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Directions of Practical Application of Mycelial Wastes of Microbiological Production of Antibiotics in Various Areas of Industry and Agriculture (Review)[1]

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Abstract—The review systematizes various directions of practical application of mycelial wastes of microbiological production of antibiotics. At present, complex schemes of using of mycelial wastes were developed and introduced to many areas of industry and agriculture.

Keywords: biotechnology, production of antibiotics, mycelial wastes, utilization

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INTRODUCTION

In recent years, biotechnological methods are becoming more and more important for the design, elaboration and production of numerous drugs [1, 2]. Nowadays, the market of drugs produced by microbiological synthesis is estimated to be more than $100 billion, which is more than 20% of production of all pharmaceutical products [3, 4]. Antibiotics make up a substantial part of drugs produced by the use of biotechnology. However, further development of antibiotics production requires environmental protection from the negative effect of industrial wastes. Solving of this problem requires complex approach, consisting in improvement and strict control of technological processes of microbiological production of antibiotics, as well as development of new scientific ideas related to decontamination and practical utilization of wastes [5–7].

Specific character of antibiotic production consists in low yield of the target product and formation of large amount of wastes, which promotes scientific research in three directions: disposal of gas wastes, disposal of sewage wastes, and utilization of mycelial wastes [8–11]. Elaboration of various methods of disposal of gas wastes from antibiotics production is described in detail in many reviews and monographs [12–16]. Technological procedures used for disposal of sewage wastes formed in microbiological processes of industrial production of antibiotics are represented in numerous publications, of both Russian and foreign authors [17–22]. At the same time, there are no reviews on utilization of mycelial wastes of production of antibiotics (MWPA). Therefore, the goal of this review is to summarize the literature about practical application of MWPA in various fields of industry and agriculture.

Primary processing and analysis of MWPA

Utilization and decontamination of mycelial wastes is one of most important problems in antibiotics production. Intensification of the processes of microbiological synthesis of antibiotics as a result of increased concentration of growth media leads to further accumulation of mycelial wastes [23, 24]. Mycelial wastes are known to be formed as a result of separation of the liquid phase of the culture medium after biosynthesis of drugs, including antibiotics [25, 26]. The solid phase of the culture medium consists mainly of tissues of microorganisms (mycelium), residues of growth medium and compounds introduced in the

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culture liquid for better filtration. The amount of the separated wet residue varies from 10 to 20%, reaching sometimes 30% of the total volume of the culture liquid [27–29]. Along with mineral compounds, the solid phase of the culture liquid contains various organic compounds, and the inorganic part of mycelial wastes includes the compounds of calcium, magnesium, sodium, iron, silicon and phosphorus [8, 30, 31].

Since the antibiotics production is a large-scale industry, tens of tons of MWPA (calculated to dry weight) are formed each day at the enterprises producing these drugs [31, 32]. Till 70-s of the last century only a small part of MWPA was utilized, mainly in agriculture, whereas the main part was deposited, removed to the system of sewage disposal, and toxic mycelium was burned [8, 13, 18, 33]. Removal of more than two third parts of the formed MWPA to dumps, systems of sewage disposal or burning cannot be considered acceptable both from the viewpoint of environmental pollution and overloading of sewage treatment facilities, and because of nonrational approach to this type of wastes containing a lot of valuable compounds.

Taking all this into account, since the middle of 70-s of the last century, intensive studies were launched on primary processing and more detailed analysis of chemical composition of MWPA. MWPA are known to have high humidity varying from 70 to 95% and to contain organic compounds subject to fast spoiling and rotting [8, 34]. Therefore, for effective use of MWPA, technologies of filtration of culture liquid were worked out, providing formation of the maximally dehydrated precipitate and its decontamination. Filtration properties, in particular, specific resistance to filtration of MWPA, is determined by the size of separate mycelium hyphae, the type of microcolony, the character of mycelium growth [30, 33, 35]. In turn, these factors depend on species membership of the producent strain and conditions of its cultivation. MWPA consists mainly of long thread-like hyphae of 0.05 to 0.20 μm thickness, which causes high specific resistance of these precipitates and, hence, very low rate of filtration of the culture liquid after fermentation [36, 37]. To increase the rate of filtration, culture liquids are subject to different types of primary processing. Thus, substantial increase of the filtrating ability of the culture liquid after biosynthesis of streptomycin and its dehydration can be achieved by thermal treatment at the temperatures from 170 to 190°C at 25 Torr in autoclaves in 15–75 min [38]. Methods of electrochemical and electroflotocoagulation condensation of MWPA were suggested [39, 40], which lead to a substantial decrease of their humidity and volume. Besides, carrying out the processes of electrochemical treatment of MWPA at low current volume densities reduces the toxicity of the treated wastes [41]. Substantial destruction of toxic compounds contained in MWPA was achieve by the use of ultrasound devices [42], UV radiation and photochemical oxidation [43], as well as by a complex approach including electrochemical treatment, dechlorination and biosorption aerobic treatment [44–46]. An original scheme of catalytic oxidation of toxic impurities and oxidizable compounds was worked out with the use of oxysorbents [47, 48].

