CYCLOLAB

PIONEERS IN CYCLODEXTRIN-BASED INNOVATION

GETTING THE BEST OUT OF CYCLODEXTRINS

Technology presentation

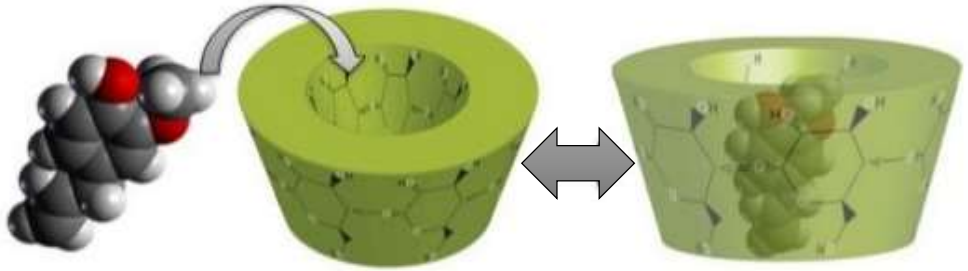
AN OUTLOOK ON THE DIFFERENT USES OF CYCLODEXTRINS IN THE PHARMACEUTICAL INDUSTRY

OUTLINE

- Traditional uses – pharma industry
- Novel uses – proteins, monoclonal antibodies
- Novel uses – non-viral gene delivery
- Novel uses - biotechnology
- Novel uses – drug delivery systems
- Novel uses – active pharmaceutical ingredients

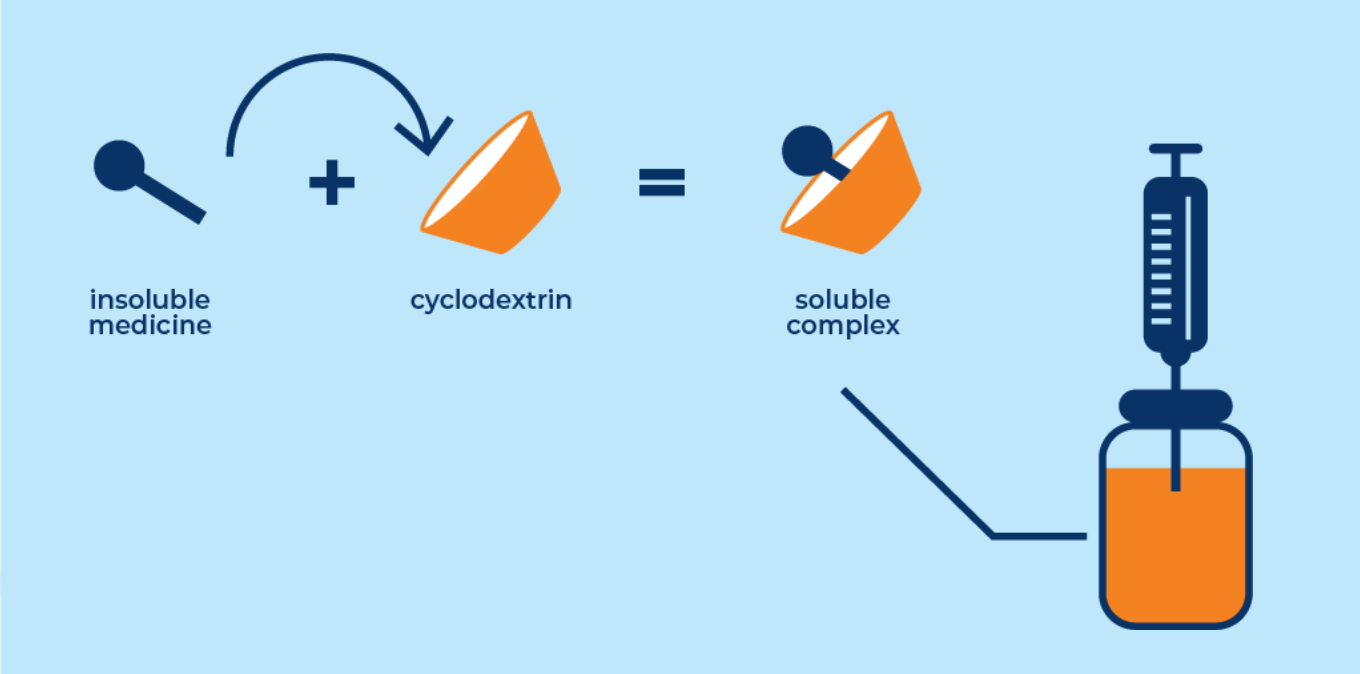
WHAT ARE CYCLODEXTRINS (CDs)?

