https://doi.org/10.31925/farmacia.2022.6.19 **ORIGINAL ARTICLE**

SYNTHESIS OF (*S*)-ALANYL-(*S*)-β-(THIAZOL-2-YL-CARBAMOYL)-α-ALANINE, DIPEPTIDE CONTAINING IT AND *IN VITRO* INVESTIGATION OF THE ANTIFUNGAL ACTIVITY

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Abstract

Enantiomerically enriched (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine amino acid was synthesized by the method of asymmetric synthesis, Ni(II) planar complex of glycine was used as an initial complex. After purification and cleavage of the metal complexes, an amino acid with high enantiomeric purity (> 99%) was isolated. Using the activated ester method for the peptide synthesis by the synthesized non-protein amino acid, N-tertbutoxycarbonyl-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine dipeptide was synthesized. As a result of studying the antifungal activity of the obtained compounds, it was found that the synthesized compounds suppressed the growth of all investigated fungal strains, and the antifungal activity of N-tertbutoxycarbonyl-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine dipeptide was more pronounced compared to the initial non-protein amino acid, when using a 0.1 M solution in the case of *Aspergillus flavus* ATCC 10567 strains.

Rezumat

A fost sintetizat aminoacidul (S)-β-(tiazol-2-il-carbamoil)-α-alanină, îmbogățit enantiomeric, prin metoda de sinteză asimetrică, iar complexul planar Ni(II) al glicinei a fost utilizat ca și complex inițial. După purificarea și scindarea complexelor metalice, a fost izolat un aminoacid cu puritate enantiomerică ridicată (> 99%). Folosind metoda esterului activat, a fost sintetizată dipeptida N-tertbutoxicarbonil-(S)-alanil-(S)-β-(tiazol-2-il-carbamoil)-α-alaninei. Ca urmare a studierii activității antifungice a compușilor obținuți, s-a constatat că aceștia au suprimat creșterea tuturor tulpinilor fungice investigate. Activitatea dipeptidei N-tertbutoxicarbonil-(S)-alanil-(S)-β-(tiazol-2-il-carbamoil)-α-alanină 0,1 M a fost mai pronunțată în comparație cu cea a aminoacidului neproteic inițial în cazul tulpinilor de *Aspergillus flavus* ATCC 10567.

Keywords: peptides, antifungal, enantiomer, synthesis

Introduction

In recent years, fungi have been recognized as an integral part of our commensal microbiota in various parts of the body, *e.g.* intestines, oral cavity, skin, lungs, vagina [1-3]. Fungi have been used as a food source and for food processing for thousands of years [4]. Fungi are also commonly used in many industrial processes, including the production of peptides, enzymes, vitamins, organic acids and antibiotics [5, 6].
However, in addition to useful properties, fungi are pathogens for humans. Inpatient and outpatient fungal infections have increased dramatically in recent years. It is calculated that fungal diseases affect more than one billion people worldwide, out of which 150 million suffer from severe infections [7].
They range from superficial and subcutaneous infections that worsen the life quality by the skin lesions, keratinized tissues and mucous membranes [8] to systemic infections that can be life-threatening, involving the brain, heart, lungs, liver, spleen and kidneys, the latter being especially alarming in immuno-compromised patients with HIV/AIDS or autoimmune diseases as well as in those undergoing anticancer chemotherapy or organ transplantation [9].
Four main classes of antifungals prevail in the market. They are azoles, which inhibit the synthesis of ergosterol; polyenes that interact physicochemically with steroles of fungal membranes; echinocandins, inhibiting glucan synthesis; and fluorinated pyrimidines that hinder pyrimidines metabolism resulting in inhibition of DNA and RNA biosynthesis [10].
The development of antibiotic resistance, the increase in diseases associated with immunodeficiency, and the limitation of available therapeutic agents and options are the basis for the search for new therapeutic agents. These new antifungal drugs should be less toxic, affect the intended target, or have a broad spectrum of action. The range and mechanisms of action of new antimicrobial agents against pathogenic fungi are aimed at limiting the development of

resistance. Taking into account these requirements, antimicrobial peptides with antifungal activity are today powerful candidates due to their high antimicrobial action and selectivity [11].

