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Eco-friendly-made selenium products of mushroom origin for use in agriculture (review)

© 2019. O. M. Tsivileva ORCID: 0000-0002-5269-349X,
Institute of Biochemistry and Physiology of Plants and Microorganisms,
Russian Academy of Sciences,
13, Prospekt Entuziastov, Saratov, Russia, 410049,
e-mail: tsivileva@ibppm.ru

Wood-decaying higher fungi attract attention as the possible participants of the plant wastes biodestruction processes, as well as the producers of unique complex of biologically active substances. Myconanotechnology has become a rapidly developing area of nanoscience and biotechnology. Broad spectrum and diversity in mushrooms could lead to an exciting potentiality and interdisciplinarity of this science. General aspects of the mushrooms' implementation relevance in the context of comparison to other organisms, as bacteria and plants, testify in favor of the mycogenic synthesis of nanoparticles. Primary and secondary fungal metabolites are capable of reducing readily the chemical elements in compounds to occur nanoparticles with definite size and shape in controlled non-hazardous processes.

Current biotechnological applications of selenium are undoubtedly very wide. Chemically synthesized Se-conjugates and elemental selenium are known to possess antimicrobial properties. However, more ecologically safe and beneficial approaches to manufacture the Se-based products are current challenge. In this relation, of especial interest are the selenium-enriched preparations of mushroom origin owing to their availability, biocompatibility, and proved biological activity. The approach developed in our works recently would allow the bioproduction of submicrostructured elemental selenium-based composites using the edible and medicinal mushrooms' cultures to be put into practice. We demonstrated the occurrence of bacteriostatic and bactericidal effects of the agents under study. Even one decade ago the review of published works on myconanotechnology did not operate with the terms "mushroom" or "selenium", and were related solely to lower fungi and metals, the real mechanism of biosynthesis of nanoparticles remaining unclear. Contemporary studies favor the supposition on advisability of further research into the mushroom-originating selenium bionanocomposites as the agents for agricultural recovery from the bacterial pathogens. Myconanotechnology of selenium could represent a novel approach to the development of antimicrobial nanomaterials.

Keywords: selenium, mushrooms, selenized mycelium, Se-fortified products, biocomposites, biological activity.

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Селенсодержащие продукты экологически чистой переработки высших грибов сельскохозяйственного назначения (обзор)

© 2019. О. М. Цивилева, д. б. н., в. н. с.,
Институт биохимии и физиологии растений и микроорганизмов
Российской академии наук,
410049, Россия, г. Саратов, пр-т Энтузиастов, д. 13,
e-mail: tsivileva@ibppm.ru

Дереворазрушающие высшие грибы привлекают внимание исследователей как возможные участники процессов биодеструкции растительных отходов, а также как продуценты уникального комплекса биологически активных веществ. Миконанотехнология становится быстроразвивающейся областью нанонауки и биотехнологии. Широкий спектр и разнообразие свойств высших грибов способствуют высокому потенциалу и мультидисциплинарности миконанотехнологии. Оценка основных аспектов актуальности применения грибов для изготовления наноструктурированных объектов с точки зрения сравнения с другими организмами, такими как бактерии и растения, свидетельствует в пользу микогенного синтеза наночастиц. Первичные и вторичные грибные метаболиты способны легко восстанавливать химические элементы в их соединениях с образованием наночастиц определённого размера и формы в контролируемых условиях процессов, не опасных для человека.

Перечень современных биотехнологических применений селена весьма внушителен. Синтезированные химическим путем Se-конъюгаты и элементный селен обладают антимикробными свойствами. Однако в соответствии с вызовом современности требуются более экологически безопасные и эффективные подходы к изготовлению селенсодержащих продуктов. В этой связи особый интерес представляют обогащённые селеном препараты из высших грибов благодаря их доступности, биосовместимости и доказанной биологической активности. Необходимо развитие новых подходов, позволяющих реализовать биопродукцию композитов на основе субмикроструктурированного элементного селена с использованием культур съедобных и лекарственных высших грибов. Нами продемонстрировано наличие бактериостатического и бактерицидного эффекта таких агентов. Современные исследования благоприятствуют мнению о целесообразности дальнейшего изучения бионанокомпозитов селена грибного происхождения как агентов, применяемых в сельскохозяйственной практике для борьбы с фитопатогенами. Миконанотехнология селена может представлять инновационный подход к получению антимикробных наноматериалов.

