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Selective Anti - Human Rhinovirus Activity of Disoxaril Analogues. P. La Colla^, M.E. Marongiu^, A. Pani, M. Artico°, A. Mai°, S. Massa° and F. Corelli§. Depts. of ^Biologia Sperimentale, Università di Cagliari, °Scienze Chimiche, Università di Roma, §Farmaco Chimico Tecnologico, Università di Siena, Italy.

A series of compounds which are structurally related to disoxaril have been prepared and tested for antiviral activity. These analogues are characterized by :

-unsubstituted or substituted pentatomic heterocycles different from isoxazole;

-the presence of a ketocarbonyl group in the five membered aliphatic chain;

-an oxazoline ring or a carboxyethyl group linked to the phenoxy moiety.

While the majority of the test compounds were totally inactive against various DNA and RNA viruses, many of them resulted potent and selective inhibitors of the HRV-14. Among them, analogues containing a chlorine- or a methyl-substituent in tiophene, furan or pyrrole rings showed a potency comparable to that of disoxaril and its pentamethylene analogue (WIN 52035). However, due to their lower cytotoxicity, some of the analogues showed a superior selectivity index. The activity against a wide panel of HRV serotypes and structure/activity relationships will be discussed.

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Inhibition of influenza A and B viruses by 2'-fluoronucleosides, mechanism of action on virus replication. M.Tisdale, J.Tuttle, G.Appleyard, M.Ellis, S.Daluge, D.Nelson, W.Miller and T.Krenitsky. The Wellcome Research Laboratories, Beckenham, U.K., Burroughs Wellcome Co., N.C., U.S.A.

A series of 2-'Fluoronucleosides were synthesised and many found to be potent inhibitors (IC_{50}'s 0.2-1μM) of influenza A virus replication in Chick Embryo fibroblast cells (CEF). Similar activity was observed against all influenza A and B strains tested, but was at least an order of magnitude higher in Madin Darby Canine Kidney cells (MDCK). Inhibition was reversed by 2'-deoxyribosides but not ribosides suggesting that these analogues were activated by cellular 2'-deoxynucleosidekinases. Correlations were observed between anti-influenza activity and a/inhibitor triphosphate levels in the two cell lines, and b/substrate specificity of calf thymus deoxycytidine kinase. Further, the triphosphate of one analogue was shown to be a selective inhibitor of the influenza polymerase complex. *In vivo*, in the mouse pneumonia model, many analogues were potent inhibitors of influenza virus replication in the lung.