

Novel synthetic peptides inhibiting the growth of multi-drug resistant *Pseudomonas aeruginosa* strains

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Currently non-protein amino acids and peptides based thereon are widely used in biotechnology and pharmacology. Peptides composed of non-protein α -amino acids occupy a special place among active compounds. Design of many modern antibacterial, antiviral, antitumor and other drugs is based on the property of non-protein amino acids and peptides either to inhibit or enhance the activity of cell targets. Short peptides synthesized from non-protein amino acids are promising alternatives to small molecule drugs. These compounds have several advantages: high activity, high specificity, targeting capabilities, minimal drug-drug interactions, low toxicity, etc.

Optically active heterocycle substituted non-protein α -amino acids and peptides based thereon have been screened for their ability to inhibit the growth of multi-drug resistant *Pseudomonas aeruginosa* strains isolated from soil. *P.aeruginosa* strain 9211 is resistant to ampicillin (Ap^R), PANSEF^R (cephalosporin of the third generation), chloramphenicol (Cm^R), amoxicillin (Amox^R) and is sensitive to augmentin (Aug^S) and kanamycin (Km^S). *P.aeruginosa* strain 9311 is Ap^R, PANSEF^R, Amox^R, Aug^R. *P.aeruginosa* strain 5249 is Ap^R, PANSEF^R, Amox^R, Aug^R, Cm^R, Km^R. All synthetic amino acids and peptides used in this study have been synthesized at the SPC "Armbiotechnology" NAS RA and YSU [1,2]. According to obtained results tripeptide alanyl-glycyl-(S)- β -[4-allyl-3-(pyridin-4'-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine, dipeptide N-formyl-methionyl-(S)- β -[4-allyl-3-(2'-chlorophenyl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine and (S)- β -[4-allyl-3-(furan-2-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine have inhibited the growth of these strains in both the medium containing antibiotics and antibiotics free. Alanyl-glycyl-(S)- β -[4-allyl-3-(pyridin-4'-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine has demonstrated bactericidal effect on the studied *P.aeruginosa* strains. Moreover this peptide has also the ability to inhibit collagenase activity (IC₅₀=11,5mM). It has been shown that these compounds have no influence on the growth of *Escherichia coli* DH5 α strain.

Alanyl-glycyl-(S)- β -[4-allyl-3-(pyridin-3'-yl)-5-thioxo-1,2,4-triazol-1-yl]- α -alanine and N-formyl-methionyl-(S)- β -[4-propyl-3-butyl-5-thioxo-1,2,4-triazol-1-yl]- α -alanine have inhibited the growth of the *P. aeruginosa* strain 9211 in the medium, containing ampicillin or amoxicillin. However, in the antibiotic free medium these peptides have no influence on bacterial growth. Taking into account these results it may be suggested that these peptides are inhibitors of bacterial beta-lactamase, similar to clavulonic acid. In contrast, these compounds do not affect the growth of *P. aeruginosa* 9311 and *P. aeruginosa* 5249. Thus, the above mentioned peptides can overcome multi-drug resistance of *P.aeruginosa* strains. Their antibacterial properties depend on both the growth conditions (medium) and peptide structure.

References

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