PERIÓDICO TCHÊ QUÍMICA
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AVALIAÇÃO DAS PERSPECTIVAS DE ESTUDAR E USAR COGUMELOS DO AZERBAIJÃO COMO PRODUTORES EFICAZES DE SUBSTÂNCIAS BIOLÓGICAMENTE ATIVAS

ASSESSMENT OF THE PROSPECTS OF STUDYING AND USING MUSHROOMS OF AZERBAIJAN AS EFFECTIVE PRODUCERS OF BIOLOGICALLY ACTIVE SUBSTANCES

ОЦЕНКА ПЕРСПЕКТИВЫ ИЗУЧЕНИЯ И ИСПОЛЬЗОВАНИЯ ГРИБОВ АЗЕРБАЙДЖАНА КАК ЭФФЕКТИВНЫХ ПРОДУЦЕНТ БИОЛОГИЧЕСКИ АКТИВНЫХ ВЕЩЕСТВ

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RESUMO

Na pesquisa realizada, os macromicetes xilotróficos foram pesquisados como produtores potenciais de substâncias ativas biológicas usadas hoje em dia para diversos fins nas práticas mundiais que se espalham no Azerbaijão e algumas de suas características (atividade biológica de metabólitos sintetizados, toxicidade, atividade antimicrobiana) dinâmica da formação de biomassa.). Ficou claro que fungos como *Ganoderma lucidum* (Curtis) P. Karst., *Laetiporus sulphureus* (Bull.) Murrill, *Pleurotus ostreatus* (Jacq.) P. Kumm, *Schyzophyllum commune* Fr e *Trametes versicolor* (L.) Lloyd consideravam uma perspectiva O produtor de substâncias ativas biológicas está amplamente espalhado nas florestas do Azerbaijão, e algumas delas são até espécies dominantes de xilomicobióticos inerentes à natureza do Azerbaijão. Como resultado de estudos com cepas isoladas desses fungos, foi demonstrado que, tanto na solução de cultura (CS) quanto nos micélios vegetativos (VB), existem metabólitos com atividade biológica. O resultado da pesquisa também ficou claro que a atividade antimicrobiana da SC em todos os casos é maior do que nos extratos de água ou álcool da biomassa seca (1,1-1,2 vezes), embora defina a atividade biológica geral dos extratos de VB para a relação de *Paramecium caudatum* dá um efeito de aumento mais alto. Além disso, as cepas ativas selecionadas não ficam atrás das cepas conhecidas em termos da quantidade de biomassa formada (até 8,7 g/l em 7 dias) e manifestações de formas de atividade biológica. Isso fornece uma base séria para realizar a produção de substâncias biologicamente ativas para finalidades diferentes (alimentos, rações, medicamentos e outras) em sua base.

Palavras-chave: *substâncias biologicamente ativas, macromicetes xilotróficos, biomassa, efeitos tóxicos, atividade antimicrobiana*.

ABSTRACT

In the carried out of the research, Xylotroph macromycetes have been researched as a perspective producer of bıologıcal actıve substances used for various purposes today in world practice which spread in Azerbaijan and some of their features (the biological activity of synthesized metabolites, toxicity, antimicrobial activity and dynamics of biomass formation). It became clear that fungi such as *Ganoderma lucidum* (Curtis) P. Karst., *Laetiporus sulphureus* (Bull.) Murrill, *Pleurotus ostreatus* (Jacq.) P. Kumm, *Schyzophyllum commune* Fr and *Trametes versicolor* (L.) Lloyd considered as a perspective producer of bıologıcal actıve substances is widely spread in the forests of Azerbaijan, and some of them are even dominant species of xylomicobiot inherent in the nature of Azerbaijan. As a result of studies with isolated strains of these fungi, it was shown that

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both in the culture solution (CS) and in the vegetative mycelia (VB), there are metabolites with biological activity. The result of research also became clear that antimicrobial activity of CS in all cases is higher than in water or alcohol extracts of dry biomass (1,1-1,2 times), although it defines the overall biological activity of VB extracts to the relationship of *Paramecium caudatum* gives a higher increase effect. In addition, the selected active strains do not lag behind the known strains in terms of the amount of biomass formed (up to 8.7 g/l in 7 days) and manifestations of forms of biological activity. This gives a serious basis to realize the production of biologically active substances for different (food, feed, medical and other) purposes on their basis.

Keywords: *biologically active substances, Xylotroph macromycetes, biomass, toxic effects, antimicrobial activity*.

