discovered by paleontologists and radiologists in some dinosaur fossils dating back as far as 100 million years. The earliest known evidence of this condition in humans was recovered from preserved Egyptian and Incan mummies, and even more ancient finds, including a Neanderthal skull (35,000 bc) and a Neanderthal rib affected by fibrous dysplasia (120,000+ bc), to name a few.[40] The first written records regarding cancer are found in the Edwin Smith Papyrus, an ancient Egyptian medical text dating back to around 1600 bc, and describe, in addition to wounds, injuries, and fractures, most likely what was cancer of the breast.[41] The Kahun paryri (around 1825 bc) contains details of conditions that fall under the modern definition of cancer. Hippocrates of Kos (460–370 bc), an ancient Greek physician who is now recognized among the most outstanding figures in the history of medicine, had already distinguished several kinds of cancer, referring to them with the Greek word *karkinós,* meaning crab or crayfish, due to the noticeable resemblance between the cross section of some tumors and these sea creatures.[41] In the millennia that followed, this pathologic state was observed and documented by numerous physicians around the globe. Many generations of researchers were eager to reveal the hidden mechanisms behind this disease and finally discover the real cure.

However, some basic understanding of the clinical picture of cancer, including the process of metastasis, was established only at the end of 19th century, mostly because of the development and incorporation of microscopic methods in medicinal studies.

The word "cancer" is a very broad term uniting large numbers of various pathologic conditions that can develop and manifest within the body. The technical name commonly used for these conditions is malignant neoplasms. The National Cancer Institute (www.cancer.gov) distinguishes more than 100 different types of cancer in humans. Nowadays, cancer has been established as 1 of 2 leading causes of death worldwide (the other cause involves cardiovascular diseases). These top 2 causes accounted for 46.1% of all deaths in the United States in 2013. The figures and projections of the global cancer burden presented in the new edition of the *World Cancer Report*42 draw the public's attention to current frightening tendencies. The data show that the incidence of cancer has increased from 12.7 million cases in 2008 to 14.1 million in 2012. Unfortunately, this trend is projected to continue in the future, with the number of new cases expected to increase by 75% in 2025.

A total of more than 40 million new cancer cases worldwide were predicted by 2015. The estimates reported by the World Health Organization (WHO) indicate that 84 million people should have died of cancer between 2005 and 2015. Thus, cancer is killing more people than AIDS, malaria, and tuberculosis combined. In addition, in China and India—the most populated countries, with a total population now exceeding 2.6 billion people— cancer deaths are increasing largely because of smoking, an unhealthy and unbalanced diet, and ecological problems such as air and water pollution. According to WHO, the total number of cancerrelated deaths on the planet should reach 17 million/ year by 2030.[42]

The 5 most common sites of cancer diagnosed among men in 2012 were the lungs (16.7%), prostate (15.0%), colorectum (10%), stomach (8.5%), and liver (7.5%). Lung cancer demonstrated the highest incidence (34.2% per 100,000), and prostate cancer had the second highest incidence (31.1% per 100,000). The 5 most common sites of cancer among women were the breast, colorectum, lungs, cervix, and stomach, with an incidence of 25.2%, 9.2%, 8.7%, 7.9%, and 4.8%, respectively.[42] Breast cancer had a significantly higher incidence than any other cancer, at 43.3% cases per 100,000 people; the next highest incidence in women was recorded for colorectal cancer (14.3% per 100,000). Among the 4 major categories of noncommunicable diseases—cardiovascular diseases, chronic diabetes, respiratory diseases, and cancer—the main cause of death around the world on national, regional, and global levels is now recognized as cancer.[42]