It is known that the requirements claimed to information about the composition and properties of wastes of microbiological production of antibiotics tighten up because of ecological problems [49, 50]. Different groups of researchers analyzed the content of the components of organic part of mycelial wastes from the production of a large group of antibiotics: penicillin, levorin, oleandomycin, streptomycin, tetracycline, fusidin, kanamycin, lincomycin, oxytetracycline, phenoxymethylpenicillin, erythromycin and monomycin [8, 37, 51]. It was shown that lipids account for 10.32–24.30%, carbohydrates 13.88–51.36%, aminoacids 1.05–16.44%, and proteins 4.02–59.92% of organic part of MWPA. For determination of total nitrogen content in MWPA, a modified Kjeldahl method was suggested [52]. For identification and quantitative determination of the components of MWPA it was suggested to use modern physicochemical methods, like gas chromatography and mass-spectrometry [53].

Use of MWPA in Agriculture

As mentioned above, one of the first directions of utilization of MWPA is agriculture. In view of this, in the present review we will discuss possible ways of practical use of MWPA as fertilizers, as nutrition additives for animal husbandry, and against cotton wilt.

Use of MWPA as Fertilizers

Nowadays, one of the most important tasks in agriculture is the increase of productivity of agriculture with simultaneous preservation and reproduction of the soil fertility [54, 55]. As follows from the world agricultural experience, the solvation of this problem requires, along with the use of local organic fertilizers (manure of agricultural animals, guano, compost, straw, green manures and plant residues), a wide use of non-traditional sources of organic compounds [56–58]. One of additional resources of different organic compounds finding application as fertilizers is the use of wastes of microbiological production of drugs, in particular, MWPA. In connection with this, comprehensive agrochemical and ecological assessment of the use of MWPA is required. Thus, chemical composition and physico-chemical properties of MWPA were investigated in reviews [59, 60], the coefficients of the use of nutrition elements when applying fertilizers prepared by using MPWA were calculated, and possible effect of MWPA on the expansion and development of diseases of agricultural crops was assessed.

Different groups of researchers suggested rather simple schemes for primary treatment of MWPA in order to prepare fertilizers, which include the use of mineral acids, accelerated filtration of the reaction mass by using perlite and neutralization of the obtained aqueous filtrate used as a fertilizer [56, 61, 62]. As a result of the performed comprehensive study, was obtained the organo-mineral mixture using mycelial wastes from the penicillin and streptomycin production, which was used as a fertilizer for a number of grain and vegetable cultures [63]. The author has shown that the use of the proposed organo-mineral mixture leads to a substantial increase of the crop capacity of barley, winter rye, cabbage and tomatoes. Besides, it was shown that the use of organo-mineral mixture did not lead to the increase of heavy metal content in the target grain cultures, decreased the littering of crops and harmfulness of most spread diseases of winter rye (snow mold) and barley (root rots).

Widespread in recent years has been the utilization of industrial organic wastes, including MWPA, by composting [56, 57, 64]. Composting can be performed in aerobic or anaerobic conditions, both in open ground compost pits and using mechanized lines. The final compost product contains most stable organic compounds, products of decomposition, lysed microorganisms and the products of reactions of various components. In invention [65], the primary compost used as a biologically active additive and moisture absorbent was prepared on the basis of mycelial wastes with addition of the carrier of compost microorganisms, for example, manure of agricultural animals, and material absorbing extra moisture: peat, sawdust or straw. The additives to the treated mycelial wastes of gentamicin are introduced to keep the humidity not higher than 75%, the obtained mixture is then actively mixed, and further processing of these wastes to compost is carried out at the temperature of ambient air from 20 to 30°C till the formation of the final product used as an organic fertilizer.