Ключевые слова: селен, высшие грибы, селенизированный мицелий, Se-обогащённые продукты, биокомпозиты, биологическая активность.

Wood-decaying higher fungi attract attention as the possible participants of the plant wastes biodestruction processes, as well as the producers of unique complex of biologically active substances. The trace element selenium (Se) is essential nutrition mineral. Interest in using mushrooms as a Se carrier increases. Analyzing the selenium content of mushrooms and its utilization, the contribution of mushrooms to the human's selenium demand, selenium content of mycelium cultivated under different conditions, effect of technology (growing) on the selenium content of mycelia, selenium species occurring in mushrooms, bioavailability of selenium in different oxidation states, one could conclude on the significantly positive trends in edible and medicinal mushrooms' implementation in this area.

Contemporary biotechnological applications of Se are very wide, including those related to antimicrobial properties. More ecologically safe and beneficial approaches to manufacture the Se-based antibacterial agents are current challenge. In this relation, of especial interest are the selenium-enriched preparations of higher-fungal origin owing to their availability, biocompatibility, and potentiality for agricultural recovery from the bacterial pathogens.

Mushrooms, promising ecologically pure multipurpose material

Mushrooms are ubiquitous organisms found in almost every ecosystem and play central roles in the recycling of organic matter. Since the wild fungi play an important role to maintain the health of forests besides their medicinal importance and nutritional value in most of the cases, therefore it becomes quite necessary to explore, document and conserve this natural wealth. A considerable amount of literature has been published on the ecology, physiology, genetics, and biotechnology of mushrooms. Edible mushrooms are readily available at any food market owing to their commercial cultivation [1]. The mushrooms do not merely constitute a highly nutritious source of food. More recently, attention has focused on a second area of exploitation following the discovery that many of these fungi produce a range of metabolites of intense interest to the pharmaceutical and food (e. g. flavour compounds) [2].

Relatively low levels of commercial cultivation of the mushrooms limit their availability for use as food and medicine [3]. A good alternative to mushrooms' fruit bodies production is provided in this respect by the submerged fermentation. The process offers several advantages including a fast growth and high biomass productivity [4], compact and controlled environment and shortened production time [5]. This resourceful biotechnological approach in the mushrooms application has been used widely to yield bioactive compounds (polysaccharides, glycoproteins, selected low-molecular substances) in different basidiomycetes [6, 7], as well as mycelial biomass itself. The latter is valuable not only as food and fodder supplement, but also as the intermediate product, seeding material, for obtaining fruiting bodies [8]. Mycelia formed by growing pure cultures under the submerged conditions are high-quality, consistent, safe, predictable and economical mushroom products [9, 10], and a suitable alternative to yield mushroom product fortified with selenium.

Mycogenic synthesis of nanoparticles: general aspects of relevance

The non-toxic and environmentally benign procedures for the synthesis of submicro- and nanomaterials based on green chemistry and biological processes needed to be developed [11]. More recent technological advances make better understanding of physicochemical and optoelectronic properties, as well as organization of nanoscale structures into predened 1-D (nanorods), 2-D or 3-D (nanowires) superstructures [12]. These advances have opened the door to new functionalities and applications of nanoparticles in agriculture. This resulted in relatively new, largely unexplored and rapidly growing area of myconanotechnology [13, 14]. It was necessary to extend knowledge on the mechanisms and approaches for fabrication of myconanoparticles. Various types of the mycogenic nanomaterial such as nanowires, nanofilters, nanosensors, nanofibrous mats and quantum dots (QDs) were synthesized. More and more authors researched into the problems of fungal nanofactories' work at suppressing plant pathogen, targeted delivery, interactive agrochemicals as pesticides, nanocomposites material for food packaging and extensive nano-surveillance using crop sensing and nano-enabled diagnostics [15].

