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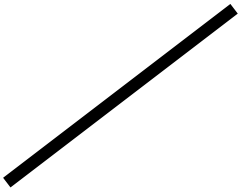

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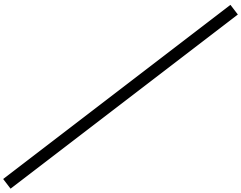

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SECONDARY METABOLITES OF THE FUNGUS *TRICHODERMA ASPERELLUM* AND THEIR BIOLOGICAL IMPORTANCE

ВТОРИЧНЫЕ МЕТАБОЛИТЫ ГРИБА *TRICHODERMA ASPERELLUM* И ИХ БИОЛОГИЧЕСКОЕ ЗНАЧЕНИЕ

TRICHODERMA ASPERELLUM ZAMBURG'ININGIKKILAMCHI METABOLITLARI VA ULARNING BIOLOGIK AHAMIYATI

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Abstract

Today, the increasing demand for food and the use of synthetic pharmaceutical chemical compounds in the agricultural production of fruits and vegetables are causing a growing number of negative changes in public health and the soil environment. Metabolites produced by Trichoderma species serve as a sustainable alternative for controlling plant diseases and mitigating harmful substances released by fungi. As part of this study, we presented a literature review of several metabolites concerning Trichoderma spp regarding the biologic activity and isolated some secondary metabolites concerning T. asperellum and described their activity. We summarize and group various antifungal secondary metabolites of Trichoderma spp. We consider in full detail some aspects concerning phytopathogenic fungi, their chemistry and biosynthesis. For the isolation of metabolites, thin-layer chromatography was performed for detection using columnar chromatography and the obtained substances were investigated by GS-MS analysis. As a result, it was found that the chloroform:methanol (5:1) system is characterized by a number of substances that differ from the metabolites that are separated from the other solvent system.

Аннотация

В настоящее время растущий спрос на продукты питания и использование синтетических фармацевтических химических соединений в сельскохозяйственном производстве фруктов и овощей приводят к растущему числу негативных изменений в общественном здоровье и почвенной среде. Метаболиты, продуцируемые видами Trichoderma, служат устойчивой альтернативой для борьбы с болезнями растений и снижения воздействия вредных веществ, выделяемых грибами. В рамках данного исследования мы представили обзор литературы по биологической активности нескольких метаболитов Trichoderma spp, а также выделили некоторые вторичные метаболиты T. asperellum и описали их активность. Мы обобщаем и группируем различные противогрибковые вторичные метаболиты Trichoderma spp. Мы подробно рассматриваем некоторые аспекты, касающиеся фитопатогенных грибов, их химии и биосинтеза. Для выделения метаболитов была проведена тонкослойная хроматография с использованием колоночной хроматографии, а полученные вещества были исследованы методом газохромато-масс-спектрометрии (ГХ-МС). В результате было установлено, что система хлороформ:метанол

(5:1) характеризуется наличием ряда веществ, отличающихся от метаболитов, выделенных из другой системы растворителей.