Various complex technological schemes for utilizetion of MWPA were worked out based on their primary treatment with chemical reagents or using methods of bioengineering [66–68]. The effect of fertilizers obtained on the basis of MWPA on the agrochemical properties and enzymatic activity of turf-podzol soils was analyzed and a substantial increase of crop capacity of agricultural products grown on them was shown.

Use of MWPA in Animal Husbandry as Nutrition Additives

As was mentioned above, MWPA is a rich source of proteins, carbohydrates, lipids and aminoacids, that makes it quite acceptable to use them as nutrition additives for animal husbandry. However, direct application of MWPA in animal husbandry is difficult because of residual content of antibiotics reaching from 500 to 20000 antibiotics activity units per 1 g of dry substance [8, 16, 56, 57]. Feeding of such MWPA to animals and birds may cause accumulation of antibiotics in organs and tissues. The use of this meet in people dietary may cause allergic diseases, violation of microflora of the alimentary canal (appearance of resistant bacteria) and other side effects. In inventions [71, 72], for removal of residual antibiotics from MWPA was suggested to treat them with 5–25% of organic additive containing manure worm *Eisenia foetida*. As an organic additive, manure of agricultural animals, straw, sawdust or plant foliage can be used. The authors had shown that such a treatment of MWPA led to complete utilization of residual amounts of antibiotics in these wastes. Moreover, by the chemical composition (for example, the content of humus) the mycelial wormcompost exceeds the manure of agricultural animals. It is known that a high percentage of humus in compost results in an increase of the content of total nitrogen and phosphorus [54, 55]. Thus, microfield experiments on onion and radish showed that applying of mycelial wormcompost increases the yield of dry mass of spring onion and radish as compared to manure of agricultural animals by 1.5–2 times.

Bulgarian researchers described the use of protein hydrolyzate isolated from mycelial wastes of a number of antibiotics [73] as well as of dry mycelium treated with mineral acids [74], as additives to animal nutrition. Modern methods of processing of MWPA allowing to obtain nutrition additives for animal husbandry, are discussed in monograph [64]. In [75, 76] it was suggested to use as a nutrition additive the spent mycelium of the producent *Streptomyces avermitilis-56* formed in the production of avermectins. It was found that the spent mycelium of this producent is practically innocuous for feeding agricultural animals, contains biologically active compounds and shows a positive effect on the factors of natural resistance of animals. The spent mycelia from the production of benzylpenicillin and levorin, dried by special technology to humidity of 4–6%, contained all original nutrition components (proteins, lipids, carbohydrates, vitamins) and were used as fodder for fur-bearing animals in fur-breeding farms [77].

Use of MWPA Against Cotton Wilt

Cotton wilt is a tracheomycosis disease by fungi imperfecti *Verticillium dahliae* (verticillium wilt) and *Fusarium oxysporum* (fusarium wilt) [78]. The pathogen is developed in the soil, penetrates into the plant through roots and is spread in the xylem water transportation system. In both cases the disease is expressed in damage of the water transporting system of the plant, losing of turgor in tissues, darkening and thrombosis of xylem vessels, turning the leaves yellow and, finally, withering of the plant. This leads to the fact that the wilt-infected cotton either gives no crop or its quality is drastically decreased [78, 79]. To date, a whole complex of measures against cotton wilt is worked out, including selection of wilt-resistant cotton growths, cleaning of soil from wilt pathogens by the use of rational crop rotation and land management, applying of organic fertilizers activating the development of saprophytic microbes and fungi antagonistic to cotton wilt pathogen [80]. In recent years, application of MWPA against cotton wilt became very promising. In joint studies of Chinese and Israeli scientists it was suggested to use the spent mycelium *Penicillium chrysogenium* from penicillin production [81–86]. For tests, the spent dry mycelium of this antibiotic obtained after drying of the mycelial mass at 110°C for 4 h was used; such a treatment allows to obtain dry mycelium in the form of dry powder containing no penicillin. Besides, water extract was obtained from the spent dry mycelium of penicillin production, which was suspended in distilled water, stirred for 2 h, kept for 24 h at room temperature, filtered off the solid residue, stored as 10% solution at 4°C and used for the experiments during two week [83–85]. It was demonstrated experimentally that the spent dry mycelium of penicillin production and its water extract not only cause the resistance of cotton to pathogens of wilt *Verticillium dahliae* Kleb and *Fusarium oxysporum f. sp. vasinfectum*, but also showed a growth-regulating effect [81–86]. It was found that the water extract of the spent dry mycelium of penicillin showed more higher level of resistance to pathogens of cotton wilt [83, 84].

