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Selective Activity of Cholic Acid and Related Compounds Against Herpes Simplex Virus Type 2. SF Reising, N Bourne, F El-Awar and LR Stanberry. Children's Hospital Research Foundation, University of Cincinnati College of Medicine, Cincinnati, OH, USA.

Cholic acid and related bile salts have been reported to have selective activity against human immunodeficiency virus replication in vitro. We have been exploring this class of anionic surfactants as possible topical microbicides for intravaginal prophylaxis against sexually transmitted diseases. To this end we have examined the activity of cholic acid and related derivatives against HSV-2 replication in HeLa cell monolayers. Our results indicate that six bile salts: cholic acid, taurocholic acid, taurolithocholic acid, taurolithocholic acid 3-sulfate; lithocholic acid 3-sulfate and glycolithocholic acid 3-sulfate demonstrate a selectivity index greater than 1 with ED_{50} values for HSV-2 of less than 700ug/ml (<0.1%). Based on the promising in vitro activity we examined the in vivo efficacy of 5.0% cholic acid in a polyethylene glycol vehicle. Mice primed with medroxyprogesterone acetate were intravaginally administered the cholic acid preparation immediately prior to intravaginal instillation of approximately 10 LD_{50} HSV-2. Thirty percent of the mice receiving cholic acid prophylaxis survived while all of the vehicle control animals died within 20 days post-inoculation ($p<0.05$). Additional bile salts and vehicles are currently under study.

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Synthesis, Molecular Conformation and Antiherpes Activity of N^1-Substituted Analogs of (E)-5-(2-bromovinyl)-2'-deoxycytidine (BrVdCyd).

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The potency of BrVdCyd against Herpes Simplex Virus type 1 (HSV-1) in VERO cells is increased in the presence of deaminase inhibitors [Aduma *et al.*, Antiviral Res. 13, 11 (1990)]. Analogs of BrVdCyd by substitution at N(4) were synthesized to confer resistance to deamination by deaminating enzymes. N^1-Methyl-BrVdCyd was inactive against HSV-1 in VERO cells up to 512 μM (highest concentration tested), whereas N^1-acetyl-BrVdCyd (AcBrVdCyd), N^1-butanoyl-MMdCyd (BuMMdCyd) and N^4-propanoyl-MMdCyd (PrMMdCyd) were potent inhibitors of HSV-1 replication. Amide derivatives were more active than the parent nucleoside.

The molecular conformation by NMR spectroscopy was determined. The relationship between molecular conformation and antiviral activity revealed that analogs in which the N^1-substituent is proximal to C(5) of the pyrimidine ring are active.

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