Annotatsiya

Bionazorat agentlari va ularning ikkilamchi metabolitlaridan (SM) foydalanish bugungi kunda qo'llaniladigan potentsial yondashuvlardan biridir. Mikrozamburug'lar olamida Trichoderma spp. butun dunyo bo'ylab qo'llaniladigan eng bionazorat agentlaridan biri sanaladigan zamburug' turkumi hisoblanadi. Trichodermaning juda ko'pgina turlari fitopatogen zamburug'larga qarshi, mikroblarga qarshi faollikka ega bo'lgan ikkilamchi metabolitlarni ishlab chiqaruvchi mashhur mikrozamburug' sanaladi. Ushbu ikkilamchi metabolitlar to'g'risidagi batafsil ma'lumotlar, birgalikda guruhlanganda, ulardan samarali foydalanish va o'simlik patogen zamburug'larini boshqarish uchun yangi bioaktiv birikmalarni qo'llanilish sohalarini yanada chuqquroq anglashga imkon yaratadi. Ushbu tadqiqot doirasida biz Trichoderma spp ga oid bir qancha metabolitlarni biologic aktivligiga oid adabiyotlar tahlilini hamda T. asperellumga oid ba'zi ikkilamchi metabolitlarni ajratib olishni va ularni faolliklarini bayon etdik. Trichoderma spp ning turli antifungal ikkilamchi metabolitlarini umumlashtiramiz va guruhlaymiz. fitopatogen zamburug'larga qarshi, ularning kimyosi va biosintezi bilan bog'liq ba'zi jihatlarni har tomonlama ko'rib chiqamiz. Metabolitlarni ajratib olishda ustunli xromatografiya usulidan foydalanib, aniqlashda yupqa qatlamli xromotagrafiya tekshiruvi amalga oshirilib, olingan moddalar GS-MS analizi orqali tekshiruv olib borildi. Natijada xloroform:methanol (5:1) sistemasining boshqa nisbatli shunday sistema yoki boshqa erituvchilar sistemasidan ajralib chiqqan metabolilardan farq qiladigan bir qancha moddalar ajralib chiqqanligini aniqlandi.

Key words: *antifungal, antioxidant, biological control, phytopathogenic fungi, secondary metabolite, Trichoderma ssp, chromatography.*

Ключевые слова: *противогрибковые препараты, антиоксиданты, биологический контроль, фитопатогенные грибы, вторичные метаболиты, Trichoderma ssp, хроматография*

Kalit so'zlar*: antifungal, antioksidant, biologik nazorat, fitopatogen zamburug'lar, ikkilamchi metabolit, Trichoderma ssp, xromatografiya.*

INTRODUCTION

In these days, it is one of the important goals of all industries, whether it is obtaining biologically active substances or increasing soil fertility, agricultural development, using natural resources, natural ways as much as possible, to achieve good and high results. Since the fungus of the genus Trichoderma and specifically T. asperellum are among the fungi that produce a lot of active substances, as well as secondary metabolites that increase soil fertility, we referred to several studies on this subject.

In the fungal sprang named T. asperellum GDFS1009 the following metabolites: 8 olefins, 24 alkanes, 2 polyketides, 25 esters, 2 benzene, 2 acids, 1 aldehyde, 4 alcohols in total, 68 secondary metabolites were isolated using GC-MS analysis GDFS1009. 28 metabolites, such as 23 alkanes and 1 nitrile, were identified by GC-MS scan [1]. When GC-MS analysis and Chemolibrary testing were performed to investigate active compounds in fungal extracts, 49 compounds were identified among the three isolates of T. asperellum MF8. Of these, 2,3-didrotiopene, alpha-pinene, p-cymen hexadecanoic acid, 2,3-dihydro-3,5-dihydroxy-6-P-6-P, 8-methylquinoline, (Z, Z)-9,12-octadecadienic acid, methyl ether had been noted in many sources as insecticidal properties [2]. It was also found that all three strains of Trichoderma exhibited an inhibitory property against pathogens by about 70%. Of the metabolites identified in the GC\u2012MS study, mainly volatile metabolites such as ketones, esters, and alcohols had an inhibitory effect on the mycelial growth of pathogens [3]. Volatile organic compounds (VOCs) of T. asperellum T76-14 F. detected by the sealed plate method were found to be effective in inhibiting the growth of incarnatum fungi by 62.5%. The solid-phase microextraction GC/MS analysis revealed a relative phenylethyl alcohol (PEA) among the few dominant compounds emitted from T [4]. Seven molecules of VOCs and 12 molecules of nVOCs were identified as a result of GC-MS and HPLC-Q-TOF-MS assay for the detection of volatile organic compounds (VOCs) and non-volatile organic compounds (nVOCs) contained in trichoderma m filtrates [5]. When the composition of Trichoderma asperellum with Diaporthe phaseolorum (8S) was investigated using a mycorrhizal viable form: 3-hydroxypropionic acid and di-(2-ethylhexyl)phthalate and 1-hydroxy-8-methoxyanthraquinone were isolated and found to be active substances against insects, weeds, and crop pests of some species [6].From the secondary metabolites isolated from T. asperellum, the compound 6-Pentyl-a-pyrone exhibited high potent antifungal activity against M. mais [7]. T. asperellum GDFS1009 releases chitinase, glucanase, and protease that can disrupt the cell walls of fungi and contribute to mycoparasit-