Use of MWPA in Building Industry

Wide use of the wastes of antibiotics production, in particular, spent mycelial sources, in different fields of industry and, first of all, building industry, allows to develop schemes of wasteless production and reduce the level of environmental pollution [8–11]. The analysis of chemical composition of MWPA showed, that the presence in them of chemical compounds traditionally used in building industry allows a wide use of such wastes as plastifying additives to concrete mixtures [87, 88]. The plastifying effect of MWPA in most cases is due to the presence in them of aminoacids and carbohydrates. A positive factor promoting the plastifying effect of MWPA is also the presence in them of inorganic compounds: chlorides, nitrates, phosphates and sulfates of sodium, potassium and calcium, which quicken hardening and increase strength of most of building materials on the basis of Portland cement. However, not always the presence of residual carbohydrates in MWPA has a positive effect on complex and multistep processes of hydration and hardening of mineral astringents [87, 88]. In most cases is it connected with absorption of carbohydrates on the particles of non-hydrated cement and lime, which for some time prevents their contact with water. A high non-uniformity of the component composition of MWPA, in particular, a large variation of the content of carbohydrates, is due to fluctuations of microbiological synthesis [9, 11, 27, 30]. It is known that biosynthesis is characterized by a number of simultaneously occurring reactions; as a result, the degree of completeness of the processes of fermentations and realization of optimal yield of the target product are not always the same, which causes variations of the component composition of MWPA [89]. The authors believe that the simplest way to increase the uniformity of MWPA is to group the portions of MWRA from a specified number of biosyntheses of antibiotics, which allows achieve a suitable system of averaging of the component composition, which, in turn, would level out the errors of separate fermentations [87, 88].

A group of researchers has studied the effect of complex additives consisting of a mixture of spent mycelium of the producent of penicillin with calcium chloride and finely pounded chalk when introduced in concretes [90, 91]. It was shown that mycelial masses have a plastifying effect on concrete and increase its strength; in doing so, calcium chloride is an accelerator of hardening, while the chalk particles act as artificial centers of crystallization. The use of spent mycelium of the producents of monomycin and neomycin allows to improve the quality and operating characteristics of concretes [92]. The use of spent mycelial masses of oleandomycin, levorin and tetracycline for concrete production allows to reduce the cement consumption by 7–10%, to improve the laying of concrete mixtures, to prevent them from separation into layers upon transportation and to increase frost-resistance of concretes [93]. In [94] the results are given for the tests of mycelial wastes of the production of antibiotics heliomycin, nystatin, fusidin, oleandomycin and tetracycline in the production of kilning building materials. It was shown that the use of MWPA for production of keramzite allows to completely refuse from acutely deficient additives on the basis of oil products. The use of MWPA in production of agloporite road metal allows to reduce the consumption of coal and wood sawdust up to 50% in volume.

One of the most important tasks of the building industry is not only to increase the total volume of produced materials but also to expand their assortment [95, 96]. At the same time, in view of reduction of non-renewable natural resources used for production of different building materials, a search for new raw materials is required [97–99]. Promising sources for this can be large-scale organic wastes formed in different fields of industry, including MWPA. After systematic studies on the search for new raw materials for production of building materials effective plastifying additives to cement systems were obtained based on the method of hydrolytic destruction of mycelial wastes of penicillin production [100–103]. These plastifying additives were used in industrial and civil building for production of monolite blocks as well as assembling concrete and reinforced concrete constructions. Besides, on the bases of mycelial wastes of penicillin production an ecologically friendly and effective foam forming agent was obtained, and autoclave-free foam concretes and dry building mixtures for production of cellular concretes with improved physico-mechanical properties were designed [104]. It was found that foam forming agents prepared by the use of MWPA provided an increased stability of the foam, reduced the density of foam concrete and its thermal conductivity without deterioration of strength characteristics [105, 106]. A promising direction of the use of mycelial wastes of penicillin production is also their application in the production of wood pulp plates, widely used in building industry [107]. A new astringent for production of wood pulp plates was elaborated, which led to a substantial increase of their strength and a decrease of swelling. Interesting results about the preparation of setting retarder for gypsum and gypsum articles with the use of MWPA are described in [108].

