as follows: HBB > oxoglaucine > ribavirin > disoxaril > PTU-23 > arildone > S7.

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Broad Anti-Infective Activity of Viracea, An *Echinacea*-derived Product

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Echinacea is a well-studied herb noted for stimulating the human immune system. There is evidence that *Echinacea* has the potential to treat a broad range of infectious diseases. Viracea, a proprietary extraction and formulation of *Echinacea* is presently marketed as RELEEV^{TM}, a commercial OTC product for the treatment of cold sores. Preclinical data indicates this product is active against HSV-1 and HSV-2. We have evaluated the broad based anti-infective properties of these products, including RELEEV and Viracea 2,4, an unfractionated product comprised of the aerial parts of *Echinacea purpurea* and *Commiphora myrrha*. RELEEV and Viracea 2,4 were highly active against HIV-1, HIV-2, HSV-1, HSV-2, BVDV and the HCV replicon 122106. Activity against laboratory-derived strains of HIV was detected at greater than 1:30,000 dilutions though lesser levels of activity were found against clinical strains of HIV-1 and HIV-2, suggesting a mode of action involving entry inhibition. MAGI cell-based assays confirmed the ability of the natural product to inhibit HIV entry. Similar levels of activity were detected against HSV-1_{HF} and HSV-2_{MS} in VERO cells, HBV in HepG2.2.15 cells, $BVDV_{NADL}$ in MDBK cells, and against the HCV replicon in Huh-7 cells. Respiratory syncytial virus (RSV) was inhibited, though antiviral activity was not observed against Influenza A or B. Although the mechanism of action of the product against HIV and herpesviruses seems to involve cell surface effects, activity of the product against HBV and in the HCV replicon assay suggests an intracellular mode of action. The range of action of the material also extends to bacteria, where both products were inhibitory in MIC assays to Gram positive and Gram negative bacteria (*S. aureus* and *E. coli*). Thus, the anti-infective attributes render *Echinacea*-derived products amenable to continued development as a treatment for infectious disease. The potent activity against HIV, HSV, and HCV suggests the potential for the development of an effective topical microbicide. A product is being developed for that use. Currently, bioassay-guided fractionation is being performed to define the active molecules responsible for the observed anti-infective activity.

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Serine Palmitoyltransferase Inhibitor Suppresses HCV Replication in a Mouse Model

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Serine palmitoyltransferase (SPT) is a first-step enzyme in the sphingolipid biosynthetic pathway. NA255 and myriocin is an inhibitor of SPT and suppresses replication of the hepatitis C virus (HCV) replicon. However, it is still unknown whether this SPT inhibitor suppresses HCV replication in vivo. We investigated the anti-HCV effect of SPT inhibitor against intact HCV using chimeric mice with humanized liver infected with HCV genotype 1a or 1b. We administered myriocin into HCV infected chimeric mice and succeeded in reducing the HCV RNA levels in serum and liver to 1/10 to 1/100 of the levels prior to the 8-day treatment. Furthermore, combined treatment with pegylated interferon reduced the HCV RNA levels to less than 1/1000 of the control levels. In conclusion, we elucidated the inhibitory mechanism of HCV replication by SPT inhibitor in vitro and determined that SPT inhibitor inhibits HCV replication in a chimeric mouse model with humanized liver. Our results suggest that SPT may be an effective target of drugs designed to inhibit HCV replication, and that SPT inhibitor has the potential to be a lead compound in the development of new anti-HCV drugs.

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New Synthetic Histone Deacetylase Inhibitors CGMC0005 and CGMC0006 Effectively Reactivate Latently Infected Human Immunodeficiency Virus Type-1 (HIV-1) from ACH2 and J1.1 CD4+ T Cells

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Histone deacetylase (HDAC) has an important role to induce HIV latently infected cells as HIV reservoir due to the inhibitory function against virus replication by binding HIV-1 LTR promoter. In this study, we treated newly synthesized HDAC inhibitors (CGMC0005 & CGMC0006, Christal Genomics, Seoul, Korea) on the latently HIV-infected cell lines J1.1 and ACH2 to reactivate virus replication from HIV reservoir. In addition, reverse transcriptase inhibitor AZT was treated to the cells to remove viruses excised to cytoplasmor extracellular space for eradicating the latent HIV reservoir. CGMC0005 and CGMC0006 showed better or similar level of safety (CD50: 0.1–0.3 μM) in cytotoxicity compared to SAHA (CD50: 0.3 μM) or PXD-101 (CD50: 0.1–0.3 μM) used as control.