ism. As a result of RNA sequence (RNA-seq) and gas chromatography-mass spectrometry (GC-MS) analysis, T. asperellum is known to produce various antimicrobial secondary metabolites: polyketides and alkanes from GDFS1009 [8]. GC-MS analysis identified six classes of volatile compound produced by T. coningiopsis VM115 (alcohols, ethers, pyrones (lactones), acids, furans, and lipids). 6-n-pentyl-6H-pyran-2-one (6PP) was known to be one of the most abundant metabolites in this study [9]. Four fermentation extracts have also shown an attractive activity in silkworm feeding for activity induced by active metabolites of T. harzianum [10]. Three novel diterpene coninginols ABC (1–3) and two novel sesquiterpenoids, 11-hydroxy-15-drymeneoic acid (4), coninginol D (5), together with twelve known compounds (6–17), have been isolated from the endophytic fungus of Tricho7in coninginols[11]. Nine new sesquiterpenes, including carotene and cadinan derivatives, have been found in the fungus Trichoderma virens Y13-3, an algae epiphyte [12].

Eight novel high-oxygen fungal polyketides, namely 15-hydroxy-1,4,5,6-tetra-tetra-epikoninginin G (1), 14-hydroxyconinginin E (2), coninginin U (3), 4'-hydroxyconinginin U (4), coninginin V (14), koninginin B (14), 14-hydroxyconinginin B (7) and 7-O-methylconinginin B (8) together with six known relevant analogues (9-14) from the fungus Trichoderma coningiopsis QA-3 derived from the internal stem tissues of the well-known medicinal plant Artemisia argya Isolated . All of these compounds are bicyclic polyketides, containing an unusual hemiketal portion in 1-5 and a ketone group in C-1 and a 2-14 compound with a ketone group in C-5(6) [13]. Peptaibols are linear peptides composed of α, α-dialkylated amino acids, isovalin, α-aminoisobutyric acid (Aib), acetylated N-terminal, and C-terminal amino acids. They have been found to have their antimicrobial and anticancer properties, as well as antimicrobial invasion properties in plants [14, 15]. Peptaibols have been found to be produced mainly by representatives of the genus Trichoderma [16]. In another study, when an antagonistic test against Fusarium oxysporum was performed, T. asperellum ZJSX5003 and GDFS1009 had the ability to grow rapidly, and the inhibitory effect on F. oxysporum was 73% and 74%, respectively. Six identical volatile metabolites are: 3-Methyl-1-butanol, 2-Methyl-1-propanol, 3-Methyl-3-butene-1-ol, butane-2,3-diol, Acetyl methyl carbinol, and 6-n-pentyl-2H-pyran-2P (Piran-2) [17]. Two additional anthraquinones-1,8-dihydroxy-3-(hydroxymethyl) anthracene-9,10-dione Other phenolic compounds caffeic acid, trichophenol A, and izorhamnetin were detected in ethyl acetate crude extract of T. harzianum (LBAT-53) [18]. Trichoderma asperellum isolated fungus was grown from Bertholletia excelsa (Brazil nut) almond and extracted with ethyl acetate, obtained AM07Ac. Later, using HPTLC (High-Performance Thin Layer Chromatography) and nuclear magnetic resonance (1 H NMR), β-amirin, kaempferol, and brusine were identified as the main compounds [19].