In 2016, Siegel et al.[43] published projected cancer statistics for the United States, reporting that 1,685,210 new cancer cases and 595,690 cancer deaths will occur. Each year, the American Cancer Society estimates the numbers of new cancer cases and deaths and compiles the most recent data on cancer incidence, mortality, and survival. The National Cancer Institute collects data on cancer cases through the Surveillance, Epidemiology, and End Results Program, the Centers for Disease Control and Prevention (National Program of Cancer Registries), and the North American Association of Central Cancer Registries. The National Center for Health Statistics collects data on mortality. Overall cancer incidence trends (the 13 oldest Surveillance, Epidemiology, and End Results Program registries) were stable for women but declined in men by 3.1% per year (from 2009 to 2012), much of which is because of recent rapid declines in prostate cancer diagnoses. The cancer death rate has dropped by 23% since 1991, which means a decline in cancer deaths by more than 1.7 million through 2012. Despite this progress, death rates are increasing for cancers of the liver, pancreas, and uterine corpus. Cancer is now the leading cause of death in 21 states, primarily because of exceptionally large reductions in deaths from heart disease. Among children and adolescents (aged 0–19 years), brain cancer has surpassed leukemia as the leading cause of cancerrelated death because of the dramatic therapeutic advances against leukemia. To accelerate progress against cancer, both national investments and cancer research must be continued.

Cancer is known to represent a genetic disease caused by specific changes in the genes that control complicated cell machinery, including the processes of cell proliferation and apoptosis. The accumulation of genetic alterations leads to changes in the structure of DNA and chromatin and, consequently, modifies gene products and levels of gene expression. Cancer-causing genetic changes that increase the risk of the disease can be inherited from parents or can be acquired during a lifetime as a result of errors that occur in the course of normal cell division.

Modern science is still not able to identify accurately the causes of cancer in each individual case, and the origins of most common cancers remain unclear. However, a number of recognized risk factors might significantly increase a person’s chances of developing this pathologic condition. Observational studies have supplied scientists with a considerable amount of data regarding the causal relationship between different factors and cancer. Multiple data revealed that the following risk factors have a strong association with cancer: inherited genetic defects, age, exposure to cancercausing substances (carcinogens), infection with oncogenic viruses, chronic inflammation, hormone imbalances, immunosuppression, radiation (including sun exposure), unhealthy diet, obesity, and alcohol consumption. Usually, specialists emphasize a so-called trio of cancer-causing factors that can either individual or combined have an impact: inherited defects, exposure to environmental insults, and infection with oncogenic viruses. A possible fourth candidate—cell fusion—is now being thoroughly investigated. A recent study by Zhou et al.[44] suggested that cell fusion may initiate malignancy and drive tumor evolution by affecting chromosomal stability, by inflicting DNA damage that causes cell transformation, and/or by generating phenotypic diversity. It is also not yet clear how often cell fusion between normal cells leads to pathological consequences.

Advances in genetics, molecular biology, biochemistry, biostatistics, and other fields had an enormous impact on the study of the human genome and revolutionized our understanding of cancer biology at the gene level. Thus, as with the incorporation of microscopic methods, which was once a huge breakthrough in medicinal studies, the application of modern molecular methods opens new horizons for cancer research.

The treatment of cancer has become among the biggest challenges for modern science. Billions of dollars are invested in cancer research and health care programs. The National Cancer Institute reports that medical expenses associated with cancer in the year 2020 are estimated to reach at least $158 billion (in 2010 dollars). Pfizer, the world’s largest pharmaceutical company, hired about 1000 researchers for an all-out effort to develop drugs for combating cancer, a disease the company once largely ignored. In addition, the company decided to scale back on cardiovascular research and made cancer drugs one of its 6 focus areas. About 20% of Pfizer’s more than $7 billion budget for research and development is spent on cancer research, and 22 of roughly 100 drugs being tested are anticancer drugs.[45] One of the major complications associated with conventional cancer treatments, especially chemo- and radiotherapy, is the substantial damage to and weakening of the patient’s natural immunological defenses caused by treatment. In addition, most anticancer drugs available in the market today are not target-specific and cause a number of side effects and complications during therapy of various types of cancer. All these factors emphasize the urgent need for developing effective yet less toxic and more tolerable drugs.

The human immune system represents a complex network uniting structural components of different levels (molecules, cells, tissues, and organs) and various biochemical processes and interactions aimed to maintain the integrity and normal functioning of an organism while being exposed to a spectrum of environmental insults. Thus, the immune system evolved to combat threats produced by the surrounding environment, such as poisonous substances, pathogenic viruses and bacteria, and parasites and is capable of locating and neutralizing internal threats, such as cancer cells. The reaction of the immune system triggered by a specific provocation exhibits an immune response. All the diverse immune responses can be grouped into 2 general types of reactions that comprise innate and adaptive immunity. Both innate and adaptive immune systems contain humoral and cellular components.

