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Synthesis and Antiviral Activity of Novel Tricyclic Analogues of Acyclovir and Ganciclovir. B. Golankiewicz[1], T. Ostrowski[1], G. Andrei[2], R. Snoeck[2] and E. De Clercq[2]
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Continuing our study on modification of physical and biological properties of acyclovir (1) and ganciclovir (2) by transforming their guanine moiety, we synthesized a series of 3,9-dihydro-9-oxo-5H-imidazo[1,2-a]purine (1,N-2-ethenoguanine) analogues of (1) and (2) bearing substitutions in the 6 or 7 or 2 and 6 positions. Substitution in the 6 position with phenyl or 4-biphenylyl group resulted in fluorescent compounds. Novel tricyclic analogues of (1) were examined for their inhibitory effects on the replication of various strains of TK^+ HSV-1, HSV-2, and TK^- HSV-1 in E_6SM cells and of TK^+ VZV, TK^- VZV and CMV in HEL cells. Compounds 6-t-butyl, 6-phenyl and 6-(4-bromophenyl) were found to inhibit the replication of TK^+ HSV-1 and HSV-2 at a concentration of 0.2-20 μg/ml (20-500-fold lower than the cytotoxic concentration) and TK^+ VZV at a concentration of 1.0-4.0 μg/ml (15-50-fold lower than the cytotoxic concentration). The substituent at the 6 position focussed the activity of the tricyclic acyclonucleosides towards particular viruses; e.g. the 6-methyl derivative was 3-30 times more potent against HSV-1 and HSV-2 than the 6-t-butyl derivative, whereas the reverse was true for VZV. The fluorescent 6-phenyl derivative, which was inhibitory to TK^+ HSV-1 and HSV-2 at a concentration of 0.2-2.0 μg/ml (50-500-fold lower than cytotoxic concentration) and to TK^+ VZV at a concentration of 1.3-1.4 μg/ml (30-fold lower than the cytotoxic concentration), seems promising for noninvasive diagnosis of herpesvirus infections.

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Synthesis and study of structural and acyclic 6-azacytidine analogues and their substituted derivates. A.S.Shalamay, I.V.Alexeeva, L.G.Palchikovska,* L.V.Nosach, N,S.Dyachenko.** *Institute of Molecular Biology & Genetics, **Institute of Microbiology & Virology of Ukrainian Acad. Sci., Kiev, Ukraine.

Nucleosides belonging to azapyrimidine series - 6-azacytidine (AC) and their N_4-carbamoylmethylic derivate (glyacidine) have been detected to inhibit DNA-viruses reproduction (such as human adenoviruses belonging to two types, herpes simplex virus, and vaccine virus) in vitro. Antiadenoviral effect of AC has been shown to be due to inhibition of viral and virus-induced polypeptides formation. Molecular biology mechanism of AC action have not been yet satisfactory explained, metabolic pathways of this compound in the infected cell are unknown; there are some data available concerning biotransformed active AC form.

So we have realized synthesis of nonglycosidic AC analogues and their N_4-carbamoylmethylic derivates - N_1-hydroxyethoxymethyl- and N_1-tetrahydrofuranyl-6-azacytosines - and have studied their antiviral properties.

The assessment of adenoviral activities possessed by the substances synthesized as well as their putative mechanism of action are to be discussed in our report.