

Designing New Potential Antiviral and Antibacterial Biological Active Compounds Using Special Unnatural Amino Acids and Polymers



Armenia - Georgia collaboration to develop New Potential Antiviral and Antibacterial Biological Active Compounds



Funded by Japan

SDGs



Yerevan
State University
YSU



Scientific and Production Center
"Armbiotechnology" NAS RA
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PROJECT:AM-2705



Agricultural
University of Georgia

Introduction

Purpose

Scope Of Activities

Outcome

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Background and Significance

- Infectious diseases, particularly viral infections, remain a significant global health challenge. The effectiveness of existing treatments is often undermined by the emergence of drug-resistant pathogens. The COVID-19 pandemic underscored the urgent need for novel therapeutic strategies, including the development of compounds targeting previously unexplored enzyme pathways.
- **Non-protein amino acids** play a crucial role in expanding the genetic code, enabling the design of proteins with enhanced stability, catalytic properties, and novel functionalities. They are widely used in drug development to improve pharmacokinetics, bioavailability, and metabolic stability, as seen in antimicrobial peptides and fluorinated compounds.

Focus Areas



Antiviral Research:

Inhibitors targeting viral polymerases, proteases, and other enzymes critical to viral replication.



Antibacterial Research:

Focus on non-protein amino acids and peptides to replace traditional antibiotics, especially against MDR (multi drug resistance) strains.



Cancer Research:

Development of inhibitors targeting **Epidermal Growth Factor Receptor** (EGFR) and **Mitogen-Activated Protein Kinase 14** (MAPK14) as a strategy for anti-inflammatory and anticancer therapies.

Create novel bioactive compounds combating viruses and antibiotic-resistant bacteria.

- The project started in 2022 with the main objective to create new types of biological active compounds that can fight harmful viruses, such as the coronavirus, and bacteria that are resistant to antibiotics.



Research activities



Antibiotic Resistance Testing:

- ✓ Localization of antibiotic resistance genes in *P. Aeruginosa* strains was investigated through transformation studies



Synthesis of Unnatural α -amino Acids

- ✓ More than 25 new non-protein α -amino acids were synthesized.
- ✓ More than 10 dipeptides with non-protein amino acids were synthesized and purified.



Biological Activity Studies:

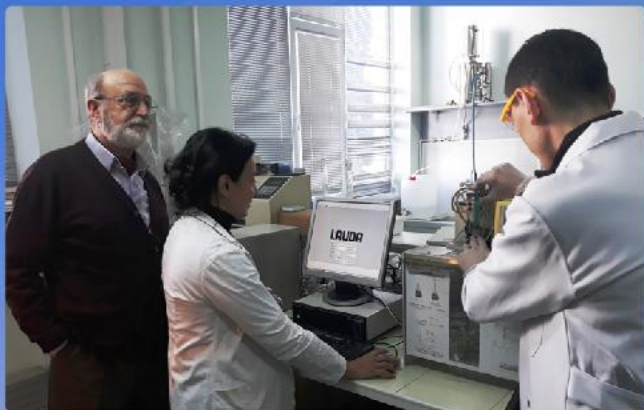
- ✓ The impact of 12 non-protein amino acids and peptides on collagenase activity was studied.



Docking Analysis for Target Receptors:

- ✓ Interaction of 14 non-protein amino acids and their peptides with Transmembrane Serine Protease 2 (TMPRSS2) was analyzed.
- ✓ Over 80 compounds were in silico tested against SARS-CoV-2 RdRp (the virus that causes COVID-19), human Epidermal Growth Factor Receptor (EGFR kinase) and Mitogen-Activated Protein Kinase 14 (MAPK14).

Achievement: Application of Research Results



Potential for Drug Development:

Several promising compounds were identified through docking studies for their interactions with critical receptors such as TMPRSS2, 3CLpro, and EGFR kinase. These compounds have potential applications as antiviral and antibacterial drugs.



Contributions to Antibiotic Resistance:

The study of antibiotic resistance genes in *P. aeruginosa* provides valuable insights into combating drug-resistant infections, an urgent global health issue. The discovery of new antibacterial compounds with activity against resistant strains could help address the growing threat of antimicrobial resistance.



Development of New Materials:

The synthesis of non-protein amino acid based polymers with high molecular weight opens new possibilities in materials science, which could lead to advancements in drug delivery systems and other biomedical applications.

Benefits to Society

Public Health Impact:

The development of novel antiviral and antibacterial compounds could lead to new treatment options for infectious diseases, and antibiotic-resistant infections, improving global health outcomes.



