

[0016] FIG. 6 shows semi-log plots of the % viable (live) cells as a function of Cohex concentration. Left plot: A549 cells. Right plot: HepG2 cells.

[0017] FIG. 7 shows linear plots of the same data as FIG. 6, showing the region of greatest cytotoxic effect. Left plot: A549 cells. Right plot: HepG2 cells.

[0018] FIG. 8 shows linear plots of the % viable (live) cells as a function of Cohex concentration. Left plot: VeroE6 cells. Right plot: 293T cells.

[0019] FIG. 9 shows results for flow cytometric assay using PI as a marker for dead cells show almost no change between 0 to ~1.2 mM Cohex.

[0020] FIG. 10 shows a curve fit of inhibition by Cohex. For purposes of fitting, the negative (-%) inhibitory % were turned into positive numbers; so 100%=100% inhibition. The IC50 for the fit was found to be 0.38 mM Cohex.

DETAILED DESCRIPTION

[0021] Hexaamminecobalt(III) (Cohex; FIG. 1), in particular the chloride salt thereof, is notable for its ability to “condense” dsDNA into toroidal-like superstructures under low salt conditions. The metal ion itself, Co(III), with its high (+)charge-density, is an ideal candidate for binding nucleotides with their high (-)charge density. Although Co(III) is not stable by itself in aqueous solutions, it is stabilized by coordinating with donor atoms (usually N) that make strong contributions to the ligand field. These coordinating donors could either be monodentate ligands, e.g., NH_3 , or polydentate chelators, such as cyclen, $\text{C}_8\text{H}_{20}\text{N}_4$. The Co(III)-chelator complexes (e.g., cobalt cyclen complexes) have been used for mechanistic studies of phosphodiester cleavage for both its efficient hydrolysis rates and kinetic inertness, whereby the kinetic inertness of Co(III) ions results in the continued binding of the complex to the hydrolyzed phosphate.

[0022] Due to the kinetic inertness of Co(III) ions, the Cohex complex sequesters the “inner-sphere” ammonia ligands from most exchange-reactions in solution; therefore, the usual interactions with solution molecules are by “outer-sphere” coordination via water bridges to the ammonia ligands and via the high charge-density of the Co(III) ion. These two characteristics play an important role in the strong attachment of Cohex to either DNA or RNA⁵ and in enabling Cohex to often substitute for hydrated $\text{Mg}^{2+}(\text{aq})$ as a cofactor in nucleic acid biochemistry. For example, Cohex complexation with 5S RNA—where Cohex was used in place of $\text{Mg}^{2+}(\text{aq})$ —was examined and found to provide no significant shifts in the λ_{max} of the absorption bands of Cohex, indicating that Cohex interaction with RNA was through outer-sphere complexation (and, of course, opposing charge attraction). It has also been reported that the number of binding sites on RNA was similar for Cohex and $\text{Mg}^{2+}(\text{aq})$ and that the number was greater than expected for simple charge neutralization of the RNA backbone. These observations demonstrate that Cohex has a great propensity to bind to nucleotides at sites similar to Mg^{2+} -binding sites and either inhibit or slow down the bio-functions of DNA and RNA.

[0023] Cohex may function as a new type of broad-spectrum antiviral compound. For example, Cohex can be effective in significantly enhancing cell viability and in depressing viral expression for Sindbis infected BHK cells, with similar significant effects of Cohex against adenovirus in A549. See US Patent Application Publication No. 2008/0182835. These observations point to the potential broad-spectrum nature of Cohex against viruses.

[0024] As disclosed herein, Cohex demonstrates antiviral properties against two additional viruses. Ebola virus is a negative-strand, filamentous, enveloped microorganism that belongs to the filoviridae family of viruses. Cohex can decrease the viral expression levels in a dose-dependent manner, in a variety of cells infected with the Ebola virus. Cohex also demonstrates antiviral properties against human immunodeficiency virus (HIV). HIV is a member of the genus lentivirus and belongs to the Retroviridae family. It has a single-strand (-)RNA genome, which is transcribed into a complementary DNA (cDNA) inside the host cell by an RNA-dependent DNA polymerase. The sense cDNA serves as a template for DNA-dependent DNA polymerase to make an antisense DNA copy, which forms a double-stranded viral DNA (dsDNA). The dsDNA is then transported into the cell nucleus where it gets integrated into the host cell’s genome. Virus replication is initiated when the integrated DNA provirus is transcribed into mRNA.

DEFINITIONS

[0025] As used herein, the term “reduce an extent of the viral infection” with regard to a patient means that the ability of viruses to multiply within a patient is at least partially reduced.

[0026] As used herein, a “patient” can be a human or other mammal.

Antiviral Uses of Cohex

[0027] It is contemplated that Cohex could be used to treat a viral infection in a patient. In one embodiment, an effective amount of Cohex is administered to a patient suspected or known to have a viral infection. Optionally, a method of treatment includes identifying a patient who is or may be in need of such treatment. The patient can be a human or other mammal, including without limitation a primate, dog, cat, cow, pig, or horse.

[0028] In an embodiment, Cohex is administered to a patient known or suspected of being infected by a virus. In a further embodiment, Cohex is administered prior to exposure of the patient to a virus. In another embodiment, Cohex is administered subsequent to exposure of the patient to a virus.

[0029] The Cohex may be administered by any of various means including orally or nasally, or by suppository, or by injection including intravenous, intramuscular, or intraperitoneal injection, or combinations of any of these.

[0030] In an embodiment, equipment for injection of Cohex in a pharmaceutically acceptable comprises at least one of a container for the compound (such as a tube, bottle, or bag), injection tubing, or an injection needle.

[0031] The quantity of Cohex effective to treat an infection can be ascertained by one of ordinary skill in the art. Exemplary amounts of Cohex include 0.5, 1, 2, 4, 8, 10, 12, 14, 16, 18, or 20 mg/kg, or more.

[0032] Viral infections that can be treated include, but are not limited to, those associated with human immunodeficiency virus (HIV), human T cell leukemia virus (HTLV), Papillomavirus (e.g., human papilloma virus), Polyomavirus (e.g., SV40, BK virus, DAR virus), orthopoxvirus (e.g., variola major virus (smallpox virus)), EBV, herpes simplex virus (HSV), hepatitis virus, Rhabdovirus (e.g., Ebola virus),