As far as we aware, even one decade ago the review of published works on myconanotechnology did not operate with the terms "mushroom" or "selenium", and were related solely to lower fungi, which were exploited for the synthesis of silver, gold, zirconium, silica, titanium, iron and platinum nanoparticles [16, 17]. Fungi are the objects that could produce great amounts of biopolymers extracellularly, and could take advantage in the downstream processing and handling of biomass, when compared to the bacterial fermentation process [18] or to the application of plants [19]. Due to slower kinetics, fungal cultures offer better manipulation and control over crystal growth and their stabilization [20]. Somewhat recently mushrooms (higher fungi) have gained an added attention from researchers. When being subjected to different kinds of unavoidable technological procedures, mushrooms' mycelia can withstand these conditions, including in bioreactors, much more better compared to plants and bacteria [21]. Many of the enzymes, polysaccharides and low-molecular metabolites secreted by fungi are capable of reducing metal and non-metal chemical elements entering the composition of the compounds – precursors of the targeted nanoparticles. Antioxidant properties of mushrooms metabolites are frequently responsible for the suitable starting chemical compound's reduction into the respective nanostructures to generate the nano-sized objects. Those primary and secondary fungal metabolites could increase the oxidation state number of the elements readily through non-hazardous processes, and allow a controlled synthesis of nanoparticles with definite size and shape [22], as nanorods, nanocubes, nanotubes, nanowires and nanosheets etc. [15] with the minor defects and more homogeneous chemical composition [23, 24]. Moreover, the interference from intracellular components, which are undesirable in most cases, is minimized owing to the extracellular secretion of fungal reductive substances.

Inorganic and organic Se: dramatically different biological effects

The trace mineral selenium (Se) is an essential element for human and animal nutrition. Selenium deficiencies in the human and animal organism are recognized worldwide to be related to a number of pathologies [25]. However, at higher Se concentrations, harmful consequences occur.

Recommended dietary intakes are not currently met by most diets, unless Se-rich foods are included. Therewith one should take into consideration a poor bioavailability of the most common inorganic forms of selenium. Selenium content in a foodstuff critically influences Se bioactivity to humans and animals. Foodstuffs processing and treatments, along with foodstuff-matrix major and minor components, affect Se bioavailability [26]. A great deal of information has been accumulated indicating that dietary form of Se is a major determinant of its efficiency [27], and the chemical form of Se plays a very important, if not a decisive role in its bioavailability [28]. A growing body of evidence indicates dramatically different biological effects of inorganic and organic chemical forms of selenium, which may explain apparent inconsistencies across studies by inadequate assessment of health risk [29]. The human or animal exposure to selenium in different chemical forms leads to not only different, but in some cases opposite nutritional and toxicological consequences [30]. It has been shown repeatedly that Se is more bioavailable to animals and humans in organic forms than in inorganic forms [25, 31, 32], and toxicity of inorganic (tetravalent) Se greatly exceeds that of organic Se [33].

The investigations aimed at the development of novel synthetic organoselenium compounds and at the discovery of naturally occurring selenium compounds that are more effective and less toxic than inorganic forms of selenium were initiated at the beginning of the 1980s. Important aspects of the modern organoselenium chemistry are the use of organoselenium reagents as catalysts (organocatalysis), green chemistry, bioinspiration, antioxidant activity. The classical synthetic application of organoselenium reagents are electrophilic, nucleophilic and free radical reagents. Organoselenium compounds find applications in organic synthesis, materials synthesis, ligand chemistry [34–36], antioxidative agents [37–39]. The synthesis and the synthetic applications of some emerging classes of selenium compounds such as hypervalent selenium species and selenoamides, address some biological aspects such as the antimicrobial activity of organoselenium derivatives and the biochemistry of selenoproteins, along with biologically relevant processes as potent therapeutic and chemopreventive agents [40, 41].

Today this area of organoselenium research is growing rapidly, and the outcomes of these investigations are highly promising. Exciting studies performed *in vitro* with respect to cellular responses showed that the dose and form of selenium compounds are critical experimental parameters.