Резюме

В ходе работы ксилотрофные макромицеты были исследованы как перспективный продуцент биологически активных веществ, используемых сегодня для различных целей в мировой практике, которые распространены в Азербайджане, и некоторые особенности (биологическая активность синтезируемых метаболитов, токсичность, антимикробная активность и динамика образования биомассы) их. Стало ясно, что такие грибы, как *Ganoderma lucidum* (Curtis) P. Karst., *Laetiporus sulphureus* (Bull.) Murrill, Pleurot us ostreatus (Jacq.) P. Kumm, *Schyzophyllum commune* Fr и *Trametes versicolor* (L.) Lloyd является перспективные продуценты биологически активных веществ и широко распространен в лесах Азербайджана, а некоторые из них являются даже доминирующими видами ксиломиобиот, присущими природе Азербайджана. В результате исследований с выделенными штаммами данных грибов было показано, что как в культуральном жидкости(КЖ), так и в вегетативном мицелии (ВМ) присутствуют метаболиты с биологической активностью. В результате исследований также выяснилось, что антимикробная активность КЖ во всех случаях выше, чем в водных или спиртовых экстрактах сухой биомассы (в 1,1-1,2 раза), хотя она определяет общую биологическую активность экстрактов ВМ по отношению *Paramecium caudatum* дает более высокий эффект увеличения. Кроме того, отобранные активные штаммы не отстают от известных штаммов по количеству образующейся биомассы (до 8,7 г/л за 7 дней) и проявлениям форм биологической активности. Это дает серьезную основу для реализации производства биологически активных веществ различного (пищевого, кормового, медицинского и др.) назначения на их основе.

Ключевые слова: биологические активные вещества, ксилотрофные макромицеты, биомассы, токсигенность, антимикробные активности

1. INTRODUCTION

Fungi one of the valuable sources of biologically active substances and these substances synthesized by them have serious perspectives to obtained the healing nutrients products and pharmacologically active preparations (Cao *et al*., 2018, Muszyńska *et al*.,2018, Sum Winnie *et al*., 2019, Sharif *et al*., 2018) . Mentioned above encountered in the vegetative mycelium of fungi, as well as in the fruits bodies formed in natural conditions (Millar *et al*., 2019, Stadler and Hoffmeister, 2015, Sułkowska-Ziaja K. *et al*., 2018). Although the number of fungi species that can form macroscopic fruits is about 14,000 (Chang, 2006), according to literature, their 2,000 are edible and 700 important as medicine (Jilinskaya, 2015).

In natural conditions, the fruity body (FB) formed by the fungi is either one-year or perennial (Bondartseva, 1998), and their reserves are limited and cannot be reached all year round. On the other side, the deterioration of the ecological situation causes fungi to contain substances that are dangerous to human health(Kokkoris *et al*., 2019), which limits the use of FB formed in the natural environment. The above-mentioned shortcomings are possible to overcome using strains taken to pure culture from FB of fungi.

Xylotropic macromistates that combining a group of fungi known to science and form macroscopic FB is one of the most widely studied objects in recent years (Alıyeva, 2019, Cör, Knez, and Knez Hrnčič, 2018, Rahi and Malik, 2016) , which is due to the fact that they are attract attention as a prospective producers (Baeva *et al*., 2019, Gargano *et al*., 2017, Taofiq *et al*., 2017)of substances used for food, feed, medical, as well as technical purposes (leather, detergent and cleaning powders, insulating materials and so on. products). A number of researches (Osinska-Jaroszuk *et al*., 2015, Ugbogu *et al*., 2019, Kryczyk-Poprawa *et al*., 2019, Wu *et al*.,

2019) have shown that their use for these purposes are ecologically safe (Ritota and Manzi, 2019, Wan and Li, 2012), economically affordable (Grimm and Wösten 2018), technically easy and even some results have already reached the production level(Sekan *et al*., 2019). Interestingly, results reached to the production level covers almost all of the above-mentioned áreas (Gehlot and Singh, 2018).

The number of fungi considered to be promising in the industry or in scientific researches is too small compared with the species known to science, and the usefulness or significance of some fungi for medicinal or for some purpose is to determine in results of general use in folk medicine or in episodic research.