- Composed of sugars
- Cyclic molecules
- Naturally occurring compounds
- Used in food, pharmaceuticals, drug delivery,
chemical industries, agriculture, etc.
- Sub-nanometer sized molecular containers with hydrophilic outer phase and hydrophobic interior properties
- Reversible inclusion complex formation



MAIN FUNCTIONAL PROPERTIES OF CDs

They form NON-COVALENT „host-guest" type inclusion complexes in a reversible manner (Szejtli,1980)



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

WHY USE CYCLODEXTRINS?
POSSIBILITIES

- Significant solubility enhancement (10 to 100.000 fold)
- Improved chemical stability
- Increased bioavailability, facilitated delivery
- Reduced aggregation
- Moderate irritation or reduced side-effects
- Maximized patient safety, complete renal elimination
- Formulation of water-insoluble APIs in all dosage forms
- Reducing API doses

CDs USED IN PHARMACEUTICALS

Parent

(Native, Unsubstituted)

- α-CD (Alfadex)
  EP, USP
- β-CD (Betadex)
  EP, USP
- γ-CD (Gammadex)
  EP, USP, JPC

Derivatives (Substituted)

- 2-hydroxypropyl β-CD (HP-β-CD, hydroxypropyl betadex)
  EP, USP
- Sulfobutylether β-CD (SBE-β-CD, betadex sulfobutyl ether sodium)
  EP, USP
- Random methylated β-CD (RM-β-CD)
  rare: nasal/ocular
- 2-hydroxypropyl γ-CD (HP-γ-CD)

CDs USED IN PHARMACEUTICALS

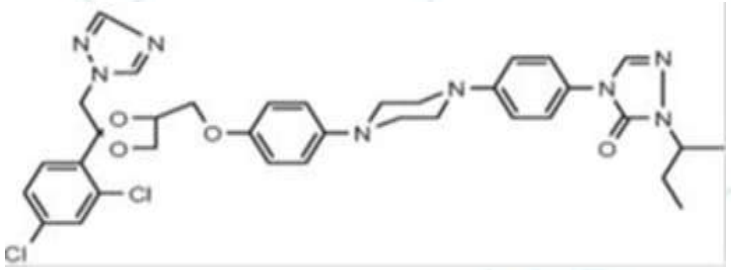
>100 pharma products on the market containing cyclodextrins

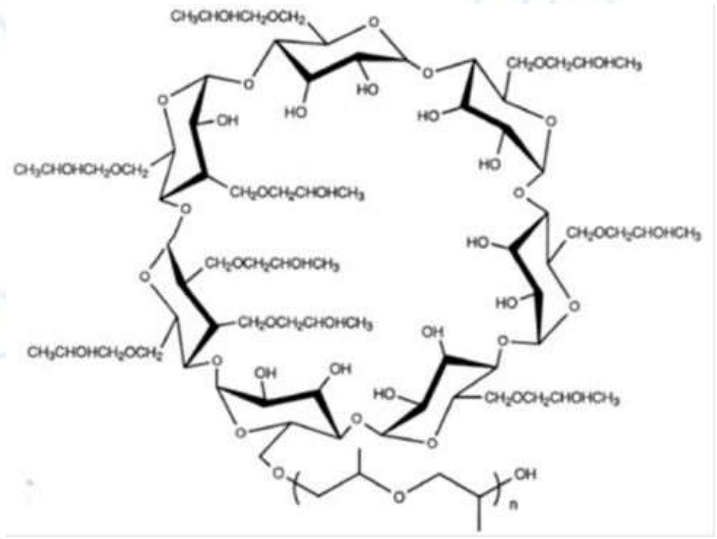
	α-CD	β-CD	γ-CD	HP-β-CD	SBE-β-CD	RM-β-CD	HP-γ-CD
ORAL		X	X	X	X		
NASAL						X	
RECTAL		X		X			
DERMAL		X	X	X			
OCULAR		X		X	X	X	X
PARENTERAL	X			X	X		X