Monoclonal antibodies, cytokine immunotherapy, vaccines and antimicrobial peptides (AMPs) have emerged as new biopharmaceuticals for the prevention or treatment of fungal infections [12].

Peptides act selectively, are effective and easy to digest [13]. According to the data of 2016, there are about 1000 or more peptides with a wide range of antifungal activity, they are peptides of both natural and synthetic origin [14].

Antifungal peptides are classified according to the structure, the nature of the impact, the origin of the peptide: natural, semisynthetic, synthetic [15].

Taking into consideration the structural units of peptides with the antifungal activity, as well as clearly expressed ranges of antifungal action of azole compounds, we aimed at synthesizing a non-protein amino acid (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine undescribed in the literature and contained in N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine dipeptide, aiming the *in vitro* investigation of the antifungal activity of the synthesized compounds. As fungal strains *Aspergillus versicolor* 12134, *A. flavus* 10567, *A. candidus* 10711, *Penicillium chrysogenum* 8190, *P. aurantiogriseum* 12053, *P. funiculosum* 8258, *Alternaria altenata* 8126, *Ulocladium botrytis* 12027, *Aurobasidium pullulans* 8269 were selected. Pathogenic and conditionally pathogenic for humans and animals species were selected as test fungi. Thus, *A. niger* often appears as the cause of otomycoses, and *A. flavus* infects the paranasal sinuses and together with other species is able to synthesize aflatoxins that have mutagenic, carcinogenic and allergic effects [16-18].

Materials and Methods

Chemistry

Materials. All reagents were obtained from commercial sources and used without further purification. Thin-layer chromatography (TLC) was carried out on Merck aluminium foil backed sheets pre-coated with 0.2 mm Kielselgel 60 F254. Column chromatography was performed on Fluka silica gel 60 (0.063e0.200 mm, 70e320 mesh) on a glass column. Melting points (mp) were determined by Elektrothermal. ^{1}H and ^{13}C NMR spectra were recorded on Varian Mercury 30000 300 MHz spectrometer using TMS as internal standard. The NMR spectra were calibrated by solvent at 7.27 ($CDCl_3$), 3.31 (CD_3OD), 4.79 (D_2O), 2.50 ($(CD_3)_2SO$) for 1H and 77.1 ($CDCl_3$), 49.15 (CD_3OD), 39.5 ($(CD_3)_2SO$) for ^{13}C. Elemental analysis was done by Euro EA3000. For the cation exchange, a column Dowex-50 (Hþ form) was used. The enantiomeric purity of the amino acids was determined by HPLC (Waters Alliance 2695 HPLC System) on a chiral phase of the Diaspher 110-Chirasel-E_1 6 m, 4.0_x 250 mm, mobile phase consisted of methanol: sodium phosphate monobasic buffer (20:80). Enantiomeric yield was proved by chiral HPLC analysis of the isolated amino acids.

Methods. A general method for the C-alkylation of glycine complexes with heterocyclic alkyl halides. 0.15 g (3.66 mmol) of freshly ground solid NaOH and 0.24 g (1.34 mmol) of the alkyl halide are added to a solution of 0.6 g (1.22 mmol) of the glycine complex in dimethylformamide under argon atmosphere. Meanwhile, the reaction mixture turns into a dark cherry-like homogeneous solution. Stirring of the solution under argon atmosphere and at room temperature (20 - 25°C) continued until complete transformation of the initial complex into the product. After the reaction is complete, the mixture is neutralized with concentrated glacial acetic acid and diluted with water. Then the precipitate of diastereomeric complexes is filtered, washed with water. The structure and absolute configuration of the isolated major diastereomer complexes were determined by spectroscopic analysis. The diastereomeric excess (*de* or stereoselectivity) of the main diastereomeric complexes formed during complexation was determined by the method of HPLC analysis of the amino acid mixture (without recrystallization) separated from the acid hydrolysate of their mixture.

