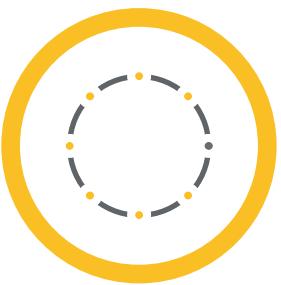


CARBOHYDE  
SUGAR IS LIFE



# Cyclodextrins

*Uses as active ingredients*



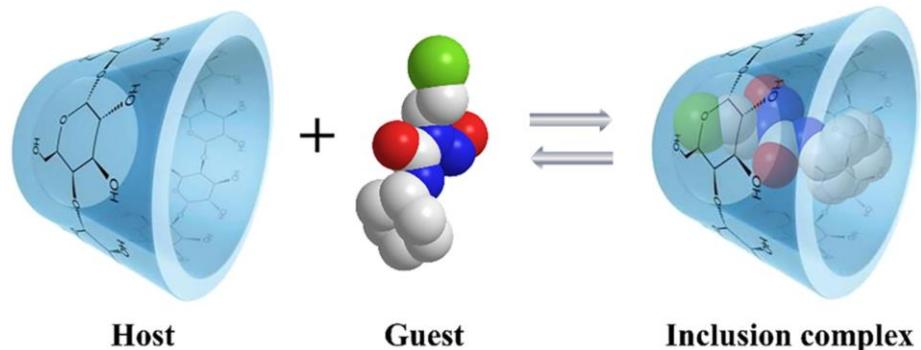
# Uses of cyclodextrins

## Traditional pharma applications

- CDs as drug complexing agents in drug delivery
- Nanosizing, solubilizing, stabilizing, etc.
- Summary of results: >100 marketed products in 2022

## Novel applications

- Active ingredients
- Monoclonal antibodies
- Gene therapy
- Targeted drug delivery
- Diagnostics & Theranostics
- Biotechnology



## Common Advantages

- Cyclodextrins may increase
  - Drug solubility
  - Wetting, dissolution rate
  - Drug stability
  - Absorbed quantity
- Cyclodextrins may decrease
  - API's dose for same efficacy
  - Taste
  - Side effects
  - Smell



# What are the "therapeutic" cyclodextrins?

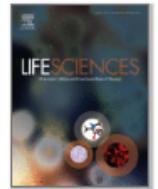
## Antidote-type cyclodextrins

- 2,6-di-*O*-methyl-BCD in hypervitaminosis (NIH)



Life Sciences

Volume 32, Issue 7, 14 February 1983, Pages 719-723



Rescue from hypervitaminosis A or potentiation or retinoid toxicity by different modes of cyclodextrin administration

Josef Pitha, Lajos Szente

Show more ▾

+ Add to Mendeley   Share   Cite

[https://doi.org/10.1016/0024-3205\(83\)90304-1](https://doi.org/10.1016/0024-3205(83)90304-1)

Get rights and content

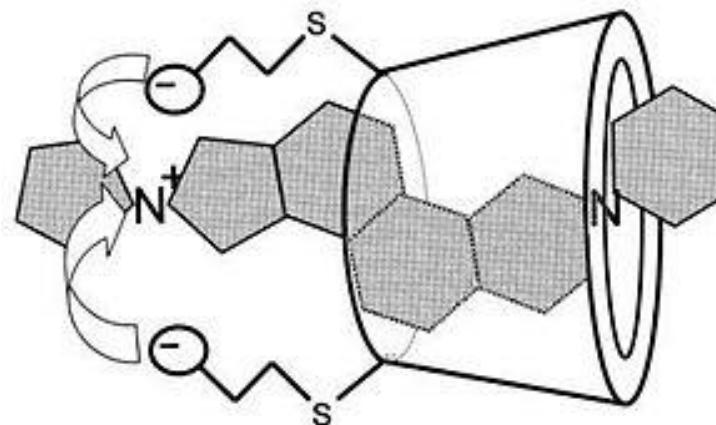
Proof of his concept: first clinical life saving action:  
rescue from retinoid intoxication in 1987

