PL11. ENZYMATIC SYNTHESIS OF NUCLEOSIDE ANALOGUES OF 1,2,4-TRIAZOLE AND THEIR ANTIVIRAL ACTIVITY

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Nucleoside analogues (or modified nucleosides) are heterocyclic nitrogenous bases of natural or synthetic origin, structurally similar to naturally occurring nucleosides, containing cyclic pentoses - ribose, deoxyribose and arabinose. Modified nucleosidesare used as antiviral, anticancer and antibacterial drugs [1-3]. Recently, the role of nucleoside analogues of 1,2,4-triazole as antiviral agents has increased. Synthesis ofsuch compounds is possible either by methods of chemical synthesis or with biocatalysis. A long multi-stage chemical synthesis has a number of significant drawbacks. "One-pot" enzymatic reactions using recombinant nucleoside phosphorylases (NP) provide an alternative way of making some nucleoside analogues and has proved to be highly effective [4]. NP catalyzes the reversible phosphorolysis of ribo- or 2'-deoxyribonucleosides to form a free heterocyclic base and ribose or 2-deoxyribose-1-phosphate (transglycosylation reaction).

In this work, we studied the substrate specificity of recombinant *E. coli* purine nucleoside phosphorylase (*EcPNP*) to 3,5-substituted-1,2,4-triazoles and evaluated the antiviral effect of the obtained nucleosides on two strains of *Herpes simplex virus* type-1 (HSV-1), including a strain resistant to the antiherpetic drug acyclovir.

The main result of study was that for the first time the new 3,5-alkyl/aryl-substituted-1,2,4-triazole nucleosides have been synthesized using enzymatic transglycosylation. The surprising ability of *EcPNP* to synthesize ribo- and 2'-deoxyribonucleosides having structurally diverse hydrophobic substituents at the 3 and 5 position of 1,2,4- triazole has been discovered. 3,5-Alkyl-substituted-1,2,4-triazole nucleosides showed remarkable anti-herpes viral effect, which is expressed in the inhibition of the development of a virus-induced cytopathic effect in a culture of *Vero E6* cells infected with various strains of HSV-1.

Keywords: Antiviral, Herpes, nucleoside analouge

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