Product complex. Yield – 70%, mp – 194 - 196°C. $[\alpha]_D^{20}$ = +1345.03° (c = 0.17; MeOH). Found, %: C 62.52; H 5.13; N 7.50; O 12.83. $C_{39}H_{38}O_6N_4SNi$. Calculated, %: C 62.50; H 5.11; N 7.48; O 12.81. ^{1}H NMR: ($CDCL_3/CCL_4$ ~1/1, δ, md, *MHz*): 1.98 (m, 1H, γ-H_a Pro); 2.08 (m, 1H, δ-H_a Pro); 2.48 (m, 1H, β-H_a Pro); 2.74 (dd, 1H, ^{2}J = 16.0, ^{3}J = 7.2, $\underline{CH_2}CH$); 2.91 (dd, 1H, ^{2}J = 16.0, ^{3}J = 2.7, $\underline{CH_2}CH$); 2.98 (m, 1H, β-$H_б$ Pro); 3.42 (dd, 1H, ^{3}J = 10.2, ^{3}J = 6.8, α-H Pro); 3.47 - 3.67 (m, 2H, γ-$H_б$ and δ-$H_б$ Pro); 3.62 (d, 1H, ^{2}J = 12.6, $\underline{CH_2}Ph$); 4.29 (dd, 1H, ^{3}J = 6.8, ^{3}J = 2.7, $\underline{CH}CH_2$); 4.39 (d, 1H, ^{2}J = 12.6, $\underline{CH_2}Ph$); 6.59 - 6.66 (m, 2H, H-3, 4 C_6H_4); 6.96 (d, 1H, ^{3}J, U$\underline{CH}$=CHN), 7.01 (d, 1H, ^{3}J = 7.6, C_6H_5); 7.14 (ddd, 1H, ^{3}J = 8.6, ^{3}J = 6.0, ^{4}J = 3.2, H-5 C_6H_4); 7.21 (m, 1H, H-4 Ph); 7.28 (m, 1H, H Ar.); 7.33 - 7.56 (m, 6H, H Ar.); 8.05 (m, 2H, H-2,6 Ph); 8.24 (d, 1H, ^{3}J = 8.6, H-6 C_6H_4); 11.70 (br., 1H, NH).

Isolation of (S)-β-(thiazol-2-yl-carbamoyl)-α-alanine. A dry residue of 0.86 mmol of the diastereomeric mixture of the product complex was dissolved in 50 mL methanol and slowly added to a 10 mL aqueous solution of 2 N HCl pre-heated at 50°C in a round-bottomed flask. After the disappearance of the red colour characteristic of the complex, the solution was evaporated under *vacuum*. Distilled water was added to the dry residue and the resulted chiral reagent was filtered. The aqueous filtrate was further extracted

with chloroform (2 x 10 mL) to completely remove the traces of the chiral reagent. The target amino acid was separated from the resulted aqueous solution by passing it through a column filled with "Ky-2x8" cation exchange resin in the H^+ form, using a 7% NH_4OH solution as an eluent. The solvent was then evaporated in a *vacuum* to dryness. The target optically active amino acid was recrystallized from aqueous ethanol and the optical purity was determined by the method of chiral HPLC analysis. Below are the physicochemical analysis data of the new synthesized amino acid. Yield – 70%, mp – 278 - 280°C. $[\alpha]_D^{20}$ = -88° (c = 0.2, H_2O:C_2H_5OH:NH_4OH = 2:2:1). Found, %: S 39.08; H 4.22; N 19.53. $C_7H_9N_3O_3S$. Calculated, %: S 39.06; H 4.21; N 19.52. ^{1}H NMR: (DMSO/CCl_4 + CF_3COOD, δ, md, *MHz*): 3.04 (dd, 1H, ^2J = 17.2, ^3J = 5.8, CH_2); 3.11 (dd, 1H, ^2J = 17.2, ^3J = 5.3, CH_2); 4.33 (dd, 1H, ^3J = 5.8, ^3J = 5.3, CH); 7.22 (dd, 1H, ^3J = 3.5, SCH=CHN); 7.47 (d, 1H, ^3J = 3.5, SCH=CHN).