European Medicinal Agency EMA/CHMP/333892/2013, Committee for Human Medicinal Products (CHMP) Background review for cyclodextrins used as excipients

CDs AS SOLUBILIZING EXCIPIENTS

Solubility of marble in water at pH 7 is about 200 ng/ml





Solubility of itraconazole in water (pH 7) is about 1 ng/ml!

HP-β-CD enables 10 mg/ml Itraconazole in aqueous system (Sporanox ™, Janssen Cilag)

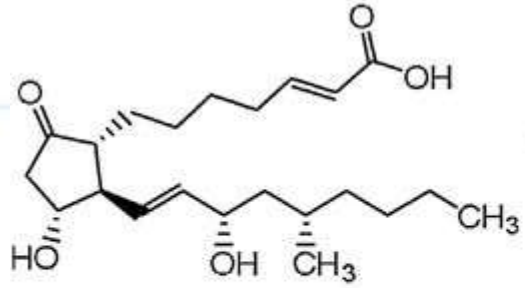
10 000 000 fold solubility increase

SOLUBILITY ENHANCEMENT OF DRUGS USING 10 M/M% SBE-β-CD VS. PURIFIED WATER

Drug	Solubility
Piroxicam	20 x
Carbamazepine	36 x
Amiodarone	50 x
Voriconazole	85 x
Delafloxacin	340 x
Ziprasidone.HCl hydrate	460 x
Aripiprazole	3350 x
Posaconazole pH 6	20 x
Posaconazole pH 3	120 x

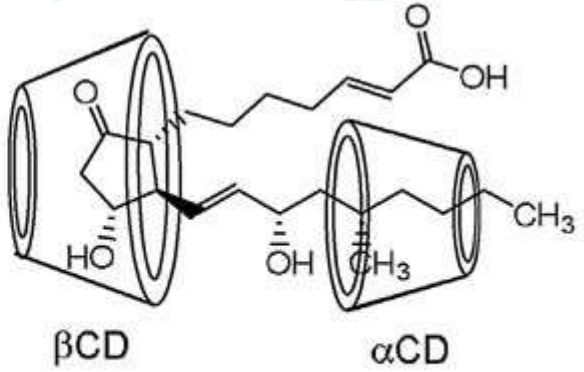
Aqueous solubilities: Pubmed database (https://pubchem.ncbi.nlm.nih.gov)
Solubility in SBECD solutions: Cyclolab results