The immune system provides several levels of protection, through which the specificity of the response gradually increases. If some pathogenic agent is able to overcome the mechanical barriers of the body, it immediately encounters the cells and mechanisms of the innate immune system. Innate immune responses are rapid, but not specific, meaning that different provocations trigger similar reactions and response patterns. Thus, innate immunity does not provide the body with continuous protection from a specific pathogen. The innate immune system comprises the following main components: physical epithelial barriers, phagocytic leukocytes, DCs, NK cells, and circulating plasma proteins, among others.[46] The presence of innate control of adaptive immunity is now a well-established paradigm.[47] Accordingly, the recognition of a microbial pathogen's features conserved by the innate immune system is mediated by pattern-recognition receptors (PRRs) that are capable of detecting conserved pathogen-associated molecular patterns. These molecular patterns may represent viral nucleic acids are several families of PRRs that can detect complex polysaccharides, glycolipids, lipoproteins, nucleotides, and nucleic acids. When a PRR identifies a pathogen-associated molecular pattern, it initiates inflammatory responses and innate host defenses. Although the mechanisms underlying the sensing of microbial organisms by different PRRs are still being investigated, it is known that PRR-mediated sensing determines the origin of the antigens and types of infection encountered and also leads to the activation of adaptive immune responses.[47]

On the other hand, the responses of the adaptive immune system manifest more slowly but are highly specific to the particular pathogen that triggers them. The adaptive immune system is able to provide long-lasting protection from the specific pathogen by creating so-called immunological memory after an initial encounter and response, leading to an enhanced response to the same pathogen in the future. Two categories of adaptive immune responses exist: humoral immunity (mediated by antibodies produced by B lymphocytes) and cellmediated immunity (mediated by T lymphocytes). B cells are produced in the bone marrow. [20,21,27] (An important immunomodulating mechanism for cancer immunotherapy is described in Mahoney et al.[48]). (...to be continued)

REFERENCES

1. Reshetnikov SV, Wasser SP, Tan KK. Higher Basidiomycota as source of antitumor and immunostimulating polysaccharides. Int J Med Mushrooms. 2001;3:361–94.

2. Van Griensven LJ. Culinary-medicinal mushrooms: must action be taken. Int J Med Mushrooms. 2009;11:281–86.

3. Wasser SP. Medicinal mushroom science: history, current status, future trends, and unsolved problems. Int J Med Mushrooms. 2010;12(1):1–16.

4. Chang ST, Wasser SP. The role of culinary-medicinal mushrooms on human welfare with a pyramid model for human health. Int J Med Mushrooms. 2012;1:95–134.

5. Pöder R. The Ice man's fungi: facts and mysteries. Int J Med Mushrooms. 2005;7:357–9.

6. Vunduk J, Klaus A, Kozarski M, Petrovic P, Zizak Z, Niksic M, Griensven LJ. Did the iceman know better? Screening of the medicinal properties of the birch polypore medicinal mushroom, Piptoporus betulinus (higher Basidiomycetes). Int J Med Mushrooms. 2015;17(12):1113–25.

7. Guzmán G. New studies on hallucinogenic mushrooms: history, diversity, and applications in psychology. Int J Med Mushrooms. 2015;17(11):1019–29.

8. Wu Y, Choi M-H, Yang H, Shin H-J. Mushroom cosmetics: the present and future. Cosmetics. 2016;3(3):22.

9. Lindequist U. The merit of medicinal mushrooms from a pharmaceutical point of view. Int J Med Mushrooms. 2013;15(6):517–23.

10. Anke T. Basidiomycetes: a source for new bioactive secondary metabolites. Prog Ind Microbiol. 1989;27:51–66.

11. Zaidman BZ, Yassin M, Mahajna J, Wasser SP. Medicinal mushroom modulators of molecular targets as cancer therapeutics. Appl Microbiol Biotechnol. 2005;67:453–68.