MATERIAL AND METHODS

Formation of fungal biomass

The fungal strain of T. asperellum is grown at intervals of 2 weeks during the Mandéls feed season. The cultivated fungal mass is separated from the cultivated liquid using filter paper (Whatman # 1.5). The collected litter mass was dried at temperatures (about 40-45°C). The dried biomass was transferred into a powder state and kept in an ethyl alcohol (96-98%) at 1:2 state and kept in a pendulum shaker at 150 μL/min for 18 h. The alcohol extract was then filtered and the filtrate was driven at 45 μm at 78.5°C in a rotary drive. This process was continued 6-9 times (until the alcohol content did not dissolve the substance). After several drives the extract mass of lard was collected and dried so that the finished mass was 16.2 g.

Fractionation technology

For extraction of the obtained dry litter mass, columnar (columnar) chromatography was used to isolate the solids. The length of the glass column is 60 cm, and it is considered to have a diameter of 12 cm. Initially, the kalonka was washed in hexane substance, then 240gr of 100/250 m size from silicagel L (Chemapol Prana-Czechoslovakia) was placed on this kalonka. And 16.2 g of biomass was thoroughly mixed with 15 g of silicagel and turned into a paroshok and put into a cocade over the silicagel. Solvents with low polarity were used to separate fractionated substances: hexane, chloroform, methanol and their various proportional systems and each separated fraction were examined by TLX analysis.

RESULTS AND DISCUSSION

The extraction of secondary metabolites from the fungus of Trichoderma asperellum has been performed in several solvents, with fractionation step by step [20]. Meanwhile, this fractionation step is performed when chloroform methanol composed of polar solvent systems is performed in a ratio of 5:1 to convert the separated metabolites into GX-MS (Fig. 1). the results of the examination and the separated substances (Table 1).

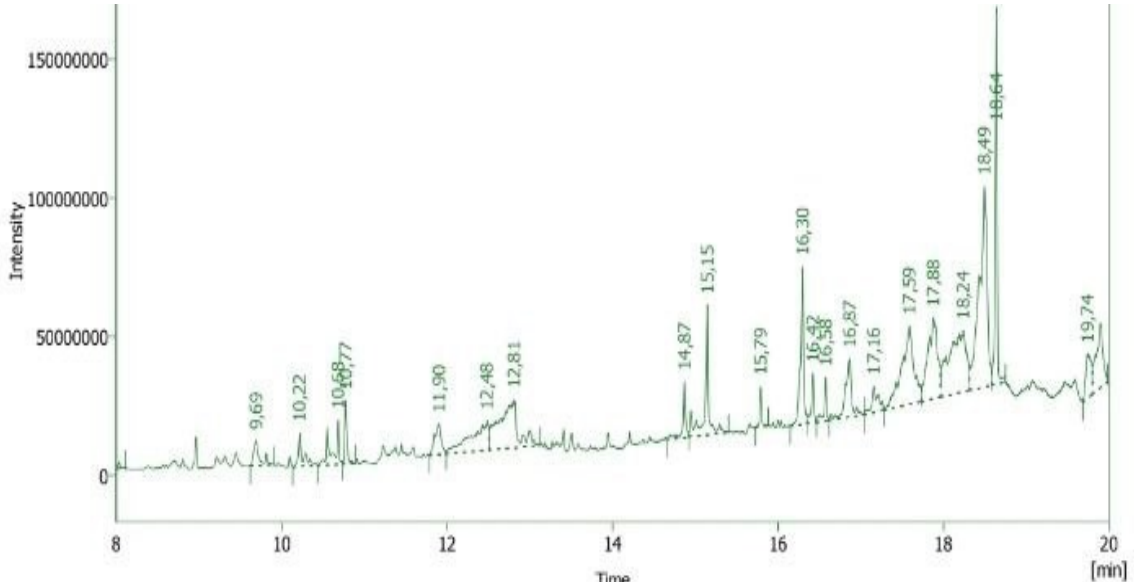

Figure 1. Gaseous liquid chromatography of the chloroform methanol 5:1 fraction

The volatile metabolites identified by chromatographic examinations were found to be the following compounds when compared with the data in the MS data library (Tab 1).