# What are the "therapeutic" cyclodextrins?



## Antidote-type cyclodextrins

- 2,6-di-O-methyl-BCD in hypervitaminosis (NIH)
- Sugammadex (MSD + generics)

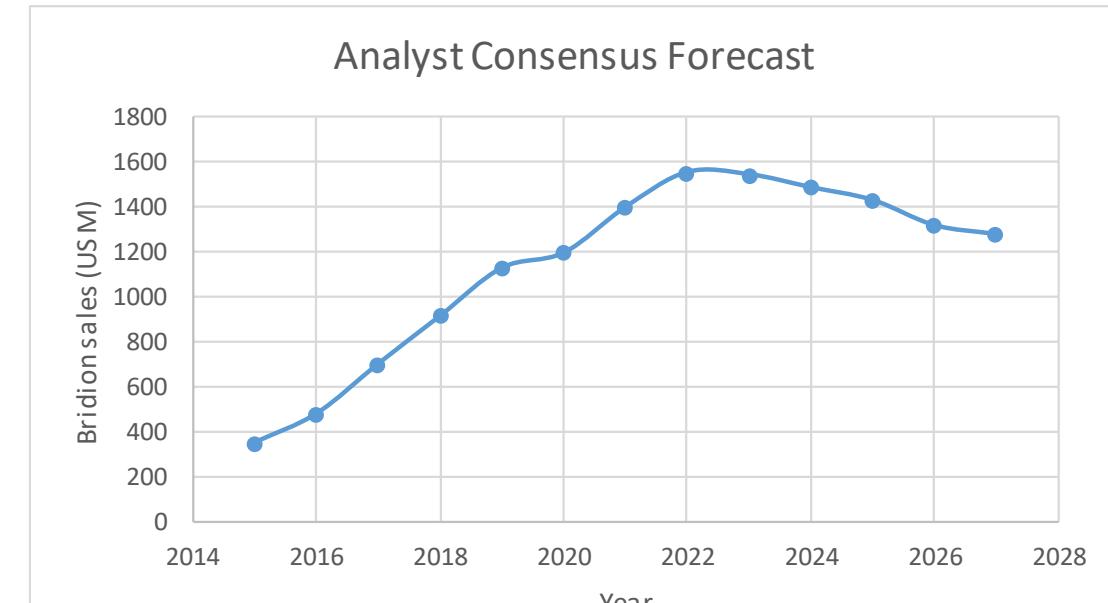


Concept: Release of neuromuscular blockade induced by rocuronium via selective removal

Approved in the EU (2008) and US (2015)



**MSD**  
INVENTING FOR LIFE



No. of companies with SGM-related patent: 50+



# What are the "therapeutic" cyclodextrins?

## Antidote-type cyclodextrins

- 2,6-di-O-methyl-BCD in hypervitaminosis (NIH)
- Sugammadex (MSD + generics)
- SBECD (REV-0100) in Stargardt disease - lipofuscin removal (Revision - Aequus)



**Weill Cornell  
Medicine**





# What are the "therapeutic" cyclodextrins?

## Antidote-type cyclodextrins

- 2,6-di-O-methyl-BCD in hypervitaminosis (NIH)
- Sugammadex (MSD + generics)
- SBEC (REV-0100) in Stargardt disease - lipofuscin removal (Revision - Aequus)
- LMWH antidote - OKL-1187 (Alveron Pharma)