The Xylotropic macromistates have been widely spread in the territory of the Republic of Azerbaijan, and the number of species registered in researches up to date is more than 200 (Akhundova, N.A. *et al*., 2019, Alıyeva, 2019, Garayeva, 2017). Among them also are encountered species like as *Ganoderma lucidum*, Laetiporus sulphureus, Lentinus eddodes, Pleurotus ostreatus, Schyzophyllum commune, *Trametes versicolor* that are used on an industrial scale for different purposes in world practice (Hapuarachchi *et al*., 2018, Hyde *et al*., 2019, Özdal *et al*., 2019, Saltarelli *et al*., 2015), as well as in the stage of study as promising producers. İn Azerbaijan is also encountered researches fungi registered as producers of BAS, and the main focus of research in this direction is focused on the perspective of their produces of hydrolase and oxidases (Musayeva, 2019). In recent times also is encountered research materials directed to the study of some fungi as a producer of polysaccharides (Muradov *et al*., 2018). The vast majority of Xylotrophic fungi known in Azerbaijan as well as in the world were not only poorly studied as BAS producers, many of them have not been involved in this study.

On the other side, researches have shown that quantitative indicator of ability to synthesize these or other BAS of separate strains belonging to the same species of fungi changes even at the level of strain (Bandara *et al*., 2019, Rahi and Malik, 2016, Zhou *et al*., 2016). This allows noting the ability to find more efficient strains of known species spreading in a particular region, which allows noting that new research in this direction in Azerbaijan is actual.

The purpose of this study is to study the possibility of effective biotechnological use of Xylotrophic macromycetes living in the natural forests of Azerbaijan as potential producers of biologically active substances, by preliminary assessment of their antimicrobial activity, their lack of metabolites with toxic action, as well as studying the dynamics of grow their biomass in culture.

2. MATERIALS AND METHODS

As an objects of the research were used strains belongs to the selected FB of fungi such as *Ganoderma lucidum*, Laetiporus sulphureus, *Pleurotus ostreatus* and *Schyzophyllum commune* collected from the different areas of Azerbaijan (Azerbaijan part of the Greater Caucasus - GC, Small Caucasus - SC, Hirkan National Park - HNP, Kura-Araz lowland - KA).

Collection of FB, primary description of the body fetus in the field, identification, taken to the pure cultures from MC, as well as the cultivation of fungi were carried out according to known methods (Bondartseva, 1998, Handbook of Mycological, 2006, Ko Y-F. *et al*., 2017, Netrusov *et al*., 2005) and those used in our previous work (Akhundova *et al*., 2019, Muradov *et al*., 2018).

To evaluate the germination process has been used a nutrient environment, which composition was as follows: (g/l): Carbon source (depending on the purpose, mono-, di-, poly-saccharides, wheat bran, wood crumbs, and others) – 10, peptone - 3, NH_4NO_3 -1,5, $MgSO_4x7H_2O$ – 0,5, NaCl – 0,5, KH_2PO_4 – 0,4. Sterilization condition is 0,5 atm, 0,5 hr. Environment after sterilization pH = 5,6.

The amount of formed biomass has been identified, bringing it to the permanent weight at the 105^0C and was expressed with g/l.

As a source of BAS has been used both culture solution (CS), as well as from the formed vegetative biomass (VB) of fungi. During the use of VB, biomass has been researched extracted separately with water (WE_1) and alcohol (AE_2). The extraction of mushroom materials was carried out according to the method specified in the work of Alvarez *et al*. (2014).

The toxicity of the biologically active metabolites obtained from solutions (CS, WE_1, and AE_2) has been clarified in relation to Tetrahymena pyriformis (a ciliate protozoan) and at the same time, was used from apparatus of BioLaT-3 and a computer with software AutoCiliataXP (Jilinskaya, 2015). For this, into the outside circle of the device's tablet are added 10 µl infusor culture and 0,5 ml of the tested solution as control was used as the primary nutrient medium. After 24 hours, the activated BioLaT-3 device was carried out counting of cells.

The assessment was carried out (Table 1) in accordance with the following main criteria (K_1 and K_k), which, for its calculation, was used from such as:

$$K_1 = N_2 / N_1 K_k \quad \text{(Eq. 1)}$$

$$K_k = N_{1k} / N_{2k} \quad \text{(Eq. 2)}$$

In equations 1 and 2, the N_1 and N_{1k} are the number of infusors in the samples and in the control, respectively, before exposure, N_2 and N_{2k} are the number of infusors in the samples and in the control, respectively, after exposure.

Bactericidal and fungicidal properties have been identified based on the ability growth of test cultures (Bhalodia and Shukla, 2011; De Lira Mota *et al*., 2012). Thus, the fungicidal activity was determined based on the amount of biomass taken from the test cultures (*Candida albicans*, *Aspergillus fumigatus, A.niger, Fusarium oxysporium and Penicillium cuclopium*), the bactericidal activity was determined based on the optical density of the cultured solution obtained from test cultures (*Bacillus subtilis, Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa*) during cultivation, compared to control.

