and 8 had to be euthanized on days 7–11 due to disseminated infection, hind limb paralysis or more than 10% of body weight loss. None of the 10 mice infected with dUY11 exposed virus shed detectable infectious virus, became clinically ill, or had to be euthanized. Mice were next vaginally treated with dUY11 or vehicle before infection. The preliminary results of these experiments suggest that dUY11 also partially protects mice from infection. In conclusion, virion exposure to RAFIs protect female mice from vaginal infection with a sexually transmitted enveloped virus.

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Evaluation of C-5 Substituted Uracil Acyclic Phosphonates as Substrates or Inhibitors for DTMP and UMP–CMP Kinases and Potential Antipox Derivatives

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In the aim of designing nucleotide phosphonate analogs able to be activated by phosphorylation in cells and to be potential antipox agents, the reaction of uracil acyclic phosphonates with human cytosolic TMP and UMP-CMP kinases was evaluated as well as with TMP kinase from vaccinia virus. Surprinsingly uracil acyclic phosphonates, with an allyl or pentenyl group as acyclic moiety, were found to be substrates of TMP kinase, but not of UMP-CMP kinase, in contrast with dUMP, phosphorylated by both enzymes. The uracil acyclic phosphonates, with vinyl, allyl or pentenyl as acyclic moiety, were also modified on the C-5 of the base by an halogen (F, Cl and Br) or a phenyl group. Several 5-halogeno-uracil derivatives were substrates for recombinant TMP kinases, with a catalytic efficiency significantly higher than AZTMP. All derivatives were found to inhibit UMP–CMP kinase activity. As shown by fluorescent competition assays, some derivatives were found to bind to UMP site and/or in some cases, surprisingly, to ATP site. The 5-halogeno-uracil derivatives specificity is presumably due to the stacking interaction between uracil and Phe72 of human TMP kinase (Phe68 of vaccinia enzyme). These derivatives should now be tested as potential antiviral molecules after chemical modification to make them available inside cells.

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Effects of PTU-23, HBBb, Ribavirin and Oxoglaucine on the Replication of Feline Calicivirus in CrFK Cells

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Effects of PTU-23, HBB, Ribavirin and Oxoglaucine on the Replication of Feline Calicivirus in CrFK Cells Julian D. Tumbarski and Angel S. Galabov Department of Virology, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria Searching for substances suppressing the replication of caliciviruses is of special interest due to their particular role in the human and veterinary infectious pathology. The investigations for a development of effective anti-calicivirus chemotherapy are important due to the lack of specific means for calicivirus infections treatment and prevention. Caliciviridae possess a RNA(+) genome and a virion structure close to one of Picornaviridae. Based on some similarities, investigations for anti-calicivirus activity of several highly efficient inhibitors of picornavirus replication were carried out. Research was done with feline calicivirus (FCV) F9 strain on Crandell's feline kidney cell line (CrFK). The following compounds were tested: PTU-23 (*N*-phenyl-*N*′-3-hydroxyphenylthiourea), HBB (2-a-hydroxybenzyl benzimidazole), known also as inhibitors of picornavirus-specific RNA synthesis, ribavirin (a broad-spectrum antiviral agent) and a recently described aporphinoid alkaloid oxoglaucine. Anti-calicivirus activity and citotoxicity were tested through CPE inhibition test and neutral red uptake assay (vs. virus inoculating doses ranging within 1 and 10,000 $CCID_{50}$). Kinetics of the effect of compounds was determined by timing-of-addition study in the one-step virus growth cycle experimental design. The compounds were added to DMEM in their maximal effective concentrations at 0 h, 1 h, 2 h, 3 h, 4 h and 5 h after the virus adsorption. The samples were freezed subsequently at 2 h, 3 h, 4 h, 6 h and 8 h. The infectious virus titer was determined by Reed and Muench. Anti-calicivirus effect in low virus inoculation doses possess all of the tested compounds. A marked activity of PTU-23 (when added during the latent period of virus replication cycle) was observed, while HBB and ribavirin (present at the same stage) showed a borderline effect.

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