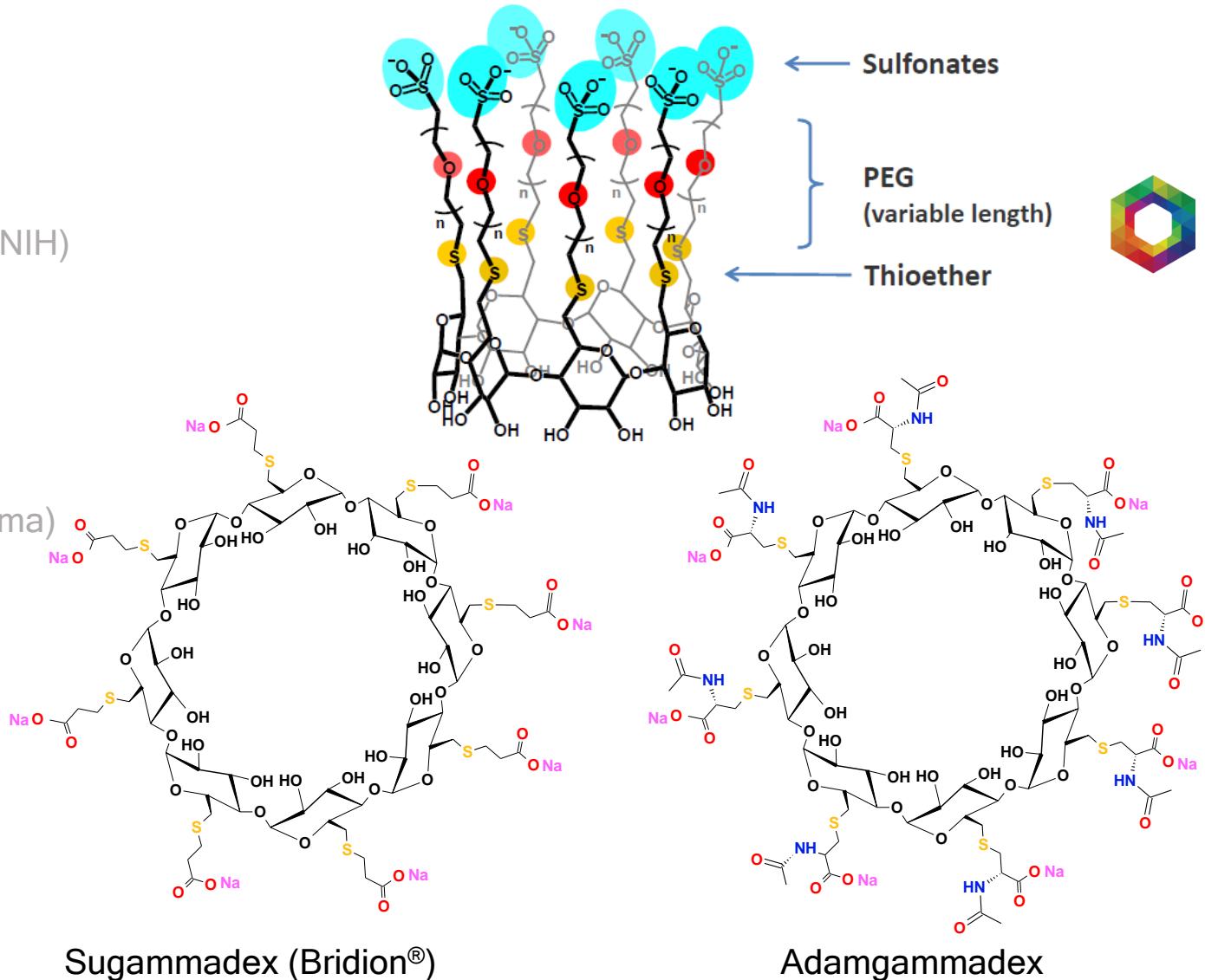
**MoA: undisclosed (reverse the anticoagulant effects of currently used direct-acting oral anticoagulants (DOACS), vitamin K antagonists, platelet inhibitors, (low molecular weight) heparins and heparin-like compounds)**

# What are the "therapeutic" cyclodextrins?



## Antidote-type cyclodextrins

- 2,6-di-O-methyl-BCD in hypervitaminosis (NIH)
- Sugammadex (MSD + generics)
- SBECD (REV-0100) in Stargardt disease - lipofuscin removal (Revision - Aequus)
- LMWH antidote - OKL-1187 (Alveron Pharma)
- Sugammadex follow-ups

