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ANTIVIRAL DRUG IZATIZON RESTORES INTERFERON ACTION. THE ENLARGEMENT OF INTERFERON ANTIVIRAL ACTIVITY SPECTRUM.

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Izatizon is a highly effective commercial liquid form of methisazone. In vitro (HEp2 cell line) study of viral genes expression (E1A, DBP-, VAI RNA-, adenovirus human, type 1), and of cell interferon alpha2 expression gene in the course of izatizon application has been provided. Early viral transcription delay and increased interferon synthesis have been observed. Inhibition of VAI RNA synthesis has been also detected. Adenoviruses are known to be resistant to interferon treatment, and the viral reproduction was not affected by recombinant human intereferon alpha2. As VAI RNA promotes the resistance of adenoviruses for interferon treatment, the antiviral effect of interferon can be markedly increased in the presence of drug. The using of izatizon led to striking stimulation of interferon action against influenza viruses and Herpesviruses. As many another viruses can posess an analogical mechanism of interferon resistance, we suppose the existing of the common mechanism of drug antiviral action.

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Antiviral Action of Glutathione: Study on the Mechanism.

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Our previous studies demonstrated that exogenous glutathione (GSH) was able to exert a strong antiviral action against both DNA and RNA viruses *in vitro*. GSH is a cysteine containing tripeptide which plays a number of important roles in cell physiology; in particular, it provides cells with reducing equivalent and functions as a major cellular antioxidant. The aim of the present study was to elucidate the mechanism(s) by which GSH induced inhibition of virus replication. We used two virus/host cell systems: i) AGMK (37RC) cells infected with parainfluenza-1, Sendai virus (SV) and ii) VERO cells infected with Herpes-1 (HSV-1) virus. In both cell lines, the intracellular content of GSH was determined, by spectrophotometric analysis, at different times after SV and HSV-1 infection, with or without addition of exogenous GSH. Endogenous GSH content significantly decreased (80% inhibition respect to uninfected cells) at early times (20-30 min) after virus challenge, and it remained at low levels until cell death. The addition of exogenous GSH at antiviral dose (15mM) to monolayers infected with SV or HSV-1, induced a significant increase in internal glutathione levels, measured after cell lysis, 24 hrs post-infection. The GSH increment was associated to the block of virus replication (93-96% inhibition respect to the control for both SV and HSV-1). PAGE analysis of ^{35}S-labelled proteins showed that the addition of exogenous GSH did not alter the pattern of cellular proteins in both uninfected and infected cells, while it specifically blocked the synthesis of some virus proteins. Immunoblot analysis using polyclonal anti-HSV and anti-SV antibodies, showed that the glycoproteins of viral envelope constitute the major target for GSH antiviral activity.