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1-Morpholinomethyl-tetrahydro-2(1H)-pyrimidinone (MCU): Selective Inhibitor of Influenza Virus Reproduction

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MCU is a compound originally synthesized by D. Sidzhakova et al. (Arch. Pharm. 315: 509, 1982). It possesses pronounced inhibitory effect on influenza virus A(H3N2) and B reproduction in cell cultures and embryonated eggs, as well as marked protective action in infected mice. MCU showed an especially high activity towards different variants of influenza virus A(H3N2) growth in embryonated eggs, even when massive virus inocula were used. MCU in ovo activity was found superior than that of rimantadine. A moderate effect of MCU was recorded against influenza virus A(H1N1) strains in MDCK cells. A MCU-resistant mutant of influenza virus A/Hong Kong/1/68 (H3N2) was obtained after five passages in chick embryos in the presence of 3 mg MCU per embryo. The comparative study of certain structural proteins isolated from MCU-resistant and MCU-sensitive mutants by ELISA with monoclonal antibody panel demonstrated some changes in the antigenic structure of 1A site of M1 protein of the MCU-resistant mutant. M1 protein is considered as a presumed target of the MCU effect on influenza virus reproduction.

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EXPERIMENTAL TRANSMISSION OF DUCK HEPATITIS B VIRUS TO PEKIN DUCKLINGS : A POTENT MODEL FOR IN VIVO EVALUATION OF ANTI-HBV DRUGS.

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We have previously demonstrated the antiviral effects of 2' fluoroarabinopyrimidine nucleosides (FMAU, FIAC) and araAMP in chronically WHV-infected woodchucks. Nevertheless, woodchuck is not very convenient in experimental practice. Thus in an attempt to develop a more suitable model, we have used experimental DHBV infection in ducklings on 3 days posthatch. We indeed observed that in these ducklings, a viremia peak lasting three weeks consistently occurs following experimental infection.In this experiment, we have assessed the antiviral drugs in this animal model. Twenty four ducklings were infected at three days of age by inoculation with an infectious DHBV DNA-containing serum. Three days after inoculation, four ducklings in each treatment group were treated twice daily by intraperitoneal injection with FMAU (0.8 and 1.6 mg/kg/day), FIAC (8 and 40 mg/kg/day) for 5 days or ara AMP (20 mg/kg/day) for 15 days. The effect of treatments was followed by the detection of DHBV DNA by dot-blot hybridization in serum samples obtained every 2 days for one month. All ducklings developped viremia. In FMAU and FIAC treated ducklings, serum DHBV DNA levels were significantly lower than in the control group. In ara AMP treated ducklings, viremia was less affected at the dose used. No weight loss and other apparent toxic side effects was observed during treatment by contrast to those reported in woodchucks.These preliminary results showed that in this duckling model FMAU and FIAC significantly inhibited experimental DHBV infection. They provide a basis for further evaluation of antiviral drugs using early experimental infection in this more convenient hepadnavirus model. In addition, duck appears less sensitive to toxic effects of antiviral compounds than woodchuck.