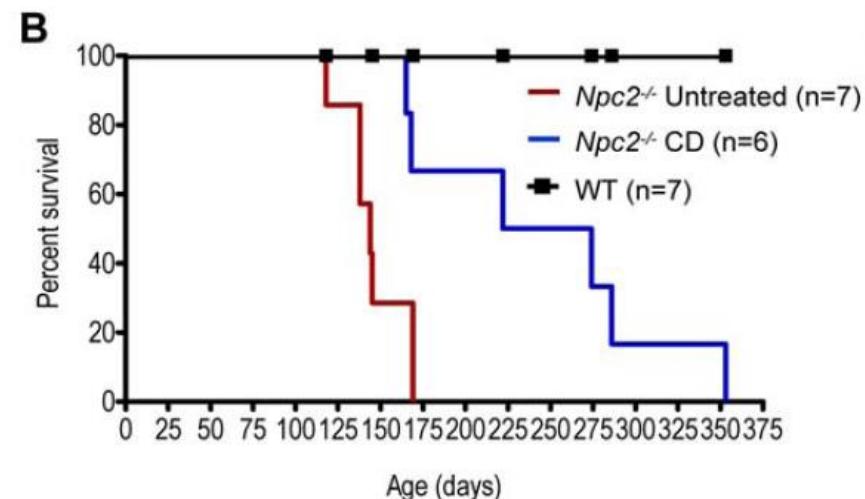


# What are the "therapeutic" cyclodextrins?

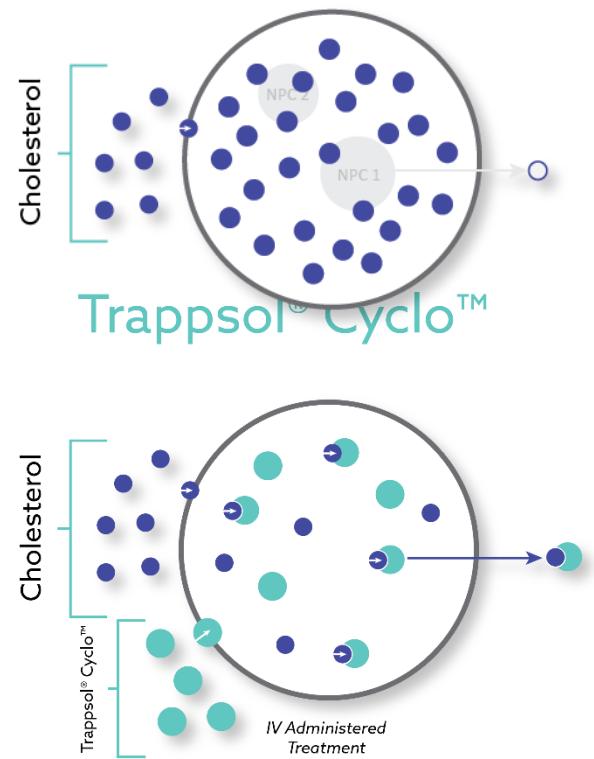


## Cholesterol(?)-targeting CDs

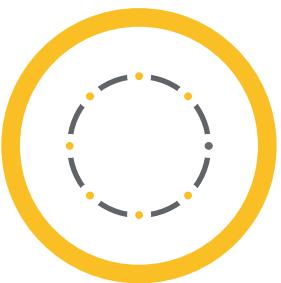
- Hydroxypropyl-BCD
  - in Niemann-Pick type C (Mandos / Cyclo Tx)  
(Adrabetadex / Trappsol Cyclo)



## Non-Functioning Lysome



cyclo  
therapeutics



# What are the "therapeutic" cyclodextrins?

## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's (Cyclo Tx)
  - in Parkinson's (Organo Tx)
  - in familiar hypercholesterolemia (Berent Tx)
  - as poison/venom antidotes (Sydney Univ)
  - FSGS (Zyversa)

Box jellyfish: Australian researchers find antidote for world's most venomous creature

Jellyfish's sting carries enough venom to kill more than 60 people



▲ University of Sydney researchers have found a 'molecular antidote' that blocks the symptoms of a box jellyfish sting if applied to the skin within 15 minutes. Photograph: Melanie Stetson Freeman/Christian Science Monitor/Getty Images

An antidote has been discovered for the world's most venomous creature, the Australian box jellyfish.