All experiments were performed in 4 replicates and all the data were statistically analyzed (Kobzar, 2006). For processing, the following equation 3 was used:

$$m / M = P \leq 0.05 \quad \text{(Eq. 3)}$$

In Equation 3, M is the average repetition rate, m is the standard deviation, and P is the Student criterion.

3. RESULTS AND DISCUSSION:

The Republic of Azerbaijan belongs to the less forested countries, and only 10,4% of its territory is covered with forests, 85 % of which is mountain and 15 % plain forests (Mamedov and Khalilov, 2002). The main trees in these forests are oak, beech, and hornbeam. This and other trees (for example, ash-tree, iron tree, lime, different fruit trees) spread in our forest at the same time is characterized as settlements and feeding places of fungi, primarily Xylotropic macromyxes. Therefore, firstly xylomyobiota of trees participating in the formation of natural forests located in ecologically different areas of Azerbaijan were evaluated according to the use of fungi in the world practice as a producer of BAS or for use in production. It has become clear that most of the xylotroph macromycetes used today as BAS producers for different purposes are found in the forests of Azerbaijan, and some of them are even dominant species of xylomicobiot inherent in the nature of Azerbaijan (Table 2).

As seen, today, among the most promising mushrooms in the world, only İnonotus obligus (Fan *et al*., 2012; Géry *et al*., 2018) are not found more accurately not before us, not in our research this mushroom was not registered. Analog thought can be said about L. eddodos (Bisen *et al*., 2010). It is true that preparations (those with pharmacological activity) taken from İ.obligus fungi are obtaining from its sterile FB (reproductive part, which the hemanophore layer does not develop), although has been noted that the drug "Befungin" taken from it has a severe effect on tumor diseases its use today for this purpose is not so useful (Jilinskaya, 2015). Other fungi are currently studied as a promising producer of both intensive cultivation and producer of BAS.

Fungi as a producer of biologically active substances used for the production of various preparation on an industrial scale, as well as promising serious prospects in this direction (Gargano *et al*., 2017, Muszyńska*et al*. 2018) are widely spread. Although all of the registered fungi by the distribution on the substrate are euritroph, different from each other by remaining features, this diversity gives itself both in their growth, as well as in the quantitative indication of biological activity of the metabolites they synthesize, which is confirmed with data presented below.

It should be noted that the mycelium of Xylotrophic macromycetes in the vegetative growth phase also has biological activity (Nikitina *et al*., 2017), for this reason, their strains which have fast growth rate, more precisely forms more biomass is considered most promising. For this reason, first of all, it has been evaluated fungi strains taken to the pure culture by these aspects. From the results became clear that the biomass of fungi formed during cultivation in the liquid nutrient medium different in quantity, and this distinction is also observed between strains belonging to the same species (Table 3). As seen, by formation biomass, the highest indicator belongs to the strains of Sch.commune and the minimal to the L.sulphureus. Taking into consideration the likelihood of biosynthetic activity and formed metabolites of each fungus that has different activity and characteristics for further research, it was considered appropriate to select one active strain of each species, namely those forms more biomass.

İn studies have also been conducted optimization of medium for selected strains such as G.lucidum AS-4, L.sulphureus AS -7, P.ostreatus AH-12, Sch.commune AH -17 and T.versicolor AN -23 and were defined component compositions of medium which is generally favorable for all of them: Carbon source - wheat bran - 8, source of additional nitrogen - peptone – 1,2 and NH_4NO_3 – 0,7, $MgSO_4x7H_2O$ – 0,3 and KH_2PO_4 – 0,1.

It should be noted that others as a source of carbon, especially glucose is a suitable substrate for growth, which is one of the facts that have been confirmed in studies, but there is another reason why we preferred to wheat bran. Thus, bran is a material produced from the wheat in the process of obtaining flour and is useful for human health (Babu *et al*., 2018; Stevenson *et al*., 2012). These components contained in biomass during its general use are causing to increase in the probability of evaluating this from the positive side. The real evaluation of this in the future should be carried out research in other aspects .

Cultural solution CS and biomass VB of active strains obtained during cultivation in optimum environments were studied both by general biology and antimicrobial activities in subsequent studies. From the results became clear that both in the CS and VB (general and antimicrobial) have metabolites that have biological activity, and the quantitative indicator of their effectiveness is characterized by different indicators depending on both selected and tested cultures. So that, solutions obtained from all active producer shows relatively low activity to bacteria used as test cultures (30-35 % reduction compared to the control), and in all of the cases, it can be assessed as a weak and moderate bactericidal activity. But related to test fungi is observed as an average (37-50 %) and strong (50-62 %) fungicidal effects.