Preparation of Adsorbents on the Basis of MWPA and Their Use for Sorption of Different Metal Ions

Preparation and the use of adsorbents (or biosorbents) obtained on the basis of MWPA allows to solve a number of ecological and practically useful tasks, in particular: (1) utilization of wastes of microbiological production of antibiotics; (2) extraction of precious metals (gold, silver and platinum metals) from different industrial solutions; (3) processing of sewage wastes containing toxic metal ions.

Use of MWPA for Preparation of Biosorbents

Taking into account a large variety of different formed MWPA and, hence, of the methods of their utilization, researches were performed to determine the expediency of preparation of adsorbents, as another way of utilization of spent mycelial masses [8, 109, 110]. In [109], the complete technological cycle for preparation of the adsorbent by the use of mycelial wastes of penicillin production was described. Preliminary, the humidity of mycelium was reduced from 84 to 54% by stepwise drying, which favored better granulation. Proper carbonization, that is, complete removal of volatile components from the formed granules, is determined by drying at fixed temperatures. Thus, in the first stage (from 20 to 360°C) the heating of granules was performed with the rate 2–7°C/min in the course of 126 min, while in the second stage (above 360°C) characterized by occurring the process of coke formation, the rate of heating was reduced to 1.5°C/min. Such a regime of the process of carbonization allowed to obtain the maximum possible strength of the carbon carcass of the adsorbent. In the last stage of preparation of the adsorbent, when the temperature in the reactor reached 500°C, activation was performed by introduction of water vapors as an activating agent into the reactor. Thus were obtained strong samples of adsorbent on the basis of spent mycelium of penicillin production with fairly high adsorption capacity [109]. Of large practical interest is activated charcoals production using MWPA. With this aim, a group of researchers worked out the technology of production of activated charcoals using mycelial wastes of tetracycline production and carbonic residue obtained by pyrolysis of used tires [110]. The obtained granulated activated charcoal MAU-5 was used for processing of sewages from antibiotics production and was not inferior to the standard activated charcoal BAU-B in adsorption of organic compounds.

Use of Biosorbents for Extraction of Precious Metals

Nowadays, large volumes of solutions with low content of silver are accumulated: washing and sewage waters from watch and jewelry plants, worked out solutions from photo and cinema industry, sewages of electronic and electrotechnical industry, from which this noble metal practically is not extracted because of low economic profitability of the processing methods [111–113]. On the other hand, in most cases, in isolation of costly metals from wastes the yield and degree of extraction of the target product is much higher than when using the primary raw material, since the process includes less number of steps, the energy consumption is substantially reduced, as well as industrial areas and areas allotted for dumps [114–116]. In connection with this, elaboration of a highly efficient and economic technology for extraction of silver from industrial solutions using cheap and readily available MWPA and biosorbents on their basis is an art-of-the-state task. Thus, the group of researchers obtained biosorbents on the basis of mycelial wastes from production of lincomycin, gentamicin, neomycin, ristomycin, levorin, penicillin and fusidin, the use of which allowed processing of industrial wastes of silver production, and the degree of extraction of silver was 93% [117]. The effect of physico-chemical parameters of adsorption on the degree and selectivity of extraction of silver from the model and industrial solutions was studied, the mechanism of isolation of silver from the solutions was suggested and the areas of silver localization in biosorbents were determined [117–119]. On the basis of studying the kinetics and mechanism of the process of adsorption/desorption adequate mathematical models for governing the processes of batch and continuous extraction of silver from industrial solutions were created [120]. In this invention, the dried mycelial masses of the production of neomycin, gentamicin and lincomycin were used, allowing selective adsorption of silver from industrial solutions, in which the content of this noble metal was 50–150 times less than the content of impurity metals copper, nickel and zinc [121]. Metal dissolving ability of MWPA was studied in the experiments with size gold extracted from non-industrial field sand pebble deposits [122]. The best results were shown when using mycelial wastes from rifamycin, ristomycin and sisomycin production; the gold concentration in the solution was 1–2 mg/L. Principal schemes of adsorption of platinum metals with the use of MWPA and spent native solutions of the antibiotics production are given in monograph [113].