PURPOSE OF USING CDs OTHER THAN SOLUBILIZING: CHEMICAL STABILIZATION



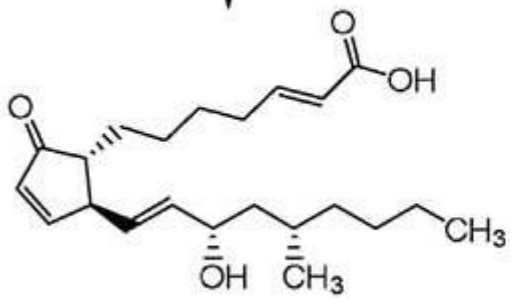
Limaprost

+ βCD + αCD

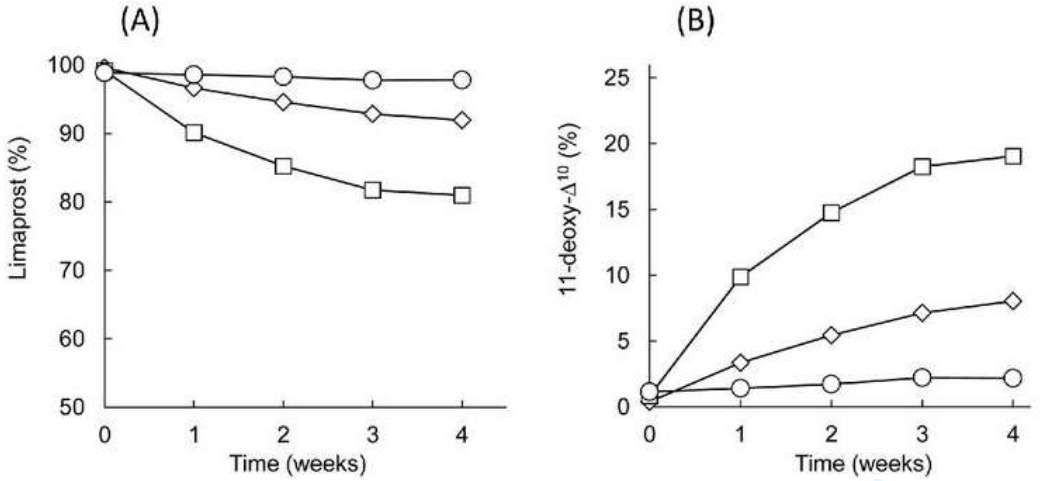


βCD αCD

Ternary limaprost/αCD/βCD complex



11-Deoxy-Δ^{10}-limaprost

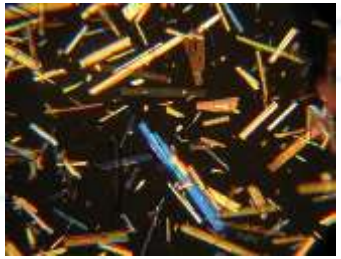


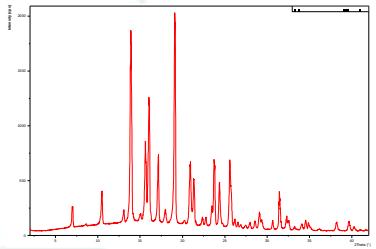
DEXOLVE™

SOLID-PHASE ENGINEERING WITH CDs

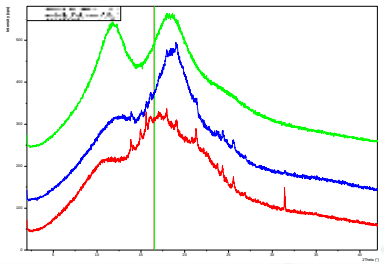
Molecular encapsulation of drugs by CDs results in:

- Molecular dispersity (each drug is surrounded by a CD ring)
- No original crystalline lattice of drug remains, amorphization
  (X-ray diffraction and DSC evidences)
- Novel solid phase (but no new chemical entity)
- Improved wetting and dissolution properties in water





Solid phase transformation



LIMITATIONS OF USING CDs FOR ENHANCED ORAL ABSORPTION

Supergeneric Approach:

Advanced drug delivery platform

+

Known active substances

Products with superior characteristics over the original brand product

Examples: Innovation in the delivery route (chewing gum/tablet, ODT, sachet)

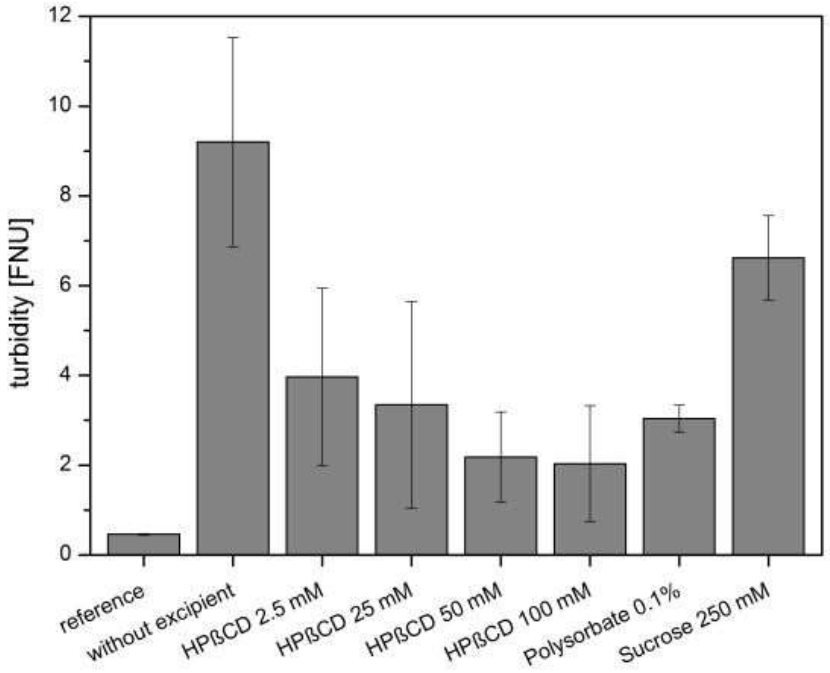
The orally applied CD complex formulation is rarely bioequivalent

