175

Seasonal Changes in Metabolism in the Woodchuck Hepatitis Virus Model Affect the Toxicity of the Antiviral Nucleoside Analog FEAU. C.J. Nielsen[1], B.C. Tennant[2], A.J. Kempf-Grote[1] and M. A. Ussery,[1] [1]DAVDP/Antiviral Research Laboratory (HFD-530), Rockville, MD 20857, [2]College of Veterinary Medicine, Cornell University, Ithaca, NY 14853

The antiviral activity of the nucleoside analog FEAU has been established in a number of in vitro and animal models including the eastern woodchuck chronically infected with woodchuck hepatitis virus. Last year, we reported initial results of studies with this model in which FEAU at 2 mg/kg daily i.p. showed unexpected toxicity in animals dosed in the winter as contrasted to animals similarly treated during summer months. A subsequent study to investigate possible seasonal changes in plasma pharmacokinetics after both i.v. and i.p dosing using an HPLC method employing the 5-methyl- congener, FMAU, as an internal standard showed no remarkable differences. It was noted, however, that a previously unidentified component in the plasma samples collected in June appeared after the third day of dosing, remained in all samples during the dosing period, then gradually disappeared after dosing stopped. No such component appeared in the winter samples. While the ultraviolet spectrum of this compound is similar to FIAU, the 5-iodo- congener, with a λ_{MAX} near 287 nm, initial mass spectral results suggest that this material is not a metabolite of FEAU. This is based on a comparison with the mass spectra of FEAU, FMAU, FIAU, and FAU, the deiodinated metabolite of FIAU. Since this unexpected component appears only in animals dosed with FEAU in the summer, it is possible that it is the product of a protective metabolic pathway that does not function at the same level, if at all, during the winter months.

FEAU =2'-Fluoro-5-ethyl-1-β-D-arabinofuranosyluracil

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176

Bone Marrow Mononuclear Cells Producing IL-1 and IL-2 Inhibited by HBV in Vitro and in Vivo

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The levels of interleukin-1 and interleukin-2 production in 16 healthy blood donors' bone marrow mononuclear cells infected by HBV in vitro and on 16 cases with chronic hepatitis B was simultaneously assayed. The evidence of virus growth is based in the detection of HBcAg in bone marrow mononuclear cells by immunoperoxidase assay. It was found that HBcAg is positive in 50%(in-vitro) and 43.7%(in vivo) respectively($P<0.05$).The level of interleukin-1 and interleukin-2 production is markedly decreased in both HBV infected groups compared with controls($P<0.01$) and interleukin-1 and interleukin-2 decreased more significantly in HBcAg positive cases than that of HBcAg negative cases($P<0.01$). There was highly significant correlation (0.001) between levels of interleukin-1 and interleukin-2. The result suggest that HBV can infect and replicate in human bone marrow mononuclear cells in vitro and in vivo. The decrease of interleukin-1 and interleukin-2 level may be closely related to the difficulty in HBV elimination.