Processing of Sewages Containing Toxic Metal Ions

The use of biosorbents prepared from mycelial wastes of production of erythromycin, neomycin, penicillin and rifamycin for sorptive extraction of uranium from industrial solutions was described [123, 124]. It was shown that the process is most effective when hydroxyapatite is added to the obtained adsorbents.

Chromium Cr(VI) compounds are known to be not only highly toxic and carcinogenic, but are also strong oxidants and may cause heavy lesions in humans even after short-term action [125, 126]. Sewages containing Cr(VI) compounds are formed in technological processes on mechanical engineering and metal-working enterprises, where chromic acid is used for etching, passivation, as well as for application of electrochemical coatings and electropolishing of steel articles [127]. Biosorbents on the basis of MWPA were obtained by different groups of researchers and successfully used for adsorption of chromium ions Cr(III) and Cr(VI) from sewages of galvanic and engineering productions [128–131]. Biosorbents obtained on the basis of MWPA were also used for sorption extraction of cerium [132], cadmium [133], lead [133, 134], zinc [135], mercury [134, 136], nickel, cobalt and copper [137, 138] from industrial sewage wastes.

Use of Hydrolyzates of Proteins, Lipids, and Aminoacids Prepared on the Basis of MWPA

Taking into account a high material index typical for drug-producing enterprises (from 9 to 180 kg/kg of production), the prospective of the use of hydrolyzates of MWPA as a component of culture media for production of antibiotics looks very promising both from the viewpoint of releasing and economy of large amounts of expensive and deficient raw materials (corn extract, sperm whale fat, hydrolyzate of casein and soya flour) and from the viewpoint of solvation of a number of acute ecological problems, related with utilization of large-scale wastes [8–11, 26–28, 139].

Different methods of hydrolysis of the peptide-containing materials are known, the highest degree of splitting of the peptide bonds is achieved in acidic hydrolysis [140, 141]. However, the biological value of the formed hydrolyzates is sometimes low because of complete destruction of vitamins, racemization of sugars and partial destruction of aminoacids, especially tryptophan. A number of scientific groups were involved in researches in order to prevent the acidic destruction of practically valuable components of MWPA. Thus, it was shown that the enzyme hydrolysis of mycelial wastes of tetracycline produc-tion with the use of industrial alkaline proteinase protosubtilin G10X allows to obtain peptide hydrolyzates with the content of aminoacids of 96–108 mg/1 g of mycelial wastes [142]. The obtained hydrolyzates can be used as components of culture media for growing microorganisms. Besides, a rather high content of aminoacids allows to use hydrolyzates also as a starting material for preparation of individual aminoacids or their mixtures. A new culture medium was elaborated, containing as a source of nitrogen the enzyme hydrolyzate of mycelial wastes of tetracycline production in the amounts from 0.02 to 0.04 g/L on the amine nitrogen [143, 144]. The use of this medium in the process of biosynthesis of tetracycline allowed to completely exclude corn extract from the composition of the medium and to increase the yield of tetracycline by 5–25%. Similar culture media for microbiological synthesis of antibiotics were elaborated on the basis of peptide hydrolyzates obtained from mycelial wastes of production of macrolide antibiotics erythromycin [145] and oleandomycin [146], as well as aminoglycoside antibiotic tobramycin [147, 148].

Preparation of Glue Compositions with the Use of MWPA

MWPA is known to contain proteins and polycarbohydrates, which are traditionally used as a basis for preparation of glues [149–151]. However, reactive groups of these polymers exist in the molecules in the bound state and cannot participate in the interaction with the surfaces of sticked objects [152]. To increase the adhesive properties of MWPA they were modified in order to make the functional reactive groups more accessible. Modification of MWPA was performed by the use of 2–12% solutions of hydrochloric acid and sodium hydroxide in the course of 4 h [153, 154]. For preparation of glue, a low-molecular fraction of hydrolyzate of dextran was used, which is a waste of microbiological production of blood substitutes, to which plastificatores, antiseptics, cross-linking agents and mycelial wastes of penicillin production were added in different ratios. The tests showed that the use of the so modified spent mycelium from the production of this antibiotic, luthern water and low-molecular fraction of dextran allows to obtain glue compositions which by their physico-chemical properties are not inferior than dextrin glue and have lower cost price [155]. The best glue compositions were shown to have the strength of gluing of 100 MPa for gluing wood and 1.5 N for gluing paper. Besides, the modified mycelial wastes of the penicillin producent can be used as an additional raw material in the production of bone glue [156]. The so prepared compositions were used for production of glue strip on a paper support and for gluing wood and paper. The tests have shown that the use of the modified spent mycelium of penicillin production as an additive to bone glue would reduce its cost price by 20–30% [153, 154].

