

CYCLOLAB



The Cyclodextrin Company



Cyclodextrin derivatives

for

Non-viral RNA/DNA/gene delivery

systems



Cyclodextrins as Non-viral gene delivery systems

Cyclodextrins are molecular containers. As of 2017, 61 products of **small molecules** are formulated with CDs.





Cyclodextrins as Non-viral gene delivery systems

Biological active substances (big molecules**), proteins, monoclonal antibodies and RNA/DNA fragments gained immense interest in product development recently**





Cyclodextrins as Non-viral gene delivery systems

Why use CDs in non-viral gene delivery:

- **Novel approach** with lot of promise and potential to protect **intellectual property**
- The systems offer **delivery to target cells**
- Act as gene delivery vectors by **condensing DNA** and forming liquid crystalline complexes with oligonucleotides
- Ability to self-assemble in aqueous solvent **forming micelles or vesicles** and can be used as hosts for the **solubilization and/or stabilization** of various compounds
- **targeted delivery** of synthetic siRNA



Cyclodextrins as Non-viral gene delivery systems

Amphiphilic cyclodextrins represent a new generation of CDs capable of forming all the assemblies expected of amphiphiles, but showing additional supramolecular properties

Self-assembling nanoparticle systems based on CD complexed siRNA has been effective in phase I clinical trials for the treatment of solid tumors



Cyclodextrins as Non-viral gene delivery systems

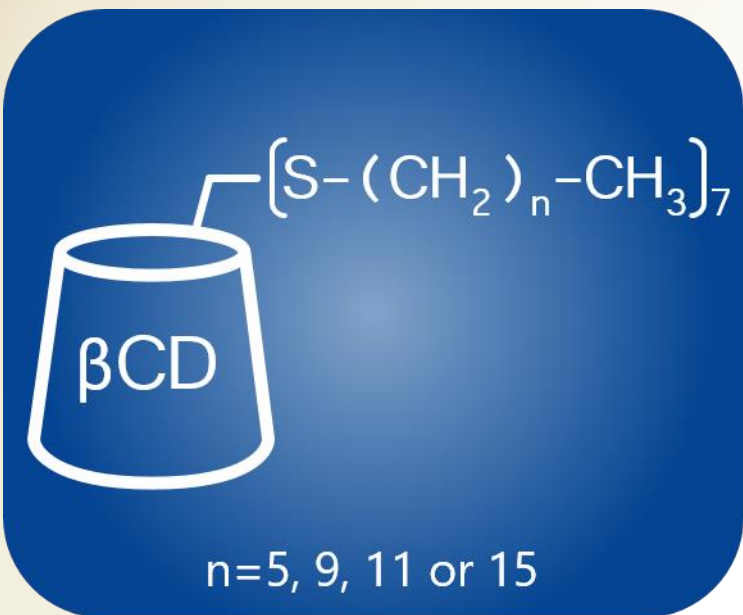
CDs are compatible in **co-formulations**: two amphiphilic cyclodextrins (CDs), one cationic and the other PEGylated or others including human transferrin (Tf) as a targeting ligand as possible.

Successful gene delivery to a **variety of cell types** (liver, intestinal epithelial in *in vivo* tumor models)

Up to 4000-fold **increase in transfection level** recorded (O'Driscoll, Eur J Pharm Sci, 2004)



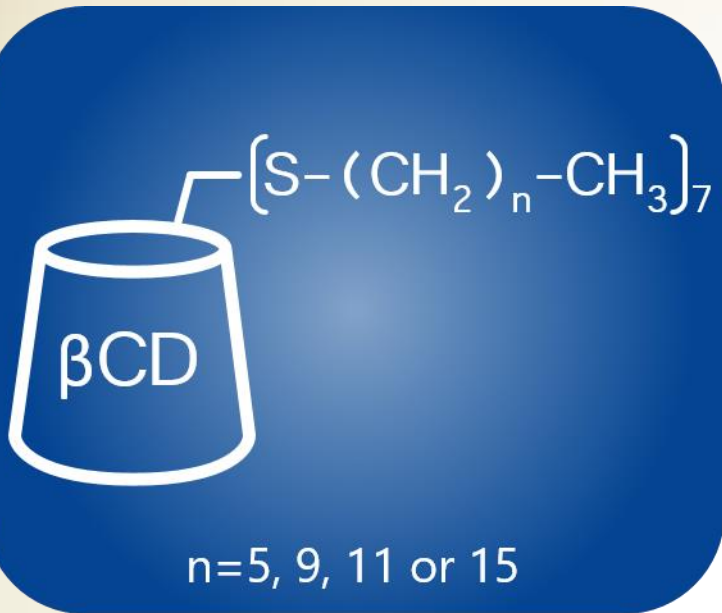
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The per-(6-alkylthio)-CDs are compounds homogeneously substituted on the primary side with apolar chains of various length (C6/C10/C12/C16). The preparation of these compounds is performed through a standard and well established procedure at CycloLab.



