

Potentiating Effect of Mizoribine on the Anti-Herpes Virus Activity of Acyclovir

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Pharmacological induction of low deoxyribonucleoside triphosphate (dNTP) levels in virus-infected cells could result in an increased antiviral effectiveness of some selective antiviral nucleoside analogues. That could be exploited as a new combined strategy in the treatment of herpes virus infections. From this point of view the alteration of antiherpes activity of acyclovir (ACV) in combination with mizoribine (N'-[β -D-ribofuranosyl]-5-hydroxyimidazole-4-carboxamide) (MZR), an inhibitor which lowers the intracellular pool of dGTP, was studied. MZR applied alone at non-toxic concentrations had no effect on herpes simplex virus type 1 (HSV-1) replication in human embryonic skin-muscle fibroblasts (HESMF). The combination of MZR and ACV acts synergistically, as measured by the virus yield assay in the above mentioned system. The potentiating effect of MZR on the anti-HSV-1 activity of ACV was reversed by guanosine (Guo). In this case dGTP could be considered as the "key metabolite" responsible for the higher effectivity of the combination of drugs.