Miscellaneous Routes of Practical Use of MWPA

A group of authors proposed to use spent mycelial wastes of production of penicillin, tetracycline and rifamycin as reagents for modification of clay-lime components of potassium ores in order to substitute the expensive derivatives of carboxymethylcellulose, which are used in manufacturing of potassium fertilizers [157]. Mycelial wastes of neomycin and erythromycin production treated with mineral acids (sulfuric, nitric or hydrochloric) can be used for neutralization of industrial sewages as well as for removal of poorly soluble phosphates [158]. Indian researchers have shown that the use of MWPA as an additive to culture medium in the microbiological process of ethanol production led to the increase of the yield of the target product [159]. In [160, 161], the possibility of using MWPA for manufacturing of rubber technical articles was shown. Combination of MWPA with suspensions of caoutchoucs (latexes) in the presence of a softener a highly filled polymer product was obtained called as a bioelastic material.

It is known that as foam extinguishers in microbiological production of antibiotics vegetable and animal fats as well as synthetic analogues of lipids are used [9, 11, 28–30, 36]. Lipids isolated from mycelial wastes of oxytetracycline and fusidin production have been successfully used as foam extinguishers in the process of fermentation of these antibiotics [162]. The performed tests have shown that lipids isolated from MWPA are good substitutes of natural fat and do not decrease the yields of antibiotics as compared to the enzymatic processes in which animal fat or synthetic foam extinguisher were employed. Interesting results were obtained on elaboration of the technology of chitin-glucan complex isolated from MWPA [163]. On the basis of the chitin-glucan complex, adsorbents were obtained, which found application for clarifying and sterilizing filtration of biological liquids [164, 165]. Very promising are the studies connected with the possibility of production of fuels on the basis of MWPA. Thus, the principal possibility was shown for the use of mycelial wastes of neomycin production as a carbon-containing raw material, which by its physicochemical characteristic is comparable with heavy oil (mazuts) [166]. Preparation of fuel components was described on the basis of a number of MWPA isolated by means of special technology based on their stepwise pyrolysis [167].

Invention [168] reports the use of mycelial sources from the production of antibiotics of penicillin series for refining of spent mineral oils, in particular, transformer oil. This invention can be used on oil-refining and regeneration plants in different fields of industry. It is known that for mechanical engineering and motor-building different lubricating oils are widely used. Of special importance for improving the properties of lubricating oils is the search for, and the use of chemically active compounds called additives [169, 170]. We have studied the possibility of the use as additives to lubricating oils the mycelial wastes of antifungal antibiotics levorin, nystatin, mycoheptinum, amphotericin B and griseofulvin [171]. It is known from the literature, that the additives used for improving the lubricating oil properties are divided to anti-friction, anti-wear and extreme pressure additives [172–174]. Most of anti-wear and extreme pressure additives contain sulfur, phosphorus and halogens. The elemental analysis has shown that mycelial wastes of production of antifungal antibiotics levorin, nystatin, mycoheptinum, amphotericin B and griseofulvin contain 5.25–7.43% of phosphorus, 1.36–2.07% of chlorine and 2.57–3.89% of sulfur [171]. The tests carried out in comparison with the known additives DF-11 and triallylphosphite have shown that the search for additives to lubricating oils among MWPA products is a promising direction of their use in mechanical engineering and motor-building.

Therefore, the directions of practical use of MWPA elaborated during the two last decades are characterized by a wide range of applications, high efficiency and relative simplicity as well as low cost of apparatus-technological solutions. A state-of-the-art task of microbiological production of antibiotics is to work out multipurpose low-waste biotechnological processes which would allow to more effectively use the material after the fermentation not only for preparation of antibiotics but also with the aim of maximum utilizetion of wastes, first of all MWPA, thus providing a substantial increase of technical-economic indices and improving of ecological aspects of industrial production of these drugs very important for public health.

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