

PLENARY PRESENTATIONS

ENZYMATIC SYNTHESIS AND ANTIHERPETIC ACTIVITY OF ALKYL-SUBSTITUTED 5-PHENYL-1,2,4-TRIAZOLE-3-THIONE DEOXYRIBOSIDES

**I.V. Fateev¹, S.A. Sasmakov², N.Kh. Akhmedova², A.A. Ziyaev², V.L. Andronova³,
R.S. Esipov¹, Sh.S. Azimova², A.I. Miroshnikov¹, I.D. Konstantinova¹**

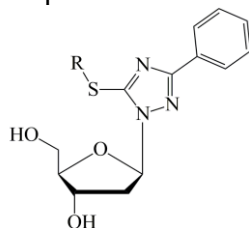
¹*Shemyakin and Ovchinnikov Institute of Bioorganic Chemistry, Russian Academy of Sciences, Miklukho-Maklaya St. 16/10, 117997 Moscow, Russia*

²*S.Y. Yunusov Institute of the Chemistry of Plant Substances, 77, Mirzo-Ulugbek Str., Tashkent, 100170, Uzbekistan*

³*D. I. Ivanovsky Institute of Virology (N.F. Gamaleya Research Center of Epidemiology and Microbiology, Ministry of Healthcare of the Russian Federation), Gamaleya St. 18, 123098 Moscow, Russia*

1,2,4-Triazole derivatives have a wide range of biological activities. The most well-known drug that contains 1,2,4-triazole as part of its structure is the nucleoside analogue ribavirin, an antiviral drug. Finding new nucleosides based on 1,2,4-triazole is a topical task. The aim of this study was to synthesize deoxyribosides of 1,2,4-triazole-3-thione derivatives and test their antiviral activity against herpes simplex virus.

Previously synthesized 5-phenyl-1,2,4-triazole-3-thione was reacted with alkyl iodide or alkyl bromide in the presence of potassium carbonate in dry acetone. In this way, methyl, ethyl, propyl, and butyl derivatives were synthesized. All the compounds were substrates for *E. coli* purine nucleoside phosphorylase (PNP), so enzymatic synthesis of their deoxyribosides was performed.



- (I) R = CH₃
(II) R = CH₃-CH₂
(III) R = CH₃-CH₂-CH₂
(IV) R = CH₃-CH₂-CH₂-CH₂

The antiherpetic activity of the synthesized bases and nucleosides was investigated. Both cytotoxicity towards *Vero E6* cells and antiviral activity increase with increasing length of the substituent at position 3 in 1,2,4-triazole.

The octanol/water partition coefficient (logP), which is a characteristic of lipophilicity, was calculated for the substances tested for antiviral activity. For both heterocyclic bases and nucleosides, an increase in lipophilicity generally leads to an increase in both toxicity and antiviral activity. For all nucleosides, a linear decrease in the CC₅₀ value is observed with increasing LogP. Additionally, for all nucleosides, a linear decrease in the IC₅₀ value is observed with increasing LogP.

A study of the substrate specificity of PNP, in relation to several homologues of 5-phenyl-1,2,4-triazole-3-alkylthione, is currently underway.