Selenium-enriched food of mushroom origin

The addition of selenium to the diet through dietary supplements or fortified food/feed becomes increasingly common owing to the frequently suboptimal level of this microelement in standard nutrition in many countries [42]. One of the basic questions arising in relation to Se-fortified food is on the threshold quantities of selenium causing unexplored harmful consequences of using common food. The content of selenium in food of not-fungal-origin, i. e. plants and animals, depends critically on the selenium content in environment. Thus, the selenium concentration in such nutrient products is highly variable [43]. The bioavailability of selenium from fish can be modified by the presence of various contaminants, including arsenic and mercury [44].

Satisfaction of the human selenium requirements can be considerably contributed from mushrooms, since the selenium enriched mushroom mycelia are valuable functional foods. It is obvious that risks and benefits of Se intakes should be quantified and balanced. The mushrooms are commonly used food product and dietary supplement convenient to apply in the selenium-fortified form. Mycelia of many tested mushroom species at submerged growing are satisfactory Se-sources due to the fact that Se-concentrations absorbed from the sodium selenite-enriched medium could achieve tens percent of its content in the medium [45]. The mycelial selenium content could be several times higher than in fruiting bodies.

In order to optimize fortification process and yields, selenium enrichment in the cultivation substrate can be an approach to increase the Se concentration in fruiting bodies of mushrooms. Popular mushrooms with high commercial values and thus cultivated world wide appeared to contain nutritionally significant but yet insufficient amounts of Se [46]. Most of edible mushroom species examined are selenium-poor (< 1 μg Se/g dry weight) [47]. So, the solution is artificial growing of basidiomycetes. A particularly rich source of selenium could be obtained from selenium-enriched mushrooms that are cultivated on a solid media fortified with selenium.

Growth-compost irrigated with sodium selenite solution appeared to cause the increase in the selenium level in button mushroom, *Agaricus bisporus* by tens times compared to the control mushroom irrigated solely with water [48]. The enrichment of *Lentinula edodes* (shiitake mushroom) fruit bodies with Se could be performed by adding the sodium selenite to the cold-shock water used to induce primordial formation in arti cial logs [49]. Thus, selenium-enriched fruit bodies are industrially cultivated as functional food or medicinal food in China and Southeast Asia and could provide an efficient way in delivering functional organic Se. However, the composition of selenium substances, as well as the distribution of the main bioactive components, remain still unknown [50].

Se^0 mycosynthesis from inorganic Se-salts

Evaluation of the efficacy of supplementation of several medicinal mushrooms with inorganic selenium salts (Na_2SeO_3 and Na_2SeO_4) attracted the attention of many researchers in 21st century. Submerged mycelium of *Lentinula edodes* accumulated selenium from the cultivation medium very effectively. Selenium was well bioavailable from the mycelial preparations in *in vitro* and *in vivo* tests [51]. The speciation of selenium in Se-enriched mycelial cultures testified to the fact that the main part of Se in the tested mycelium was in the zero (elemental selenium) and IV oxidation states. *Phanerochaete chrysosporium*, too, was found to be a selenium-reducing organism, capable of synthesizing elemental Se from selenite but not from selenate [52]. Studies with *Ganoderma lucidum*, *Agrocybe aegerita*, and *Hericium erinaceus* showed that the growth of *G. lucidum* fruit bodies was observed with up to 0.8 mM Se accompanied by the highest total Se content, macroscopic changes in the fruiting bodies of the examined mushrooms, and color changes of fruiting bodies [53]. Biotechnologically important mushrooms fortified with inorganic Se, as *Ganoderma lucidum, Pleurotus ostreatus, Pleurotus eryngii, Pleurotus pulmonarius, Flammulina velutipes, Ganoderma applanatum, Lenzites betulinus, Trametes hirsuta* were explored [54] in respect to their morpho-physiological characteristics, as well as biological activities. During cultivation on selenite-enriched medium, the appearance of mycelium of brick-red color with significant morphological and ultrastructural changes in comparison with the control was observed. Hyphal density was lower, the cell wall was thick with more expressed extracellular matrix, septa were abundant, and branch frequency and occurrence of clamp-connections were rare. Cytological analysis demonstrated that the majority of selenium was accumulated in cell membrane and vacuoles, while changes taking place in a cell wall were insignificant [54].