From the result of research became clear that antimicrobial activity of CS in all cases is higher than in water or alcohol extracts of dry biomass (1,1-1,2 times), although it defines the overall biological activity of VB extracts to the relationship of *Paramecium caudatum* gives a higher increase effect (Table 4). As seen, the growth effect of the materials obtained from the separate strains differs from each other by quantitative indications, but this difference is not too significant.

The discovery of a relatively high growth effect when using CS allows us to note that metabolites with antimicrobial activity are extracellular and are characterized by low molecular weight. So that, a sufficient amount of first metabolites in biomass and to use this by other living things as foodstuffs become easier. Those that synthesized as a manifestation form of adaptive properties and characterized as mainly second metabolites (Keller, 2019, Macheleidt *et al*., 2016) are secreted out of fungi cells.

Apparently, the characterization of the growth effect of strains with similar indicators is due to the fact that the metabolites that caused the growth effect or contain compounds are similar to the extent that these facts are true, future studies will clarify.

Finally, in relation to the data presented in Table 4, an issue it can be said that none of the strains selected as an active producer is observed metabolites with toxic effects and the presence of biological activity components in all received materials is no doubt.

4. CONCLUSIONS:

Thus, from the carried out of research became clear that today the majority of Xylotropic macrometers as a promising producer of BAS used for various purposes in the world practice is also widely spread in Azerbaijan. Thus, the absence of metabolites with toxic effects as in CS as well as in the VB and possession their both general and antimicrobial activity in the future a serious basis for the organization of various BAS production based on them.

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Table 1. *Assessment of toxicity of obtained solution with respect to the Tetrahymena pyriformis infusion*

Growth coefficient of *Tetrahymena pyriformis* infusion within 24 hours of exposure (K_1)	**Assessment of toxicity**
K_1 < = 0,5	Solution is toxic
K_1 > = 0,9	The solution is not toxic

Table 2. *The general characteristic of Xylotrophic macrometers located in the natural forests of Azerbaijan and considered promising as a perspective BAS in the world*

№	**Recorded species**	**Registered area**	**Characterization according to highlight substrate**	**Ecolo-trophic relationships, the color of the decay**	**Characterization according to the distribution degree**	**Hyphal system**
1	*Ganoderma lucidum*	BC, HNP	Evrytoph	Saprotroph, white	Casual and rare species	Trimitik
2	*Laetiporus sulphureus*	BC, HNP, SC		Polytrophy, brown	Frequently encountered	Dimitik
3	*Pleurotus ostreatus*	BC, HNP, SC, KA		Polytrophy, white	Frequently encountered	Dimitik
4	*Schyzophyllum commune*	BC, HNP, SC, SC		Polytrophy, white	Dominant	Dimitik
5	*Trametes versicolor*	BC, HNP, SC, KA		Saprotroph, white	Dominant	Trimitik

Table 3. *Evaluation of Xylotroph macromycetes by the amount of biomass formed in the liquid nutrient medium*

№	The name of the registered species	Number of checked strains	The total amount of formed biomass (7 day, g/l)
1	*G.lucidum*	5	5.2-7.8
2	*L.sulphureus*	5	4.5-6.5
3	*P.ostreatus*	5	6.6-8.4
4	*Sch.commune*	5	6.5-8.7
5	*T.versicolor*	5	5.8-8.1

Table 4. *Toxic activity of strains of Xylotrophic macromysacies selected as an active producer in relation to Tetrahymena pyriformis*

№	Recorded species	The number of primary cells (cell/300 µl)	The number of cells after 16 hours (cell/µl)	Increase coefficient
		VB (Extraction with water)		
1	*G.lucidum AS-4*	160	319	2.00
2	*L.sulphureus AS -7*	145	290	2.00
3	*P.ostreatus AH-12*	150	314	2.09
4	*Sch.commune AH -17*	148	320	2.16
5	*T.versicolor AN -23*	156	315	2.02
6	Water	147	185	1.26
		VB (Extraction with 1 % alcohol)		
1	*G.lucidum AS-4*	151	405	2.68
2	*L.sulphureus AS -7*	157	408	2.60
3	*P.ostreatus AH-12*	152	398	2.62
4	*Sch.commune AH -17*	149	410	2.75
5	*T.versicolor AN -23*	143	356	2.49
6	Alcohol	137	167	1.22
		CS		
1	*G.lucidum AS-4*	159	290	1.82
2	*L.sulphureus AS -7*	162	298	1.84
3	*P.ostreatus AH-12*	142	250	1.76
4	*Sch.commune AH -17*	155	287	1.85
5	*T.versicolor AN -23*	158	275	1.74
6	The liquid nutrient medium	140	201	1.43