RESEARCH ARTICLE | ATHEROSCLEROSIS

## Cyclodextrin promotes atherosclerosis regression via macrophage reprogramming

SEBASTIAN ZIMMER, ALENA GREBE, SIRIL S. BAKKE, NIKLAS BODE, BENTE HALVORSEN, THOMAS ULAS, MONA SKJELLAND, DOMINIC DE NARDO, LARISA I. LABZIN, [...], AND

EICKE LATZ

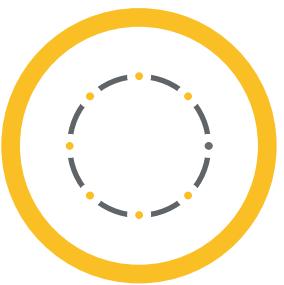
+15 authors

[Authors Info & Affiliations](#)

SCIENCE TRANSLATIONAL MEDICINE • 6 Apr 2016 • Vol 8, Issue 333 • p. 333ra50 • DOI: 10.1126/scitranslmed.aad6100



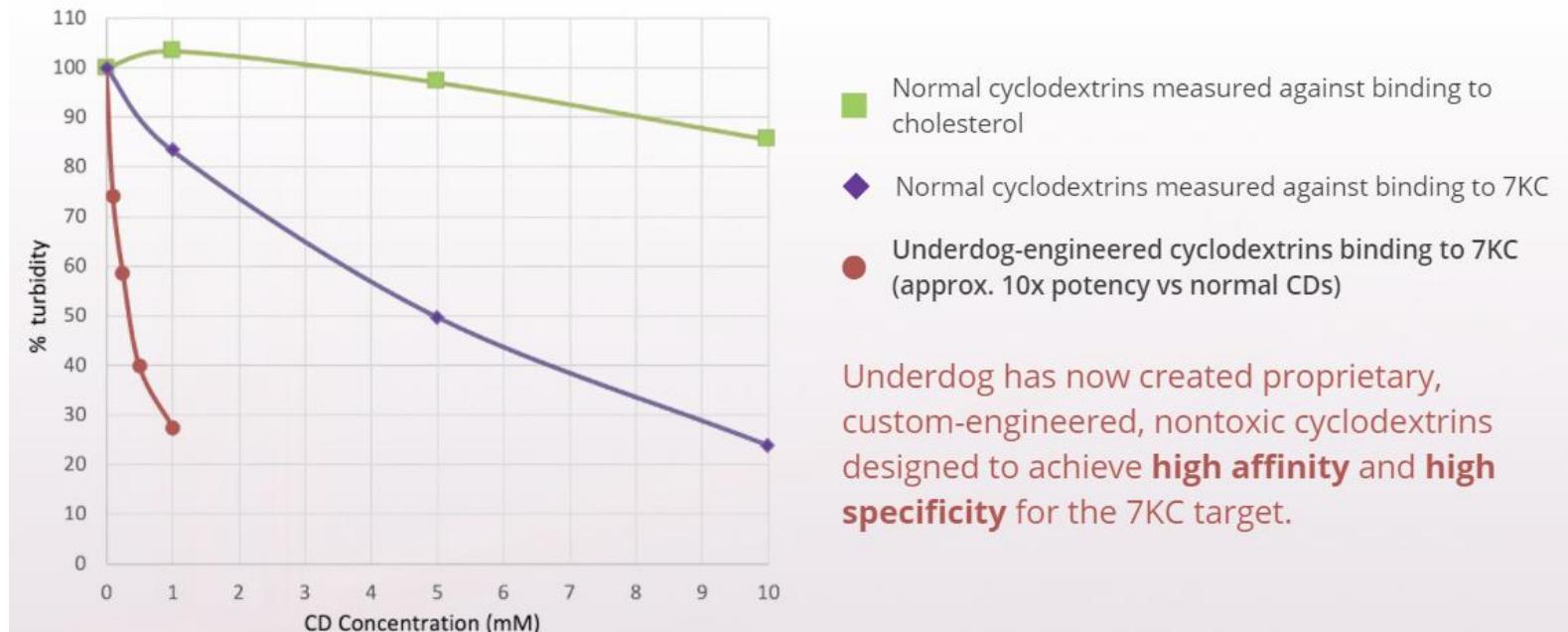
Beren Therapeutics (stealth)