Instead of supergeneric approach:

- Preclinical (toxicology) studies
- Dose finding studies

with the cyclodextrin complexes of drug candidates

Cyclodextrin's effect on Ig B aggregation



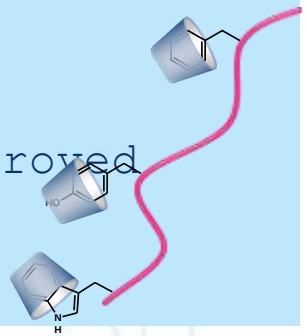
Turbidity of 1.8 mg/mL IgGB aqueous solution after 1 h stirring

Hartl (2013)

CDs IN PROTEIN FORMULATIONS

Why use CDs in protein and biological formulations?

- Safer than current excipients (e.g. Tween) – no peroxide formation, corresponding immunogenicity, degradation
- Prevention of aggregation, delayed folding
- Less protein adsorption onto container surface
- Reduced/maintained viscosity, improved injectability
- Life-cycle management

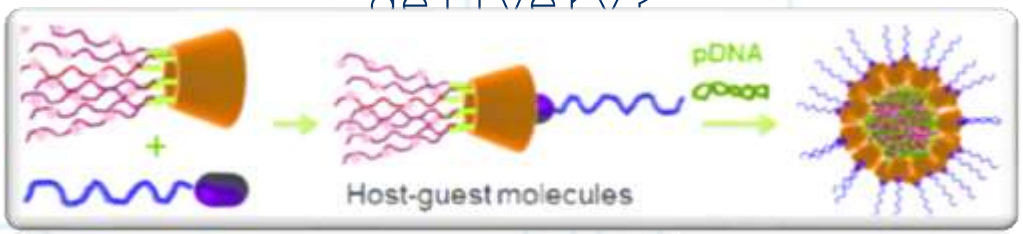


Protein without CD | Protein + CD1 | Protein + CD2 | Protein + CD3

Cyclodextrins' effect on insulin aggregation after stirring

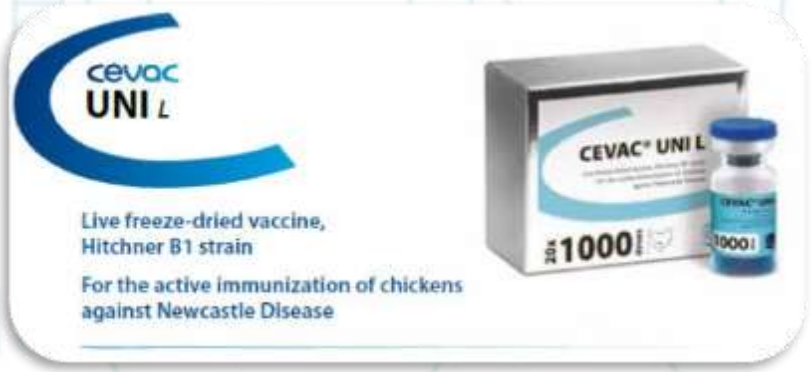
CDs IN siRNA FORMULATIONS

Why use CDs in non-viral gene delivery?

