ISSN 0003-6838, Applied Biochemistry and Microbiology, 2018, Vol. 54, No. 2, pp. 211–214. © Pleiades Publishing, Inc., 2018.
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Isolation, Purification, and Biological Activity of Secondary Metabolites from *Trichoderma asperellum* F-1087

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Received April 28, 2017

Abstract—The secondary peptide metabolites produced by the *Trichoderma asperellum* strain F-1087 were isolated, and their properties were studied. It has been shown these metabolites at concentrations of 0.08 and 0.02 mg/mL inhibit the human prostate cancer cell line by 97 and 34%, respectively.

Keywords: secondary metabolites, *Trichoderma asperellum*, PC-3
DOI: 10.1134/S000368381802014X

INTRODUCTION

The genus of fungi *Trichoderma* is widely distributed in different climatic zones; they occupy a variety of habitats. These fungi can be isolated from a large number of natural and artificial substrates [1, 2]. The survival of these fungi in different climatic zones is caused by their high adaptability, as well as the wide metabolic variety of strains, their high reproductivity, and their competitiveness [3].

Mycelial fungi, including molds, are effective producers of secondary metabolites (products of the producer's vital activity) that possess biological activity and influence the environment of the producer by suppressing the growth of other microorganisms [4–7]. Many secondary metabolites do not have a definite function and are often synthesized under certain cultivation conditions, for example, stressful ones [8, 9]. Some of them are of interest to the pharmaceutical industry (enzymes and antibiotics) [10, 11].

The purpose of this work was to isolate and characterize the secondary peptide metabolites of the mold fungus *T. asperellum* F-1087.

MATERIALS AND METHODS

The object of the study was the *Trichoderma asperellum* F-1087 strain isolated from the soil of the Murzikhinsky II burial ground (Republic of Tatarstan, Russia). The strain was deposited in the All-Russia Collection of Industrial Microorganisms under the registration number F-1087.

To obtain the seeding material, the fungus *T. asperellum* F-1087 was grown on Czapek nutrient medium of the following composition (g/L): glucose 30, $NaNO_3$ 3.0, K_2HPO_4 1.0, $MgSO_4 \cdot 7H_2O$ 0.5, KCl 0.5, $FeSO_4 \cdot 7H_2O$ 0.01, and agar-agar 15. Cultivation was carried out in the dark for 14 days at 28°C [12]. After 14 days of growth, the formation of a dark green pigment was observed.

Mycelium with a portion of the solid medium was placed in a liquid nutrient medium of the following composition (g/L): glucose 5, KH_2PO_4 0.8, KNO_3 0.7, $CaCO_3$ 0.06, $MgSO_4$ 0.5, $ZnSO_4$ 0.01, $CuSO_4$ 0.005, $FeSO_4$ 0.001, $MnSO_4$ 0.01 and distilled water 1 L; H_3PO_4 was added to a concentration of 1.75%; and mycelium was cultured in 1000-mL conical flasks containing 500 mL of the medium for 12 days on a Helicon shaker (Germany) at a platform rotation speed of 80 rpm at 28°C. During cultivation of the fungus, the product yield, the morphological state of the culture, and the absence of extraneous microflora were monitored.

After the cultivation was completed, the culture liquid (CL) of *T. asperellum* F-1087 was separated by filtration through a layer of gauze and centrifuged at 4800 *g* for 15 min. Ethyl acetate (Khimmed, Russia) was poured onto the resulting supernatant in a 1 : 1 ratio, stirred, and incubated for 24 h at 4°C. In this case, a clear separation of the boundaries of the two phases was observed. The upper phase (ethyl acetate) was evaporated to a volume of 1 mL on a Heidolph vacuum rotary evaporator (Germany) for 4 h at 30°C and then dissolved in 50 mL of acetonitrile (Merck, Germany).