12. De Silva DD, Rapior S, Sudarman E, Stadler M, Xu J, Alias SA, Hyde KD. Bioactive metabolites from macrofungi: ethnopharmacology, biological activities and chemistry. Fungal Divers. 2013;62:1–40.

13. Dai YC, Yang ZL, Ui BK, Yu CJ, Zhou LW. Species diversity and utilization of medicinal mushrooms and fungi in China (review). Int J Med Mushrooms. 2009;11:287–302.

14. Lo HC, Wasser SP. Medicinal mushrooms for glycemic control in diabetes mellitus: history, current status, future perspectives, and unsolved problems (review). Int J Med Mushrooms. 2011;13(5): 401–26.

15. Rahman MA, Abdullah N, Aminudin N. Interpretation of mushroom as a common therapeutic agent for Alzheimer's disease and cardiovascular diseases. Crit Rev Biotechnol. 2016;36:1131–42.

16. Chihara G, Hamuro J, Maeda Y, Arai Y, Fukuoka F. Fractionation and purification of the polysaccharides with marked antitumour activity especially lentinan from Lentinus edodes (Berk.) Sing. (an edible mushroom). Cancer Res.1970;30:2776–81.

17. Zhang M, Cui SW, Cheung PC, Wang Q. Antitumor polysaccharides from mushrooms: a review on their isolation, structural characteristics and antitumor activity. Trends Food Sci Technol. 2007;8:4–19.

18. Zhang Y, Li Sh, Wang X, Zhang L, Cheung PC. Advances in lentinan: isolation, structure, chain conformation and bioactivities. Food Hydrocoll. 2011;25:1996–2006.

19. Zhang Y, Kong H, Fang Y, Nishinan K, Phillips GO. Schizophyllan: a review on its structure, properties, bioactivities and recent development. Bioactive Carbohydr Diet Fiber. 2013;1(1):53–71.

20. Lee DH, Kim HW. Innate immunity induced by fungal β-glucans via dectin-1 signaling pathway. Int J Med Mushrooms. 2014;16(1):1–16.

21. Guggenheim AG, Wright KM, Zwickey HL. Immune modulation from five major mushrooms: application to integrative oncology. Integr Med (Encinitas). 2014;13(1):32–44.

22. Wu JM, Doonan BB, Hsieh TC, Yang Q, Yang XT, Ling MT. Recent advances and challenges in studies of control of cancer stem cells and the gut microbiome by the Trametes-derived polysaccharopeptide PSP (review). Int J Med

Mushrooms. 2016;18:651–60.

23. Zhuang C, Wasser SP. Medicinal value of culinary-medicinal Maitake mushroom Grifola frondosa (Dicks.:Fr.) S.F.Gray (Aphyllophoromycetidae). Int J Med Mushrooms. 2004;6:287–313.

24. Boh B, Berivic M. Grifola frondosa (Diks.:Fr.) S.F. Gray (Maitake mushroom): medicinal properties, active compounds, and biotechnological cultivation. Int J Med Mushrooms. 2007;9:89–108.

25. Hobbs C. The chemistry, nutritional value, immunopharmacology, and safety of the traditional food of medicinal split-gill fungus Schizophyllum commune Fr.:Fr. (Schizophyllaceae). A literature review. Int J Med Mushrooms. 2005;7:127–40.

26. Lin Z-B. Lingzhi. From mystery to science. Beijing: Peking University Press; 2009.

27. Mahajna J, Dotan N, Zaidman BZ, Petrova RD, Wasser SP. Pharmacological values of medicinal mushrooms for prostate cancer therapy: the case of Ganoderma lucidum. Nutr Cancer. 2009;61:16–26.

28. Hobbs C. Medicinal value of turkey tail fungus Trametes versicolor (L.: Fr.) Pilát (Aphyllophoromycetidae). Int J Med Mushrooms. 2004;6:195–218.

29. Mizuno T, Zhuang, Abe K, Okamoto H, Kiho T, Ukai Sh, Leclerc S, Meijer L. Antitumor and hypoglycemic activities of polysaccharides from the sclerotia and mycelia of Inonotus obliquus (Pers.:Fr.) Pil. (Aphyllophoromycetidae). Int J Med Mushrooms. 1999;1:301–16.

