type of the substrate as well as on the presence of HIV particles and their concentration. We have seen the changes of maxima heights and their half-widths. The DS curves have shown in experiment the non-Debye behavior what could be attributed to the fractal clustering process occurring and changing at various stages of virus–cell interaction. The maxima registered for SC sample were sheared to the lower frequency region after the time needed for viral nucleic acid replication what indicates directly the emerging of newly created virions and their dissemination over the population of non-infected SC. The real significance of the applied DS method could be understood while recognizing it sensitivity to the presence of the particles having certain dipole moments and interacting with the dielectric SC ambient. The general sensitivity of DS is in the range of 0.5–2.5% depending on the instrumentation used. We have shown experimentally that the DS method could be applied for the quantitative independent description of the virus–cell interaction at various stages beginning from the infection emerging for various types of virus–cell pairs due to its general physical modeling. It could be applied both in drug design tests, anti-viral therapy trials as well as in clinical and laboratory practice.

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59
Placental and Monocyte-derived Macrophages have Different Secretome

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It is well documented that placental macrophages (PM) show lower levels of HIV-1 infection than monocyte-derived macrophages (MDM) and that soluble factors secreted in the placenta can inhibit viral replication. We tested the hypothesis that HIV-1 inhibitory factors are secreted by PM and differentially expressed in PM and MDM using proteomics. Cells were cultured for 12 days and supernatant was collected. To characterize PM supernatants, the protein profiles of PM were compared to MDM using the protein chip assay (Ciphergen). The weak cationic exchange (CM10) and metal affinity (IMAC30) surfaces provided the greatest number of protein peaks. Subsequently, proteins were separated by 1D SDS-PAGE and identified by LC–MS/MS. Significant differences were found in four protein peaks with *m/z* values of 6075, 6227, 11,662, 14,547, between PM and MDM supernatants on the CM10 chip and in three protein peaks with *m/z* values of 6158, 7740, 11,934 on the IMAC chip confirming our hypothesis. Proteins were sequenced and identified with high confidence. Worth noting are four peaks that were identified as over-expressed in PM corresponded to fatty acid binding protein-3 (FAB) (14,858 Da) corresponding to the 14,547 *m/z* SELDI-TOF protein peak. Also FKBP 12 (11,951 Da) corresponding with 11,934 *m/z* protein peak, thioredoxin (11,737 Da) and closely correlates with the 11662 *m/z* protein peak. Apolipoprotein E (ApoE, 7558 Da) corresponding to 7740 *m/z* peak. FAB plays a role in transport of fatty acids; FKBP 12 is a peptidil cis–trans isomerase's which aids in the folding of proteins and binds with high affinity to the V3 loop of the HIV-1 envelope glycoprotein; thioredoxin is and antioxidant molecule that could help control viral infection by reducing oxidative stress in macrophages; ApoE mediates binding, internalization and catabolism of lipoprotein particles, and can reduce viral entry. The identity of these proteins found increased in the PM secretome will be validated by Western blots as they could play a role in the inhibition of HIV-1 infection observed in PM.

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60
Inhibition of Human Rhinovirus Replication by Some Antivirals

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Human rhinoviruses, members of the Picornaviridae family, are among the main causative agents of viral upper respiratory tract infections and particularly of common cold. These infections are often mild and self-limiting, but multiple during the human life. The frequent appearance of HRV infections and their economic importance in terms of employee absenteeism, physician visits, and medication costs makes them a subject of primary importance. HRV infections can also be associated with more serious medical complications like acute otitis media, sinusitis, pneumonia and bronchiolitis in infants and young children. Rhinoviral infections commonly cause exacerbations of disease in individuals with underlying respiratory disorders. Until now there is no registered clinically effective antiviral chemotherapeutic agent for treatment of diseases caused by HRVs. Apart from the symptomatic therapy, the hope for an effective treatment of these diseases is the development of broad spectrum antirhinoviral drugs. The topic of the present study is antirhinovirus effect of several picornavirus replication inhibitors with different mode of action against the replication of human rhinoviruses. Monolayer cultures of human cervical carcinoma (HeLa Ohio-I) cells in 96-well tissue culture plates were used in the viral CPE-inhibition test. The action of the compounds at various viral inoculation doses (100, 1000 and 10 000 $CCID_{50}$) was studied to quantitate the antiviral activity and the cytotoxicity of the compounds. The neutral red uptake assay was used. The following compounds have been tested: ribavirin (a large-spectrum viral inhibitor, mostly of RNA viruses), arildone, disoxaril, S7, PTU-23, HBB and oxoglaucine (a compound efficient against enteroviruses initially characterized in our laboratory). The effect of the combinations of most active compounds has been studied. Two of the tested compounds, HBB and oxoglaucine, show the highest activity with a selectivity ratio (CC_{50}/IC_{50}) exceeding 137 and 190, respectively, against 100 cell culture infectious doses 50. According the activity of the tested compounds they can be arranged

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

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61
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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62
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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63
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.