# What are the "therapeutic" cyclodextrins?

## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's
  - in Parkinson's
  - in atherosclerosis
  - as poison/venom antidotes
  - FSGS
- CD-dimers in atherosclerosis



- Normal cyclodextrins measured against binding to cholesterol
- ◆ Normal cyclodextrins measured against binding to 7KC
- Underdog-engineered cyclodextrins binding to 7KC (approx. 10x potency vs normal CDs)

Underdog has now created proprietary, custom-engineered, nontoxic cyclodextrins designed to achieve **high affinity** and **high specificity** for the 7KC target.



# What are the "therapeutic" cyclodextrins?

## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's
  - in Parkinson's
  - in atherosclerosis
  - as poison/venom antidotes
  - FSGS
- CD-dimers in atherosclerosis
- "Next generation" CDs in Niemann Pick C
  - HPACD
  - Sugar-appended CDs
  - Peptide-CD conjugates
- HPGCD
- polyrotaxanes
- CD polymers



Albert Einstein College of Medicine



National Institutes  
of Health





# What are the "therapeutic" cyclodextrins?

## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's
  - in Parkinson's
  - in atherosclerosis
  - as poison/venom antidotes
  - FSGS
- CD-dimers in atherosclerosis
- „Next generation“ CDs in Niemann Pick C
- Methyl-BCD (S-1229) in pulmonary inflammation (CF, asthma, etc)

**MoA: reverse the surfactant dysfunction in conditions such as CF, ventilator-induced lung injury (VILI) asthma, COPD, bronchiolitis, ALI & ARDS via cholesterol sequestering**





# What are the "therapeutic" cyclodextrins?



熊本大学  
Kumamoto University

## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's
  - in Parkinson's
  - in atherosclerosis
  - as poison/venom antidotes
  - FSGS
- CD-dimers in atherosclerosis
- „Next generation“ CDs in Niemann Pick C
- Methyl-BCD in pulmonary inflammation (CF, asthma, etc)
- Methyl-BCD and derivatives in cancer therapy