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These compounds are the ideal substrates for the preparation of amphiphilic cyclodextrins. The secondary side can be modified with polar groups such as oligo(ethylene glycol) units thus generating an amphiphilic structure and further modification can lead to the introduction of ionic groups.

A. Mazzaglia et al.: Novel Amphiphilic Cyclodextrins: Graft-Synthesis of Heptakis(6-alkylthio-6-deoxy)- β -cyclodextrin 2-Oligo(ethylene glycol) Conjugates and Their-Halo Derivatives.

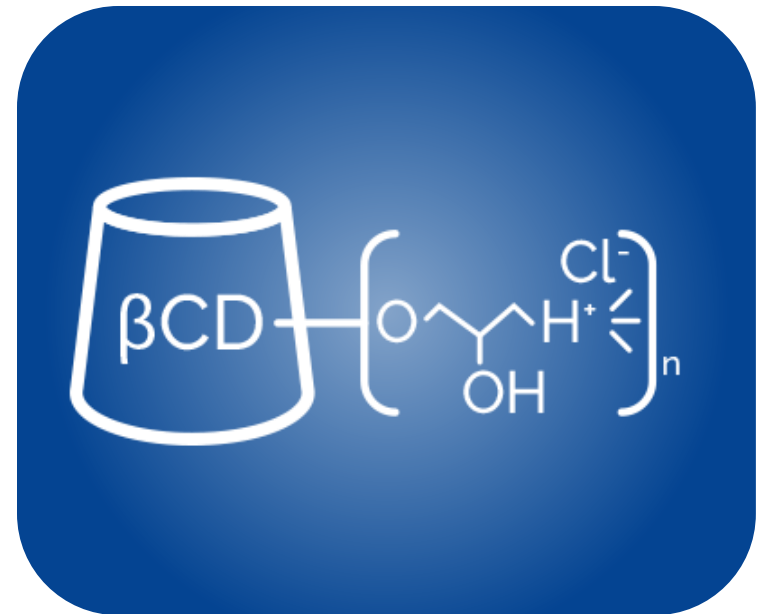
C.M O'Driscoll et al.: Cationic and PEGylated Amphiphilic Cyclodextrins: Co-Formulation Opportunities for Neuronal Sirna Delivery

C.M O'Driscoll et al.: Cell transfection with polycationic cyclodextrin vectors



Cyclodextrins as Non-viral gene delivery systems

Cyclolab offers a wide range of cationic cyclodextrins that are ideal host molecules to interact with RNA and DNA fragments. These may be available as permanently charged (quaternary amines), pH dependently charged (primary amines) and even as polymers of these products.





Cyclodextrins as Non-viral gene delivery systems

List of commercially available precursor products at CycloLab

Product name
Per-6-hexylthio-BCD
Per-6-decylthio-BCD
Per-6-dodecylthio-BCD
Per-6-hexadecylthio-BCD

Several further types of long-chain precursors can be custom prepared and completed with permanent cationic groups to yield amphiphilic gene delivery systems.

**For any other specific derivative to be designed,
please reach out to us for discussion at info@cyclolab.hu**



Cyclodextrins as Non-viral gene delivery systems

List of commercially available cationic CDs at CycloLab

Product code	Product name
CY-2024	6-Monodeoxy-6-monoamino-beta-cyclodextrin hydrochloride
CY-1065	Hexakis(6-deoxy-6-amino)-alpha-cyclodextrin heptahydrochloride
CY-2065	Heptakis(6-deoxy-6-amino)-BCD
CY-3065	Octakis(6-deoxy-6-amino)-GCD
CY-1099	(2-Hydroxy-3-N,N,N-trimethylamino)propyl-alpha-cyclodextrin chloride
CY-2099	(2-Hydroxy-3-N,N,N-trimethylamino)propyl-beta-cyclodextrin chloride
CY-3099	(2-Hydroxy-3-N,N,N-trimethylamino)propyl-gamma-cyclodextrin chloride
CY-2055	Heptakis(2,3-di-O-methyl)-hexakis(6-O-methyl)-6-monodeoxy-6-monoamino-beta-cyclodextrin hydrochloride
CY-2056	6-Monodeoxy-6-monoamino-random-methyl-beta-cyclodextrin hydrochloride
CY-2066	Heptakis(2,3-di-O-methyl-6-deoxy-6-amino)-beta-cyclodextrin heptahydrochloride
	Polymers of derivatives CY-x099, CY-x065 and CY-2024

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