

## IN VITRO CYTOSTATIC ACTIVITY OF 8-SUBSTITUTED AND TRICYCLIC ANALOGUES OF ACYCLOVIR

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*In vitro* cytostatic activity of 8-substituted and tricyclic analogues of acyclovir: B. HŁADOŃ, T. GOŚLIŃSKI, H. LASKOWSKA, D. BARANOWSKI, T. OSTROWSKI, J. ZEIDLER, P. RUSZKOWSKI, B. GOLANKIEWICZ. *Pol. J. Pharmacol.*, 2002, 54, 45–53.

Out of a series of twenty 8-substituted or/and 1,N-2-bridged (tricyclic) derivatives of acyclovir (a selective antiherpetic drug), known to be nontoxic to normal cells, seven compounds were found to exhibit moderate cytostatic activity in KB human tumor tissue culture system with ED<sub>50</sub> activity values ranging from 0.052–0.094 × 10<sup>-3</sup> mole/l.

The structure-activity relationship analysis indicated that the primary factors determining their cytotoxicity were: 1) bromine atom at the C-8 position of the bicyclic derivatives and 2) unsubstituted appended ring in the tricyclic derivatives. Combination of two structural elements carrying the cytotoxicity gave diverse effects, enhancement or decrease in activity depending on particular cases.

Two compounds (of four selected), 8-bromoacyclovir and 1,N-2-ethenoacyclovir, having unsubstituted 9-[(2-hydroxyethoxy)methyl] chain, showed approximately 2-fold increase in their cytotoxicity against HeLa tumor cells in the presence of the induced microsomal generating system suggesting that their cytotoxicity depends on the drug metabolic transformation into their active metabolites (intermediates) *via* MFO-system, and that structural unit of this chain is essential for abovementioned activation.

Presently found remarkable cytotoxic selectivity of acyclovir analogues against KB and HeLa tumor cells together with previously reported in the literature specific cytotoxic activity of acyclovir against murine leukemia L 1210 cells seem to be encouraging for further investigation of this class of compounds in other tumor systems.

**Key words:** *acyclovir analogues, cytotoxic activity*