

Cytotoxic Activity of 1,2,4-Triazole Derivatives as Nucleoside Analogues with Antiviral Potential

Tosheva Nigora Arziyevna

Sasmakov Sobirdjan Anarmatovich

Azimova Shakhnoz Sadikovna

*Acad. S.Yu. Yunusov Institute of the Chemistry of Plant Substances, Academy of
Sciences of the Republic of Uzbekistan, MirzoUlugbek Str. 77, Tashkent, 100170,
Uzbekistan; nika1705@bk.ru*

Abstract.

The cytotoxic activity of 1,2,4-triazole-containing nucleoside analogues was evaluated in tumor and normal cell lines. The compounds showed no cytotoxic effects, in contrast to reference drugs, indicating high selectivity and supporting their potential as safe antiviral agents.

Keywords:

1,2,4-triazole; nucleoside analogues; antiviral agents; cytotoxicity; tumor cell lines; selectivity; medicinal chemistry

The development of novel nucleoside analogues remains a priority in modern medicinal chemistry due to their ability to incorporate into nucleic acids and inhibit key enzymes of nucleotide metabolism, including DNA and RNA polymerases as well as ribonucleotide reductase [1]. Particular interest is focused on modified nucleosides containing heterocyclic fragments that enhance biological selectivity and therapeutic efficacy.

We investigated a series of newly synthesized 1,2,4-triazole-containing nucleosides with pronounced antiviral activity. These compounds are structural analogues of natural nucleosides and are potentially capable of participating in replication and transcription processes, as well as interacting with cellular enzymatic

systems [2]. The presence of a 1,2,4-triazole moiety significantly alters the electronic and spatial properties of the molecules, enhancing their interaction with viral enzyme active sites and nucleic acids.

The aim of the present study was to evaluate the cytotoxic activity of 1,2,4-triazole derivatives—5-methylthio-, 5-ethylthio-, and 5-propylthio-1-(2-deoxy- β -D-ribofuranosyl)-3-phenyl-1,2,4-triazoles—on tumor and normal cell lines. The experiments were conducted on HeLa and HEP-2 tumor cell cultures, as well as on normal Vero B cells and fibroblasts, within a concentration range of 10–100 μ M. Doxorubicin and cisplatin were used as reference cytotoxic agents.

The studied compounds did not exhibit cytotoxic effects on HeLa or HEP-2 tumor cells, indicating the absence of inhibitory influence on tumor cell proliferation. Similarly, no significant cytotoxicity was observed in normal cell lines, in contrast to the reference drugs, which demonstrated pronounced toxicity even at low concentrations.

Thus, the investigated 1,2,4-triazole derivatives represent promising candidates for further pharmacological and molecular biological studies as potential antiviral agents characterized by high selectivity and low cytotoxicity.

Recent References

1. Polina N Kamzeeva., et al. Recent Advances in Molecular Mechanisms of Nucleoside Antivirals. *Current issues in molecular biology*. 2023 Aug 17;45(8):6851–6879.
2. Ilya V. Fateev., et al. Synthesis of Substituted 1,2,4-Triazole-3-Thione Nucleosides Using *E. coli* Purine Nucleoside Phosphorylase. *Biomolecules*. Volume 14, Issue 7; 2024 June.