Synthesis of N-tert-butoxycarbonyl-(S)-alanine. 0.587 g (0.0066 mol) of alanine was added to a 0.5 M aqueous solution of 0.7 mL sodium hydroxide in a flat-bottomed flask, to which 0.37 g (0.0044 mol) of $NaHCO_3$ dissolved in 5 mL of water was added, stirred with a magnetic stirrer at room temperature until the alanine was dissolved, and then 1.44 g (0.0066 mol) of di-tert-butylpyrocarbonate dissolved in 6.6 mL of isopropanol was added. After adding the materials, the mixture was stirred at room temperature for 2 hours, the reaction progress was monitored by TLC, which showed that the reaction was complete after 2 hours, then the reaction mixture was diluted to 50 mL and the excess reagent was extracted with ethyl acetate (2 x 20 mL). 6 mL of 10% citric acid solution was added to the aqueous solution and re-extracted with ethyl acetate (2 x 20 mL), the extracts were combined and washed with NaCl saturated aqueous solution, dehydrated with anhydrous sodium sulfate. After decanting, organic solvents were evaporated under *vacuum* at 50 - 60°C. The target product was recrystallized from ethyl acetate-hexane mixture in the ratio of 1:3, filtered and dried under vacuum (50 - 60°C). White powdery crystals were obtained, the reaction yield was 70% (0.87g of N-t-BOC-(*S*)-alanine). The authenticity, chemical and optical purity of the resulted N-t-BOC-(*S*)-alanine protected amino acid were checked and confirmed with the literature data. N-t-BOC-(*S*)-alanine. Specific rotation value: $[\alpha]D20_{Sample}$ = -26.3° (c = 2; acetic acid), $[\alpha]D20_{literatue}$ = -260 (c = 2; acetic acid). Melting temperature. $T_{melt.\ sample}$ = 86 - 89°C, $T_{melt.\ literature}$ = 83 - 89°C [19].

Synthesis of N-tertbutoxycarbonyl-(S)-alanyl-N-oxysuccinimide ester. 0.87 g (0.0046 mol) of N-t-BOC-(*S*)-alanine and 0.579 g (0.005 mol) of N-hydroxysuccinimide were placed to a flat-bottomed flask, dissolved in a mixture of 5.8 mL of dioxane and 1.56 mL of methylene chloride by mixing with a magnetic stirrer at room temperature; a calcium chloride tube was attached to the flask to avoid moisture. After the materials were dissolved, the reaction mixture was cooled to 0°C and 1.004 g (0.00487 mol) of dicyclohexylcarbodiimide, previously dissolved in 1.5 mL of dioxane, was added in small portions within 15 min at 5 min intervals, during which the reaction mixture turned from transparent to white, which indicates the progress of the reaction with the formation of dicyclohexylurea. The reaction mixture was stirred for an additional 1 hour at -2 - 0°C, then the cooling was removed and stirring was continued for another 1 hour at room temperature. The course of the reaction was monitored by the TLC method (chloroform/methanol/ethyl acetate 4/2/1). After completion of the reaction, the precipitate formed was filtered to get rid of dicyclohexylurea and the reaction mixture was immediately used to obtain dipeptide.