30. Balandykin ME, Zmitrovich IV. Review on Inonotus obliquus (Basidiomycota). Realm on medicinal applications and approaches on resources estimation. Int J Med Mushrooms. 2015;17(2):95–104.

31. Hsieh PW, Wu JB, Wu YC. Chemistry and biology of Phellinus linteus. Biomedicine (Taipei). 2013;3:106–13.

32. Maruyama H, Ikekawa T. Immunomodulation and antitumor activity of a mushroom product, proflamin, isolated from Flammulina velutipes (W.Curt.:Fr.) Singer (Agaricomycetidae). Int J Med Mushrooms. 2007;9:109–22.

33. Matsuzawa T. Studies on antioxidant effects of culinarymedicinal bunashimeji mushroom Hypsizygus marmoreus (Peck) Bigel. (Agaricomycetidae). Int J Med Mushrooms. 2006;8(3):245–50.

34. Holliday H, Cleaver M. Medicinal value of the caterpillar fungi species of the genus Cordyceps (Fr.) Link (Ascomycetes). A review. Int J Med Mushrooms. 2008;10:209–18.

35. Stamets P, Wasser SP, Ferreira da Eira A, Didukh MY, de Amazonas MAL. Is widely cultivated culinary-medicinal royal sun Agaricus (the Himematsutake mushroom) indeed Agaricus blazei Murrill? Int J Med Mushrooms. 2002;4:267–90.

36. Wang H, Fu Z, Han Ch. The medicinal values of culinary-medicinal royal sun mushroom (Agaricus blazei Murrill). Evid Based Complement Alternat Med. 2013;2013:842619.

37. Reshetnikov SV, Wasser SP, Nevo E, Duckman I, Tsukor K. Medicinal value of the genus Tremella Pers. (Heterobasidiomycetes) (review). Int J Med Mushrooms. 2000;2(2):169–93.

38. Yassin M, Wasser SP, Mahajna J. Substances from the medicinal mushroom Daedalea gibbosa inhibit kinase activity of native and T315I mutated Bcr-Abl. Int J Oncol. 2008;32:1197–204.

39. Petrova RD, Mahajna J, Wasser SP, Ruimi N, Denchev CM, Sussan S, Nevo E, Reznick AZ. Marasmius oreades substances block NF-kappaB activity through interference with IKK activation pathway. Mol Biol Rep. 2009;36:737–44.

40. Monge J, Kricun M, Radovčić J, Radovčić D, Mann A, Frayer DW. Fibrous dysplasia in a 120,000+ year old

neandertal from Krapina, Croatia. PLoS One. 2013;8(6):e64539.

41. Hajdu SI. A note from history: landmarks in history of cancer, part 1. Cancer. 2011;117(5):1097–102.

42. Stewart BW, Wild CP, editors. World cancer report 2014. Lyon (France): International Agency for Research on Cancer; 2014.

43. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2016. CA Cancer J Clin. 2016;66(1):7–30.

44. Zhou X, Merchak K, Lee W, Grande JP, Cascalho M, Platt JL. Cell fusion connects oncogenesis with tumor evolution. Am J Pathol. 2015;185(7):2049–60.

45. Pollack A. Drug firms see fortune in treating cancer. Int Herald Tribune. 2009:15–16.

46. Dranoff G. Cytokines in cancer pathogenesis and cancer therapy. Nat Rev Cancer. 2004;4(1):11–22.

47. Iwasaki A, Medzhitov R. Control of adaptive immunity by the innate immune system. Nat Immunol. 2015;16(4):343–53.

48. Mahoney KM, Freeman GJ, McDermott DF. The next immune-checkpoint inhibitors: PD-1/PD-L1 blockade in melanoma. Clin Ther. 2015;37(4):764–82.

Call for Papers

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

Contact information

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

ISMM Secretariat Office, Beijing
Room D-1216, Jun Feng Hua Ting,
No. 69 West Beichen Road,
Chaoyang District, Beijing 100029, China.
Tel: +86-10-58772596, 87109859
Fax: +86-10-58772190
E-mail: ismm.org@gmail.com
Website: http://www.ismm2013.com/