



## RENATUS® RN-005

RENATUS® RN-005 is a novel synthetic cyclodextrin that is chemically cross-linked hydroxypropyl-γ-cyclodextrin (HPγCD) oligomer mainly consisting of dimers, trimers, and tetramers (FIGURE 1).



FIGURE 1. RENATUS® RN-005 is a HPγCD oligomer.

## Solubilization

Cyclodextrins increase water solubility of poorly soluble molecules such as free cholesterol. The oligomer structure of RENATUS® RN-005 allows more stable and efficient solubilization of cholesterol than conventional hydroxypropyl cyclodextrins (FIGURE 2).

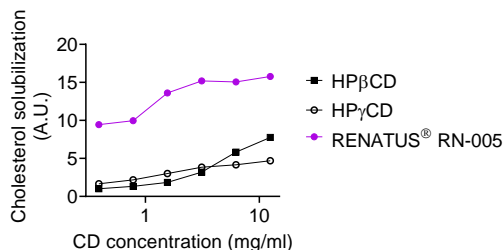


FIGURE 2. RENATUS® RN-005 increases aqueous solubility of free cholesterol.

## Minimal plasma membrane disruption

Extraction of plasma membrane cholesterol causes membrane disruption, leading to cytotoxicity and hemolytic activity. RENATUS® RN-005 minimizes cholesterol extraction from the plasma membrane and exhibits low cytotoxicity and hemolytic activity (FIGURE 3).

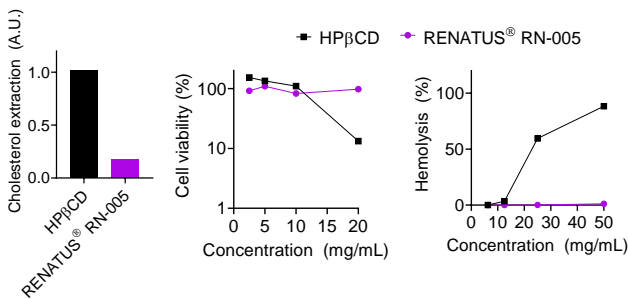


FIGURE 3. RENATUS® RN-005 exhibits minimal membrane disruption.

## Efficient cholesterol efflux

Cyclodextrins are known to mediate cholesterol efflux. RENATUS® RN-005 effectively reduces intracellular cholesterol crystal (CC) by facilitating cholesterol efflux (FIGURE 4).

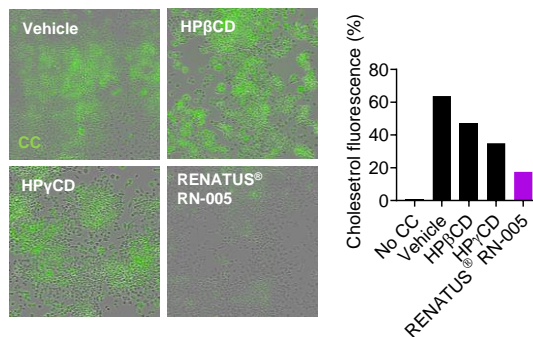


FIGURE 4. RENATUS® RN-005 induces cholesterol efflux. CD concentration : 5 mg/mL

## No ototoxicity

Some cyclodextrins cause ototoxicity when administered at a high dose due to its harmful effects on the plasma membrane of outer hair cells in the cochlea. RENATUS® RN-005 does not induce ototoxicity even at a very high dose (FIGURE 5).

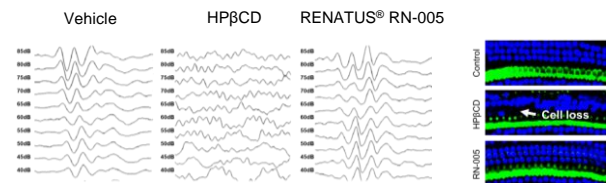


FIGURE 5. RENATUS® RN-005 does not induce hearing loss and outer hair cell loss in mice as observed by ABR test and histology. CD injection dose : 8,000 mg/kg (S.C.)

## Applications

The primary application for RENATUS® RN-005 is modulation of cholesterol metabolism. Due to its ability to avoid plasma membrane cholesterol extraction and specifically target intracellular cholesterol, it has potential to provide a safer modality to control cellular cholesterol metabolism. Other applications include formation of inclusion complexes with poorly soluble molecules. The oligomer structure has potential to allow more stable inclusion complex formation with insoluble molecules other than cholesterol and increase their aqueous solubility.

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