Layered Double Hydroxide as Inorganic Vector for Gene Therapy

Jenny Lin Gao Literature Seminar March 22, 2001

Recently, there has been considerable interest in nanohybrids which often exhibit extraordinary high synergetic and complementary behavior between two component materials.[1,2] One of the most widely used methods in this area is the intercalation chemistry. The essential advantage of this technique is that it allows some degree of modification in the geometric, chemical, electronic and optical properties of the host and guest.[3] The combination of two-dimensional layered materials and the intercalation technique create great new opportunities in the development of new hybrids materials with desired functionality.[4]

One of the layered materials, the layered double hydroxides (LDHs), also called 'anionic clays', have received considerable attention due to their technological importance in many aspects. They have been applied to catalysis,[5] separation technology,[6] purification for environmental pollutants,[7] optics,[8] medicinal applications,[9] surface modification technology[10], and nanocomposite materials engineering.[11]

LDHs can be structurally described as containing brucite- (magnesium hydroxide-) like layers in which some divalent metal cations have been substituted by trivalent ions to form positively charged sheets. The metal cations occupy the centers of octahedra whose vertices are occupied by hydroxide ions. These octahedra are connected to each other by edge sharing to form an infinite sheet. The cationic charge created in the layers is compensated for by the presence of hydrated anions between the stacked sheets. LDHs have the general formula $[M^{II}_{(1-x)} M^{III}_{x} (OH)_2] [A^{n-}]_{x/n} \cdot zH_2O$ where M^{II} is a divalent cation (Mg^{2+}, Mn^{2+}, Fe^{2+}, Co^{2+}, Ni^{2+}, Cu^{2+}, Zn^{2+}, or Ca^{2+}); M^{III} is a trivalent ion (Al^{3+}, Cr^{3+}, Mn^{3+}, Fe^{3+}, Co^{3+}, Ni^{3+}, or La^{3+}) and A^{n-} is the interlayer anion (OH^-, Cl^-, NO_3^-, CO_3^{2-}, SO_4^{2-}, *etc.*).[12]

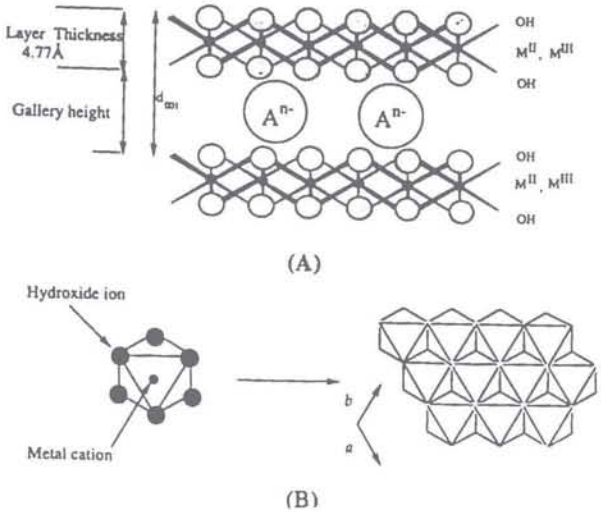

Figure 1 Schematically illustrated LDH structure.

The unique anion exchange capability of LDHs meets the requirement of inorganic matrices for encapsulating functional biomolecules with negative charge in aqueous media. Such biomolecules can be incorporated between hydroxide layers by a simple ion – exchange reactions to form bio-LDH nanohybrids. The negatively charged biomolecules intercalated in the gallery spaces would gain extra stabilization energy due to the electrostatic interaction between cationic brucite layers and anionic biomolecules. When DNA is intercalated, the hydroxide layers can play the role of a reservoir to protect the DNA from DNase degradation.[13] For its usage as gene vector for gene therapy, the hydroxide layers can be intentionally removed by being dissolved in an acidic media, which offers a way of recovering the encapsulated biomolecules.[14]

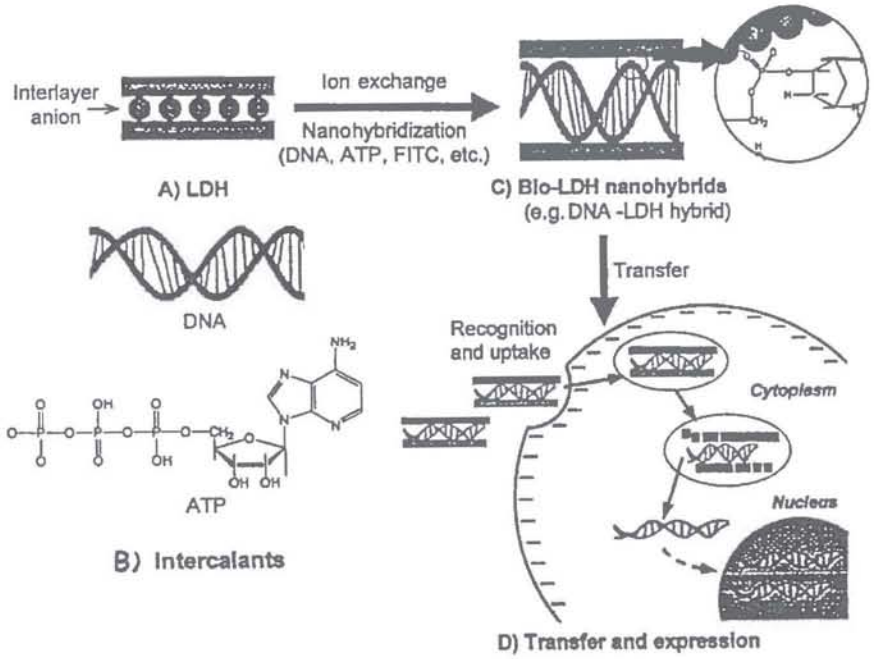

Figure 2. Schematic illustration of DNA-LDH hyridization and proposed mechanism of it into a cell

From the study of Powder X-ray Diffraction, Circular Dichroism, Infrared, and UV-visible spectra of biomolecule - LDH hybrids and the chemically well-defined biomolecules and LDH, it is concluded that the biomolecules stabilized in the interlayer space of LDH retain their chemical and biological integrity. This type of Bio – LDH hybrids exhibited pH – dependent behavior in gel electrophoresis experiment. This result strongly supported the proposal that the gene delivered by LDH can be released in the acidic regions in eucaryotic cells. Its trans-membrane delivery potential was verified by fluorescence measurement and laser scanning confocal microscopy with control experiments. A gene delivered by LDH showed 65% inhibition effect on the cancer cell growth of Human Leukemia - 60 cells.[14]

In conclusion, for the first time, the biomolecules such as CMP, AMP, GMP and DNA can be intercalated into Layered Double Hydroxides (LDH). The resultant heterostructured nanohybrids consist of one biomolecules layer and one inorganic layer

alternatively. It is expected that more and more fine-tuned inorganic materials as gene vector for gene therapy can be discovered in the future.

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