Synthesis of N-tertbutoxycarbonyl-(S)-alanyl-(S)-β-(thiazol-2-yl-carbamoyl)-α-alanine. 0.13 g (0.6 mmol) of non-protein amino acid was placed in a flat-bottomed flask with a magnetic stirrer and heated to 60°C, dissolved in 1.63 mL of 0.5 M NaOH, then 0.26 mmol of $NaHCO_3$ was added, then 0.816 mmol of BOC-(*S*)-alanine-N-oxysuccinimide ether dissolved in 2 mL dioxane was added at room temperature. After that, the reaction mixture was stirred for 3 hours at room temperature, then it was transferred to a refrigerator at 5°C. The next day, 5 mL of ethyl acetate, 3 mL of 10% citric acid solution and 0.2 g of NaCl were added to the reaction mixture and stirred for 15 min. Then the organic layer was separated, dried over sodium sulfate and the solvent was removed under vacuum at 50°C. The residue was recrystallized from ethyl acetate-hexane mixture in the ratio of 1:3. The course of the reaction was monitored by thin-layer chromatography, as a solvent system chloroform:methanol:ethyl acetate-3:2:1 was used. The reaction yield was 90%. ^{1}H NMR (300 MHz, DMSO) δ 7.88 (d, *J* = 7.1 Hz, 1H, NHCH), 7.34 (d, *J* = 3.5 Hz, 1H NCH), 6.94 (d, *J* = 3.5 Hz, 1H, CHS), 6.40 (d, *J* = 7.5 Hz, 1H, NHCH), 4.63 (dd, *J* = 13.3, 5.7 Hz, 1H, CHCOOH), 4.07 - 3.87 (m, 1H, $CHCH_3$), 3.02 - 2.83 (m, 2H, CH_2), 1.43 - 1.35 (m, 9H, $(CH_3)_3$), 1.22 (d, *J* = 7.0 Hz, 3H, CH_3). ^{13}C NMR (75 MHz, DMSO) δ 172.15 (COOH), 171.87, 171.63 (CO), 167.92 (SCN), 157.84 (CO), 137.00 (NCH), 112.34 (CHS), 77.81 ($(CH_3)_3C$), 48.20 ($CHCH_3$), 36.83 (CHCOOH), 28.09 ($(CH_3)_3$) 25.05 (CH_2), 18.22 (CH_3).

Biological activity

Investigation of untifungal activity. As objects of study *Aspergillus versicolor* 12134, *Aspergillus flavus* 10567, *Aspergillus candidus* 10711, *Penicillium chrysogenum* 8190, *Penicillium aurantiogriseum* 12053, *Penicillium funiculosum* 8258, *Alternaria altenata* 8126, *Ulocladium botrytis* 12027, *Aurobasidium*

pullulans 8269 from the National Culture Collection of microorganisms of Armenia fungal strains were selected. The effect of the synthesized compounds on the growth activity of the above mentioned fungi was investigated. In order to investigate the antifungal activity, the investigated compounds were dissolved in dimethylsulfoxide by obtaining 0.1 M solutions, which at concentrations of 0.3 mL, 0.6 mL and 0.9 mL were added to the Czapek medium in the amount of 90 mg each, with the following composition: sucrose – 30.0, sodium nitrate – 2.0, potassium hydrogen phosphate – 1.0, magnesium sulfate – 0.5, potassium chloride – 0.5, iron sulfate – 0.01, then the obtained mass was evenly distributed in 9 Petri dishes, 3 strains in each dish and three replicates. Dishes were incubated at 28°C for 5 - 7 days. The experiment was repeated three times.

Upon completion of the test, the dishes were examined with the naked eye and under a binocular magnifier, after which the antifungal activity of various concentrations of the samples was assessed by the intensity of growth and sporulation of fungi. The growth of fungi without the addition of the synthesized compounds and the addition of the corresponding millilitres of DMSO 0.3 mL, 0.6 mL, 0.9 mL served as the control.

The results of the study were compared with the control and the intensity of the growth of the fungi was observed by eye and a magnifying glass.

Results and Discussion

Chemistry. For the synthesis of the non-protein amino acid (S)-β-(thiazol-2-yl-carbamoyl)-α-alanine (5), the glycine nickel complex (1) was preliminarily synthesized according to a previously developed method [20]. At the next stage, the alkylation reaction of the amino acid residue of the complex with heterocyclic alkyl halides was studied under the conditions of basic catalysis. Thiazol-2-yl-carbamoyl-methyl chloride (2) was used as the alkylating agent. The reaction proceeded easily and rapidly in dimethyl-formamide in the presence of NaOH at room temperature. It is convenient to monitor the course of alkylation reactions by the TLC method (SiO_2, $CHCl_3$:CH_3COCH_3 (5:1), or $CHCl_3$:$CH_3COOC_2H_5$ (3:1)). As a result of alkylation of the glycine complex, a mixture of (S,S)- (3) and (S,R)- (4) diastereomeric complexes was obtained with a high excess of (S,S)-diastereoisomer (Table I). For isolation of the target amino acid, the resulting mixture of diastereomeric complexes was subjected to hydro-chloric acid degradation in 2N HCl at 45 - 50°C, the optically active target amino acid was separated from the hydrolysate by ion exchange, recrystallized from C_2H_5OH:H_2O (1/1) solution and characterized by physicochemical and HPLC analysis (Figure 1, Table I).