Considerable amount of works are focused on the effect of inorganic selenium salts' concentrations on mycelium morphological and ultrastructural features. At a relatively high selenite concentration in *Lentinula edodes* liquid nutrient medium, the excess selenium is eliminated *via* its reduction to elemental Se [55]. As for another very popular cultivated mushroom, *Pleurotus ostreatus*, the studies also showed that higher selenite concentrations caused firstly Se accumulation in *P. ostreatus* mycelium, and during the suppression growth phase, selenite was reduced to amorphous Se in zero oxidation state and this gave the mycelium and medium a reddish color [56, 57]. Hyphal morphology of *P. ostreatus* was dependent on Se concentration in the liquid medium. Electron-dense spots, visible in both the control and Se-enriched samples, were described [58] as proteinaceous bodies, since lipid bodies would be extracted during preparation for transmission electron microscopy. In the presence of Se, the number of these bodies increased, and changes in their shape, color, and size were slight. It was shown that the reduction of the ionic Se and production of amorphous Se^0 are really occurring round the bodies [58]. Selenite stress exerts a significant effect on ultra-architectural features of the fungal hyphae and spores of mushroom cultures, e. g., *Ganoderma lucidum* [59]. A number of works deals with the Se distribution among different cellular compartments, and, in particular, polysaccharide structures contained in fungal cell walls. Se-enriched submerged mycelia of *Pleurotus ostreatus* were explored in respect to the incorporation of selenium from the growth medium to mushroom [60]. A polysaccharide-containing fraction of mycelia was treated alternatively with Tris-HCl or with chitinase. Better solubility and increased contribution of low molecular mass compounds were observed in chitinase extracts (UV detection), confirming the degradation of polysacharides by the enzyme. The results obtained suggest selenium binding to chitin-containing polysaccharide structures in fungal cell walls [60]. Selenite influenced the pellet morphology of *Phanerochaete chrysosporium* by reducing the size of the fungal pellets and inducing their compaction and smoothness [52]. Analysis of *P. chrysosporium* mycelia with transmission electron microscopy, electron energy loss spectroscopy, and a 3D reconstruction showed that elemental selenium was produced intracellularly as nanoparticles.

Selenium-containing agents of mushroom origin for agricultural recovery from the bacterial pathogens

Almost all of the published works dealt with the Se-fortified fungal cultures are concerned with selenium exclusively in the form of inorganic substances, sodium selenite Na_2SeO_3 or selenate Na_2SeO_4. The source of selenium should reasonably be the organic substance 1,5-diphenyl-3-selenopentanedione-1,5 (synonyms diacetophenonylselenide, bis(benzoylmethyl) selenide, preparation DAPS-25) [61], since its low toxicity at physiological concentrations in combination with high efficiency (compared to, e. g., selenites) has been proved earlier for various living organisms. It is the source of selenium we use in our research. Appreciable positive effect of preparation DAPS-25 on the vital processes of *Lentinula edodes* (shiitake mushroom) exhibited as the change in mushroom growth parameters and lectin activity on various organic and mineral, agar and liquid media [62] was considered in relation to fungal metabolites, extracellular lectins of shiitake mushroom. Along with DAPS-25, several other compounds of the 1,5-di(4-R-phenyl)-3-selenopentanediones-1,5 series were explored involving both computations and experiment [63].

