

**COBALT HEXAMMINE AS A POTENTIAL
THERAPEUTIC AGAINST HIV AND/OR
EBOLA VIRUS**

CROSS-REFERENCE TO RELATED
APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application 61/230,287 filed on Jul. 31, 2009. This application also claims the benefit of U.S. Provisional Application 61/261,018 filed on Nov. 13, 2009. Each of these applications is incorporated by reference in its entirety.

BACKGROUND

[0002] In this specification where a document, act or item of knowledge is referred to or discussed, this reference or discussion is not an admission that the document, act or item of knowledge or any combination thereof was at the priority date, publicly available, known to the public, part of common general knowledge, or otherwise constitutes prior art under the applicable statutory provisions; or is known to be relevant to an attempt to solve any problem with which this specification is concerned.

[0003] Hexaamminecobalt(III) chloride, also called Cohex, 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 positive charge density, is an ideal candidate for binding nucleotides with their high negative 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.

[0004] 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 RNA and in enabling Cohex to often substitute for hydrated $\text{Mg}^{2+}(\text{aq})$ as a cofactor in nucleic acid biochemistry.

[0005] For example, Cohex complexation with 5S RNA—where Cohex was used in place of $\text{Mg}^{2+}(\text{aq})$ —was 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.

[0006] While certain aspects of conventional technologies have been discussed to facilitate disclosure of the invention,

Applicants in no way disclaim these technical aspects, and it is contemplated that the claimed invention may encompass one or more of the conventional technical aspects discussed herein.

BRIEF SUMMARY

[0007] Cohex can inhibit viral transcription/translation via interference with viral RNA. This interference can be either via general “blockade” of the nucleotide strands from transcription/translation or may be made more overt by attaching hybridizing oligonucleotide strands to the Cohex. It has been shown that Cohex does not hydrolyze nucleotides, but does show potent antiviral properties against the Sindbis virus and Adenovirus, which are positive single-stranded (ss) RNA, double-strand (ds) DNA, respectively, and furthermore can act as an antibiotic. See US Patent Application Publication Nos. 2008/0182835 and 2010/0004187, each of which is incorporated by reference in its entirety.

[0008] In one embodiment, a method for treating a viral infection comprises administering to a patient a hexaamminecobalt(III) compound (e.g., hexaamminecobalt(III) chloride) in an amount effective to reduce an extent of a viral infection.

[0009] In a further embodiment, a method for treating a viral infection comprises administering to a human patient a hexaamminecobalt(III) compound in an amount effective to reduce an extent of an infection of the patient with Ebola virus or HIV.

[0010] In another embodiment, a kit for delivery of a hexaamminecobalt(III) compound by injection comprises a hexaamminecobalt(III) compound in a pharmaceutically acceptable carrier, and equipment for delivery thereof by injection, wherein the equipment comprises at least one of a container, injection tubing, or an injection needle.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 is an illustration of hexacoordinated Co(III), hexaamminecobalt(III) (chloride counterions not shown), and magnesium(II) hexahydrate, $\text{Mg}(\text{H}_2\text{O})_6^{2+}$, both form octahedral coordination geometry with their respective ligands.

[0012] FIG. 2 is a double-Y semi-log plot is shown of the decrease in RT activity (left), as a measure of viral activity, or uninfected cell viability (right) for HIV-1 NL4-3 isolate. “% VC” means “% Virus Control” and “% CC” means “% Cell Control.”

[0013] FIG. 3 is a double-Y semi-log plot is shown of the decrease in RT activity (left), as a measure of viral activity, or uninfected cell viability (right) for HIV-1 Ba-L isolate. “% VC” means “% Virus Control” and “% CC” means “% Cell Control.”

[0014] FIG. 4 plots levels of GFP expression in cells infected with Zaire Ebola GFP, normalized against infected cells with no therapeutic (+/-control). Left plot: Relative GFP levels for A549 cells as a function of Cohex concentration, from 2.5 μM to 5 mM. Right plot: Relative GFP levels for HepG2 cells as a function of Cohex concentration

[0015] FIG. 5 plots the levels of GFP expression in cells infected with Zaire Ebola GFP, normalized against infected cells with no therapeutic (+/-control). Left plot: Relative GFP levels for 293T cells as a function of Cohex concentration, from 2.5 μM to 5 mM. Right plot: Relative GFP levels for VeroE6 cells as a function of Cohex concentration.