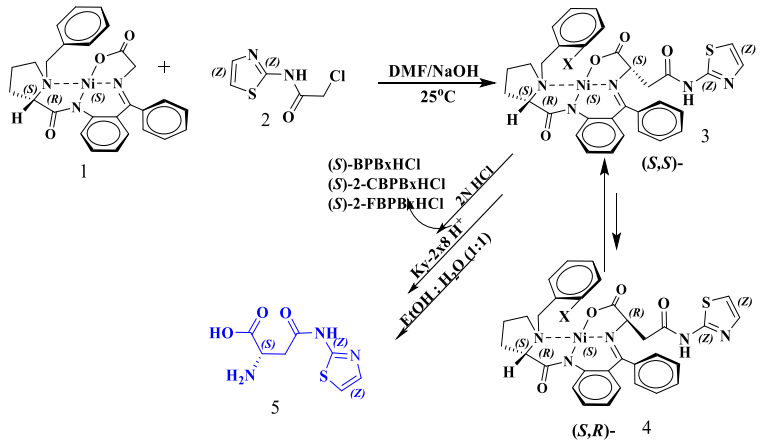
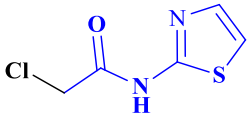
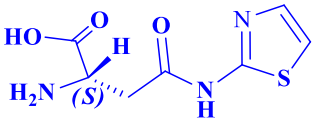


Figure 1.
The synthesis of the non-protein amino acid (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine

Table I
The chiral HPLC analysis data

Alkylating reagent	Product complex yield, %	(*S*,*S*)/(*S*,*R*) (%)*	Synthesized amino acid	Chemical yield, %	Enantiomeric yield, %
	**70**	93.23/6.77		70	98.2

For the synthesis of dipeptide containing the non-protein amino acid (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine **(5),** at the first stage, conversion of the N-t-BOC-(*S*)-alanine **(6)** to succinimide ester was carried out according to Figure 2. During the reaction, N-hydroxysuccinimide ester (HOSu) (7) and dicyclo-hexylcarbodiimide (DCC) were used as water splitting agents, and dioxane and methylene chloride were used as solvents. As a result of the reaction, carried out according to a previously developed method, stable N-tert-butoxycarbonyl-(*S*)-alanyl-N-oxy-succinimide ester (8) was obtained [21]. At the next stage, in the presence of 0.5N aqueous NaOH in dioxane medium, the condensation reaction of the activated ester of N-BOC-(*S*)-alanine with (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine (5) amino acid was carried out at room temperature. As a result, N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine **(9)** dipeptide was synthesized (Figure 2).

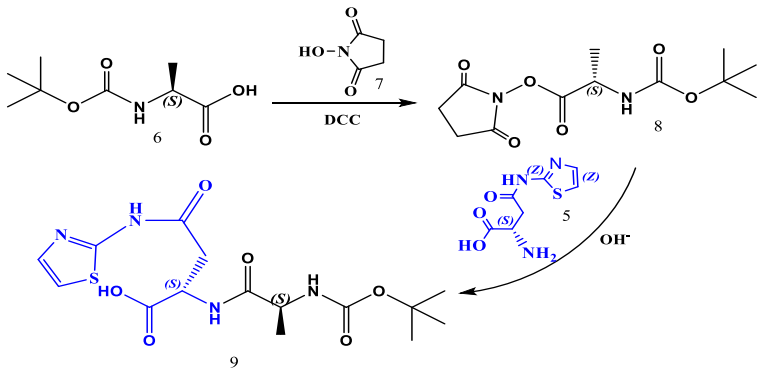


Figure 2.
The synthesis of N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine

Biological activity

Antifungal activity. The results are shown in Table II. Upon addition of (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine and N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine, test-fungi in comparison with the control showed evident inhibition of sporulation and mycelium growth, which enhanced with the increase in the concentration of the studied substances in the nutrient medium (Table II, Figure 3 and Figure 4).