HACETTEPE  
ÜNİVERSİTESİ



UNIVERSITÄT  
DES  
SAARLANDES



ICM  
Institut régional du Cancer  
Montpellier | Val d'Aurelle

**MoA:**  
triggering apoptosis, lower cell proliferation rate, hinder MDR

Affecting cholesterol homeostasis → cell growth inhibition  
→ apoptosis

Targeted therapy, tumour growth inhibition

# What are the "therapeutic" cyclodextrins?

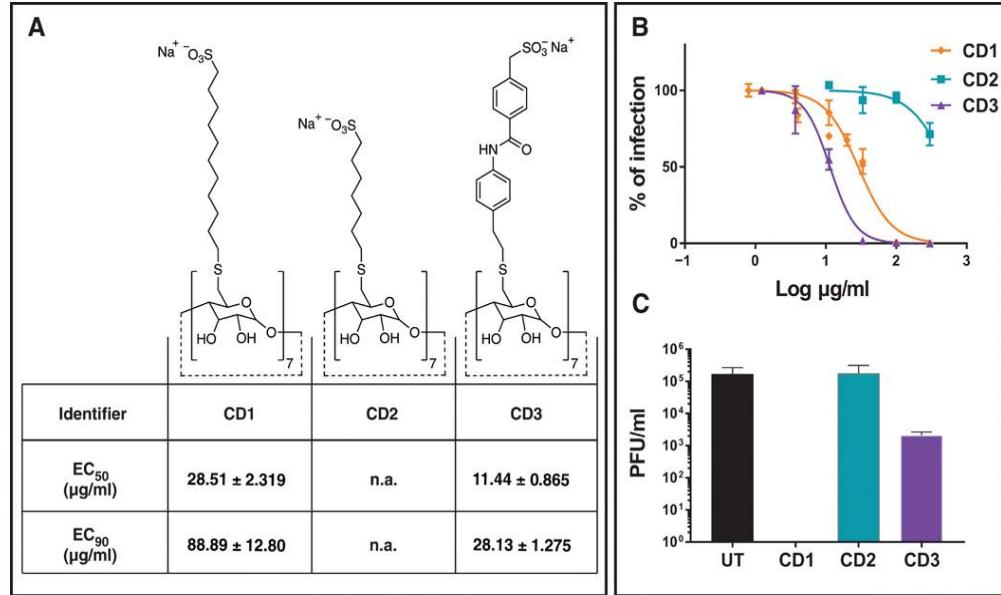


## Cholesterol(?)-targeting CDs

- Hydroxypropyl-BCD
  - in Niemann-Pick type C
  - in Alzheimer's
  - in Parkinson's
  - in atherosclerosis
  - as poison/venom antidotes
  - FSGS
- CD-dimers in atherosclerosis
- „Next generation“ CDs in Niemann Pick C
- Methyl-BCD in pulmonary inflammation (CF, asthma, etc)
- Methyl-BCD and derivatives in cancer therapy
- Sulfated CDs as antivirals



ÉCOLE POLYTECHNIQUE  
FÉDÉRALE DE LAUSANNE



- Evaluating modified, tailor-made CD against HSV-2
- Candidate proved to be active against several HS-dependent [heparan sulphate-dependent] viruses
- „exhibits a broad-spectrum virucidal, irreversible mechanism of action, presents a high barrier to viral resistance, and is biocompatible“



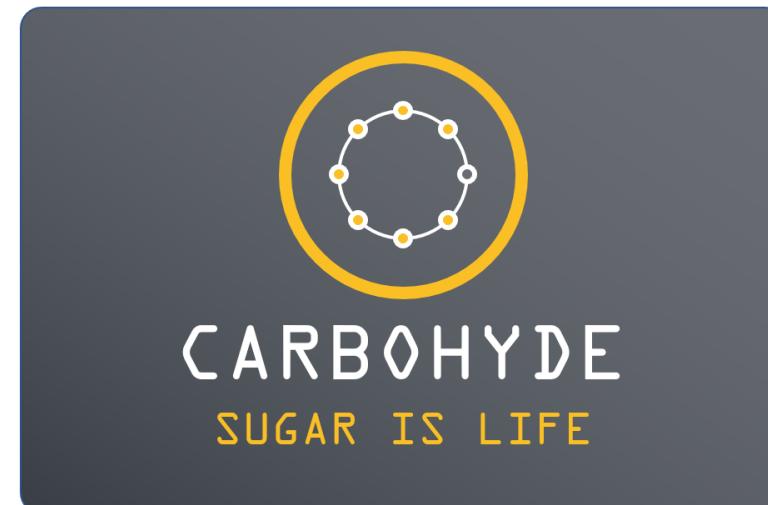
# Thank you!

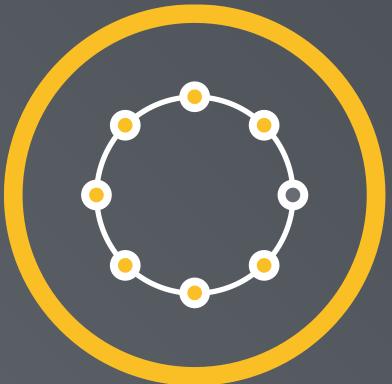
## Take Home Message

- CDs are widely evaluated in therapy
- Real challenges are in upcoming areas
  - Vaccines
  - mAbs
  - Gene therapy
  - Targeted drug delivery / therapy
  - Biotechnology
  - NCE development

## Reality & Next steps

- No novel cyclodextrin on the pharma market for almost 20 years
- New applications pose two big challenges
  - Understanding MoA
  - Designing new CDs
- Forming new consortia and collaborate with an industrial mindset





CARBOHYDE  
SUGAR IS LIFE



For any questions:

*[info@carbohydr.com](mailto:info@carbohydr.com)*