Antimicrobial Resistance Solutions:

By identifying compounds that target resistant bacteria, the research contributes to the fight against antimicrobial resistance (AMR), which is critical for ensuring the continued effectiveness of antibiotics in treating infections.



Scientific Advancement:

The results of this research add to the global scientific knowledge on antiviral and antibacterial drug development, providing valuable data for future studies and potential clinical applications.



Publications in High-Impact Journals

Molecular Catalysis
Vol. 100, December 2024, 114188

Synthesis and evaluation of new mono- and binuclear salen complexes for the α -alkylation reaction of amino acid substrates as chiral phase transfer catalysts

Anahit M. Hovhannisyants, Anna S. Teymasyan, Anna F. Mkrtchyan, Karapet R. Ghazaryan, Ela V. Minasyan, Olga L. Dollechen, Mikayel S. Chobanyan, Hayk Zakaryan, Giovanni N. Rovito, Ashot S. Saghyan

Synlett

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Asymmetric Synthesis of Derivatives of Amino Acids via Michael Addition Reaction and their Biological Study

Anna S. Teymasyan, Anna F. Mkrtchyan, Karapet R. Ghazaryan, Ela V. Minasyan, Olga L. Dollechen, Mikayel S. Chobanyan, Hayk Zakaryan, Giovanni N. Rovito, Ashot S. Saghyan

Synthesis of enantiomerically enriched β -substituted analogs of (S)- α -alanine containing 1-phenyl-1H-1,2,3-triazole groups

Original Article | Download | Published: 01 December 2024
Volume 55, article number 67, (2024) | The Article

Amino Acids

Abstract
A synthesis of new enantiomerically enriched derivatives of (S)- α -aminoacetic acid, containing in the β -position 1,2,3-triazole groups coupled with *o*-, *m*- and *p*-substituted alkyl residues, was developed based on Cu(I) catalyzed (3+2)-cycloaddition of azides with alkynes. As the starting materials was used the square-planar Ni(II) complex of the Schiff base of propargylglycine with the chiral auxiliary DPE (Benzylpyrrolidone) and 1,4-substituted phenyl azides. The assignment of the (S)-absolute configuration of the α -carbon atom of the amino acid residue of the main diastereomeric complexes of the cycloaddition products was carried out on the basis of positive Cotton effects in the region of 400–500 nm of the circular dichroism spectra. The target amino acids were isolated from acid hydrolyses of diastereomeric complexes using ion-exchange deprotection and crystallization from aqueous ethanol. Additional confirmation of the absolute configuration and determination of the enantiomeric purity of the target amino acids were carried out by chiral HPLC analysis. As a result, seven new non-proteinogenic (S)- α -amino acids, containing in the β -position a 1,2,3-triazole moiety, were synthesized.

molecules

Synthesis, Characterization, and Study of Catalytic Activity of Chiral Cu(II) and Ni(II) Salen Complexes in the α -Amino Acid C- α Alkylation Reaction

by Anna S. Teymasyan, Anna F. Mkrtchyan, Hamlet N. Ghazaryan, Mary V. Hovhannisyants, Robert V. Hakobyan, Karapet R. Ghazaryan, Anna S. Teymasyan, Ela V. Minasyan, Olga L. Dollechen, Mikayel S. Chobanyan, Hayk Zakaryan, Giovanni N. Rovito, Ashot S. Saghyan

ChemistrySelect

Unnatural Phosphorus-Containing α -Amino Acids and Their N-FMOC Derivatives: Synthesis and In Vitro Investigation of Anticholinesterase Activity

Anna S. Teymasyan, Anna F. Mkrtchyan, Aram S. Poghosyan, Samik A. Dacaryan, Lela A. Stepanyan, Menika H. Hovhannisyants, Anna S. Teymasyan, Aram S. Poghosyan, Samik A. Dacaryan, Lela A. Stepanyan, Menika H. Hovhannisyants, Anna S. Teymasyan, Aram S. Poghosyan, Samik A. Dacaryan, Lela A. Stepanyan, Menika H. Hovhannisyants

Graphical Abstract

Synthesized unnatural α -amino acids and their FMOC derivatives, highly pure in enantiomeric form, inhibit AChE and BuChE. AChE activity varied from 14.5 to 77.6, while (S)-2-((2H-fluoren-5-ylmethoxy)carbonyl)amino-3-((diisopropylphosphoryl)propanoic acid) peaked at 7.13%. Anti-BuChE properties ranged 4.6–71.8, with (S)-2-amino-3-((diisopropylphosphoryl)propanoic acid) showing 71.8 activity.

Anticholinesterase property

Team



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