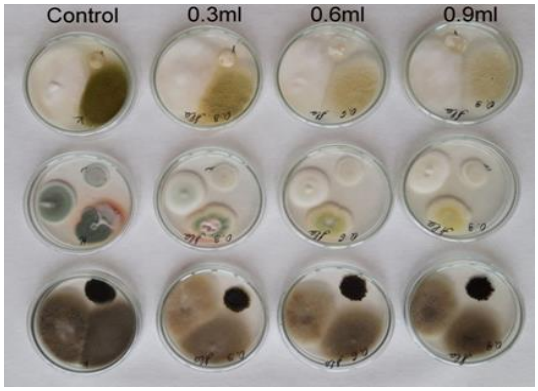


Figure 3.
Assessment of the antifungal activity of N-BOC-(S)-alanyl-(S)-β-(thiazol-2-yl-carbamoyl)-α-alanine replicates were repeated without exception

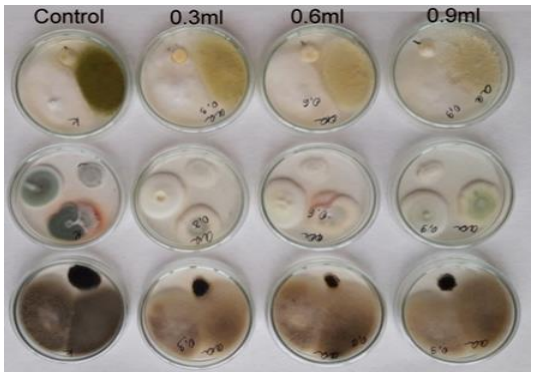


Figure 4.
Assessment of the antifungal activity of (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine replicates were repeated without exception

As can be depicted in Table II, the antifungal activity of N-t-Boc-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine dipeptide is more pronounced compared to the initial non-protein amino acid in the case of 0.9 mL volume of *Aspergillus versicolor* 12134 strain, and the synthesized compounds mainly show equal effects on the selected fungal strains.

Table II

Assessment of the antifungal activity when adding (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine and N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine

Names and numbers of strains according to MDC	(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine			N-BOC-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine		
	0.3 mL	0.6 mL	0.9 mL	0.3 mL	0.6 mL	0.9 mL
Aspergillus versicolor 12134	+	+	++	+	++	+++
A. flavus 10567	+	++	+++	+	++	+++
A. candidus 10711	+	++	++	++	++	++
Penicillium chrysogenum 8190	+	+	++	+	+	++
P. aurantiogriseum 12053	++	+++	+++	+	++	+++
P. funiculosum 8258	+	+	+	+	+	++
Alternaria alternata 8126	+	+	++	++	++	++
Ulocladium botrytis 12027	+	+	++	++	++	++
Aurobasidium pullulans 8269	+	+	++	+	+	+

+++ – active inhibition of mycelial growth and sporulation: ++ – moderate inhibition of mycelial growth and sporulation; + – inhibition of sporulation

Conclusions

The non-protein amino acid (*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine was synthesized by the asymmetric synthesis, on the basis of which, applying the activated esters method of classical peptide synthesis, it was possible to synthesize N-tertbutoxycarbonyl-(*S*)-alanyl-(*S*)-β-(thiazol-2-yl-carbamoyl)-α-alanine dipeptide undescribed in the literature. Antifungal activity studies revealed that both the synthesized amino acid and dipeptide inhibited the growth of all tested fungal strains.

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Conflict of interest

The authors declare no conflict of interest.

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