Table 1

Substances degraded by fractionation in chloroform methanol 5:1 system

No	Metabolite name	Molecular formula	Molecular mass g/mol	Time to Absorption
1	Octadecanedioic acid	C18H36O2	284.4772	11,900
2	Pyrimidine-2,4-dione,1,2,3,4-tetrahydro-5-methyl-1-[2-hydroxymethyl-3-dione]	C9H12N2O5	228.20	12,481
3	L-Pyroglutamic acid	C5H7NO3	129.11	12,807
4	n-Hexadecanoic acid	C16H32O2	256.4241	15,147
5	Oleic Acid	C18H34O2	282.4614	16,297
6	2-Butenoic acid, 2-methyl-, 2-(acetyloxy)-1,1a,2,3,4,6,7,10,11,11a-decahy	C29H40O9	532.6	17,157
7	2,4-Cyclohexadien-1-one,3,5,6-trihydroxy-2-isovaleryl-4,6-bis(3-methyl-2-b)	C21H30O5	362.46	17,587
8	Pregn-4-ene-3,20-dione,16,17-epox, (16a)	C21H30O2	316.5	17,877

9	Oxiraneoctanoic acid, 3-octyl-, cis-	C18H34O3	298.4608	18,239
10	Octadecanoic acid, 2-hydroxy-1,3-propanediyl ester	C18H36O2	284.47	18,494
11	Diisooctyl phthalate	C24H38O4	390.6	18,640
12	Linoleic acid ethyl ester	C18H32O2	280.5	19,741

Biological significance of extracted substances

This chloroform: non-dissociated metabolites in other fractionation steps in the methanol system: 2-Butenoic acid, 2-methyl-, 2-(acetyloxy)-1,1a,2,3,4,6,7,10,11,11a-decahy, Pyrimidine-2,4-dione, 1,2,3,4-tetrahydro-5-methyl-1-[[2-hydroxymethyl-3-dione, Pregn-4-ene-3,20-dione, 16,17-epoxy-, (16a), L-Pyroglutamic acid, 2,4-Cyclohexadien-1-one, 3,5,6-trihydroxy-2-isovaleryl-4,6-bis(3-methyl-2-b) And so on. When we study the properties of the compound Pyrimidine-2,4-dione,1,2,3,4-tetrahydro-5-methyl-1-[2-hydroxymethyl-3-dione], it is revealed that in many bioactive molecules it retains potential biological activity, which is a common building block for which the pyrimidine nucleus retains, while tetrahydro-pyrimidine derivatives are among the substances that retain anti-cancer, anti-inflammatory, antimicrobial and antioxidant properties. The presence of methyl and hydroxymethyl groups may have a further influence on its biological activity and interaction with biological targets [21]. L-pyroglutamic acid, also known as pedolic acid or 5-oxoproline, is a naturally occurring derivative of amino acid possessing different biological properties. It acts as a metabolite of the glutathione cycle in the body and may affect the cholinergic system of the brain. It is found in the brain, spinal fluid, skin and blood, and is the skin's natural moisturizing factor. It also has potential roles in taste perception, and its effects on plants, especially under stress, have shown antifungal activity against Phytophthora infestans, a plant pathogen of some L-pyroglutamic acid derivatives [22, 23, 24]. Humulon is an optically active cyclic ketone and is 3,5,6-trihydroxycyclohexa-2,4-diene-1-one, composed of two 3-methylbut-2-en-1-yl substituents at position 4 and 6, and also a 3-methylbutanyl group at position 2. It plays a role as an antibacterial drug, antioxidant, cycloxigenase 2 inhibitor and metabolite. These are diketone, triol, cyclic ketone, aromatic ketone, and tertiary alpha-hydroxy ketone [25]

CONCLUSION

The results of the above study show that as a result of this stepwise fractionation, in the process of some other fractionation, the insoluble metabolites, i.e. organic substances, are decomposed and these substances are substances of specific biologically active properties.

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