

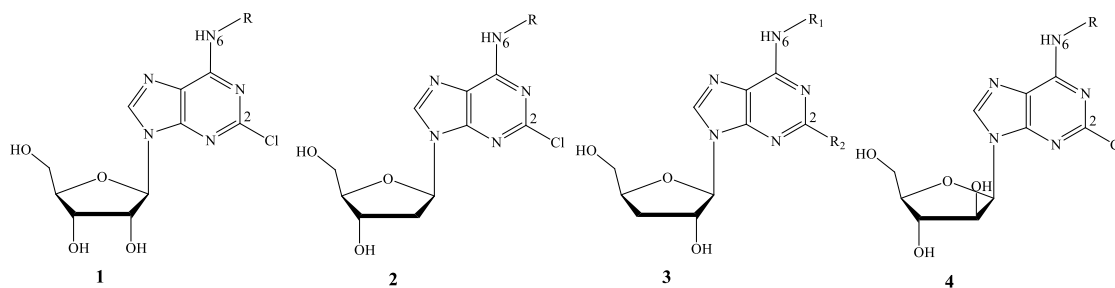
ORAL PRESENTATIONS

CYTOTOXICITY OF PURINE NUCLEOSIDES WITH C2 AND C6 SUBSTITUENTS

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A series of purine nucleoside analogues – namely the ribosides **1**, 2'-deoxyribosides **2**, 3'-deoxyribosides **3**, and arabinosides **4** – have been synthesized. These compounds bear various substituents at the C6 and C2 positions of the purine ring. At C6, the introduced groups include amide residues derived from amino acids as well as amino alcohol moieties, while the C2 position uniformly carries a halogen atom.



The cytotoxic potential of the synthesized compounds was evaluated across a panel of human and murine cell lines, including Jurkat (T-cell lymphoma), Raji (B-cell lymphoma), HEK293 (embryonic kidney epithelial cells), HepG2 (hepatocellular carcinoma), MCF-7 (breast carcinoma), L929 (mouse fibroblasts), THP-1 (monocytic leukemia), and U937 (leukemic monocytic lymphoma). Cell viability was determined by the colorimetric MTT assay, employing 3-(4,5-dimethyl thiazol-2-yl)-2,5-diphenyl tetrazolium bromide as the detection agent.

Arabinosides **4** showed low or zero cytotoxicity in all studied cell lines. For purine ribosides **1** and 2'-deoxyribosides **2** bearing a chlorine atom at C2, the introduction of a bulky substituent (an amino acid residue or amino alcohol) at C6 resulted in a marked reduction or total abolition of cytotoxic activity relative to the C6-unsubstituted analogs, namely 2-chloroadenosine (**1**, R = H) and cladribine (**2**, R = H).

In the case of 3'-deoxyribosides (cordycepin analogues) **3**, replacing hydrogen with fluorine at C2 (2-fluorocordycepin **3**, R₁ = H, R₂ = F) (1) significantly augmented cytotoxicity across all tested cell lines, whereas the parent cordycepin (**3**, R₁ = H, R₂ = H) exhibited only weak to moderate activity against a subset of lines. By contrast, the simultaneous presence of a chlorine atom at C2 and a bulky group at C6 led to a complete loss of cytotoxicity.

References:

1. Arnautova, A.O., Antonov, K.V., Zorina, E.A., Simonova, et. all., *Russ. J. Bioorg. Chem.* 2025, **51**, 1189–1205.
2. This research was funded by the Russian Science Foundation (Projects No. 24-14-00458, and No. 25-74-10097).