The biotransformation of DAPS-25 at the growth of shiitake mushroom under the liquid-phase and solid-phase culture conditions has been studied. The intensive red pigmentation of mycelium caused by the elemental selenium accumulation resulted from the organoselenium compound destruction by the mushroom *L. edodes* has been revealed. At the initial DAPS-25 concentration equal to or higher than $1 \cdot 10^{-4}$ mol/L in the synthetic liquid medium, a red color of *L. edodes* mycelium develops, the intensity and initiation time of which being related to this Se-additive concentration [64]. Starting from the results of qualitative reaction, the data of X-ray fluorescence, X-ray diffraction and GC-MS analyses, we should conclude on the *L. edodes* submerged culture capability of destructing the organoselenium xenobiotic to occur red modification of elemental selenium and to evolve acetophenone. The process of elemental selenium elimination was followed by its precipitation onto gyphae [65]. Within the framework of more recent studies, the growth parameters of more than twenty strains of xylotrophic basidiomycetes belonging to 8 genera, 13 species on liquid media enriched with selenium in organic form were studied, and the effect of 1,5-diphenyl-3-selenopentanedione-1,5 within a wide concentration range ($1 \cdot 10^{-4}$–$1 \cdot 10^{-8}$ mol/L) on the mycelial growth was observed. The culture liquids of the fungal species under study were successfully tested for their reducing and stabilizing properties toward organic selenide and elemental selenium, respectively [66].

In doing so, the mycosynthesized Se-containg bionanocomposites were manufactured and tested for biological activity. The results of studying the effect of those selenium nanocomposites on the bacterium *Clavibacter michiganensis* ssp. *sepedonicus* (*Cms*) were obtained [67]. *Cms,* a Gram-positive bacterium, causes ring rot, which is one of the most dangerous potato diseases. The effective alongside ecologically safe methods for combating *Cms* are lacking. As the agents feasible for use in this purpose, we examined the selenium biocomposites obtained from the submerged cultures of mushrooms, several microbiological techniques being implemented. The results demonstrated the occurrence of bacteriostatic and bactericidal effects of the agents under study, and favored the supposition on advisability of further research into the selenium bionanocomposites as the agents for agricultural recovery from the bacterial pathogens [67].

The impact of Se-containing biocomposites based on *Ganoderma* mushroom submerged cultures (6 species, 9 strains) grown in the presence of oxopropyl-4-hydroxycoumarins, on the bacterial phytopathogens was examined [68]. These bacterial strains used were kindly provided by the Collection of Rhizosphere Microorganisms of IBPPM RAS (http://collection.ibppm.ru). By means of such methods as the colony-forming units count, the agar well diffusion method, and the bacterial suspension turbidity measurement, the bacteriostatic and bactericidal activity of the Se-containing biocomposites was elucidated. The pioneering information on the biological activity of coumarin series compounds in their application for producing the substances of fungal origin has been provided [68].

We explored the effect of selenium biocomposites obtained from medicinal basidiomycetes *Ganoderma lucidum*, *Grifola umbellata*, *Laetiporus sulphureus*, *Lentinula edodes*, and *Pleurotus ostreatus* on the ability of *Cms* to form biofilms [69]. A decrease in the viability of the bacterial cells as a result of incubation with biocomposites was shown. The determining effect of the selenium component of the composites on the studied biological activity was stated, and the dependence of the antibiofilm-forming effect of Se-containing agents on the biological species of the fungus was found. Biocomposites based on extracellular metabolites of *Ganoderma lucidum* possess maximal activity. When biopolymer samples of fungal origin were added to the bacterial suspension, the ability of *Cms* to form biofilms differed depending on the type of biocomposite; it decreased significantly in some cases [70]. The development of selenium biotechnology should be based on natural edible and medicinal products, e. g., mushrooms, and considered to be appropriate "green" method. As being originated from the biotransformed organoselenium compound, the selenium submicroparticles possess the benefit of their non-toxic source and provide the potential multipurpose use.

Conclusive remarks

Mushrooms are recognized to be promising ecologically pure raw material. Fortification of edible mushroom cultures with the selenium-containing compounds has proven to be an effective and cost saving strategy for the prevention of Se deficiency. Of especial interest are the selenium-enriched preparations of higher-fungal origin owing to their availability, biocompatibility, and the proved biological activity. The novel aspects concerned with the essential nutrient and antioxidant Se properties have changed the views on selenocompounds. Different chemical forms of selenium possess excellent biochemical properties and have been implicated for use in agriculture. The favorable profile of newly synthesized organoselenium compounds including those explored in our research warrants their recognition as a promising option for fortification purposes. Further thorough investigation should be focused on the mechanism of Se-containing compounds' biological effect to take that into account when using the various Se sources in biotechnological fields, including the production of ecologically safe antibacterial agents.

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