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THE CONTRACEPTIVE MICROBICIDE WHI-07 PREVENTS GENITAL TRANSMISSION OF FELINE IMMUNODEFICIENCY VIRUS (FIV) IN THE VAGINAL AND RECTAL TRANSMUCOSAL MODEL FOR FELINE AIDS (FAIDS)

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INTRODUCTION: The current pandemic of sexually transmitted HIV/AIDS has created an urgent need for a new type of microbicide: one that is both a spermicide and a virucide. WHI-07 [5-bromo-6-methoxy-5,6-dihydro-3'-azidothymidine-5'-(p-bromophenyl)-methoxy alaninyl phosphate] is a potent anti-HIV spermicide. We evaluated a gel-microemulsion of WHI-07 as a single agent and in combination with a novel dual-function spermicide, vanadocene dithiocarbamate (VDDTC), to prevent vaginal as well as rectal transmission of FAIDS by chronically FIV-infected feline T cells.

METHODS: Forty-six SPF domestic cats in 7 subgroups were given a single dose of highly infectious cell inoculum (7 million FIV(Bangston)-infected feline T cells) intravaginally or intrarectally. Genital transmission of FIV was monitored in recipient cats by the appearance of plasma viral antibodies to FIV Gag proteins (p26 and p15) by Western blotting (WB), virus isolation (VI) of blood leukocytes by FIV reverse transcriptase (RT) activity and FIV-specific polymerase chain reaction (PCR). Microbicidal activity was considered effective when the treated cats did not show evidence of FIV infection (by WB, VI-RT, and VI-PCR) for up to 18 weeks postchallenge.

RESULTS: A single dose of the infected cell inoculum efficiently transmitted FIV infection when delivered into the vagina (100%) or rectum (66%). Pretreatment of the vagina or rectum (13 cats) with 2% WHI-07 or 2% WHI-07 plus 0.25% VDDTC significantly ($P = 0.004$) protected cats from genital transmission by the highly infectious

inoculum when compared with 5% Nonoxynol-9-treated (10 cats) or placebo control (13 cats) groups. Histology of WHI-07 or WHI-07 plus VDDTC-exposed cervicovaginal tissues revealed lack of mucosal toxicity.

CONCLUSIONS: Using the vaginal and rectal transmucosal model for FAIDS, our studies demonstrated that WHI-07 either alone or in combination with a vanadocene has clinical potential for the development of a dual-function anti-HIV microbicide for sexually active women.

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