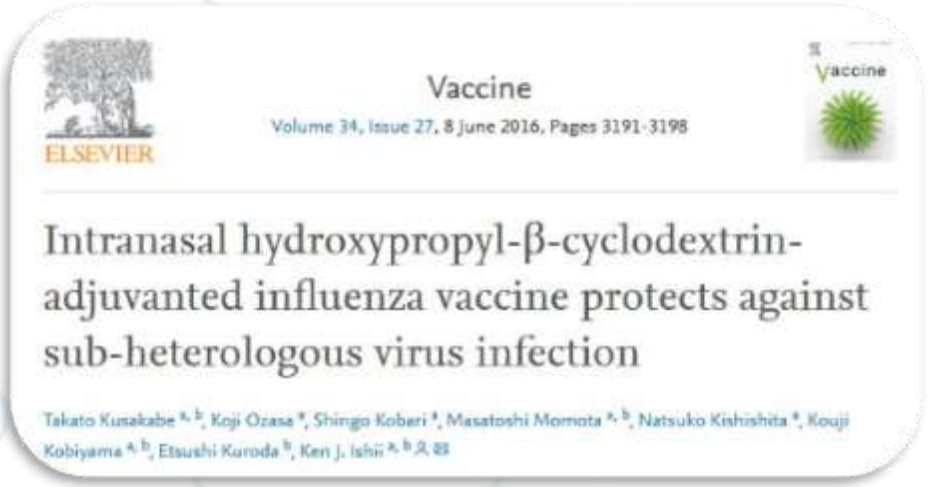


- Novel approach with a lot of promise and potential to protect intellectual property
- The systems offer delivery of synthetic siRNA to target cells
- Act as gene delivery vectors by condensing DNA and forming liquid crystalline complexes with oligonucleotides
- Ability to self-assemble in aqueous solvent forming micelles or vesicles and can be used as hosts for the solubilization and/or stabilization of various compounds
- Nanoparticle system based on CD complexed siRNA has been effective in phase I clinical trials for the treatment of solid tumors
- Successful gene delivery by modified β-CDs to a variety of cell types including liver cells and intestinal epithelial cells and to in vitro and in vivo tumor models
- Heptakispyridylamino CD, produced a 4000-fold increase in transfection level over DNA alone

CDs IN FORMULATING VACCINES



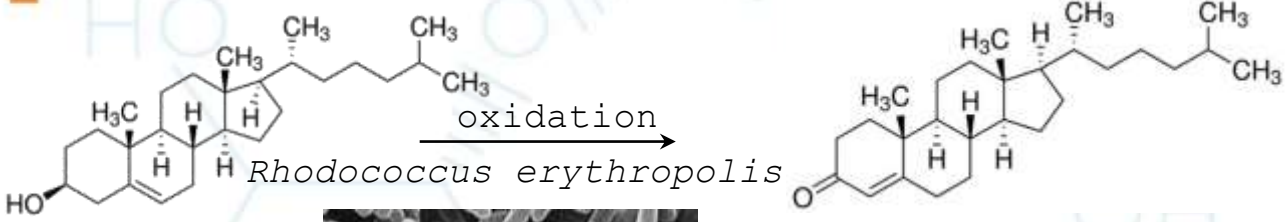
As an excipient , (2-hydroxypropyl)-beta-cyclodextrin (HPBCD) is used.



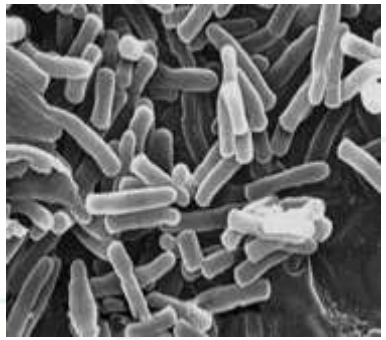
HPBCD is used in Janssen's COVID-19 vaccine. Role not diclosed: It may be anticipated though, that HPBCD acts as a effective protein stabilizer hindering aggregation and adsorption onto the container

Suvaxyn PCV™ contains inactivated recombinant Porcine Circovirus type 1, expressing the Porcine Circovirus type 2 ORF2 protein. This vaccine is used for the active immunization of pigs over the age of 3 weeks against Porcine Circovirus type 2 (PCV2). Sulfolipo-cyclodextrin (SLCD) is used as an adjuvant.

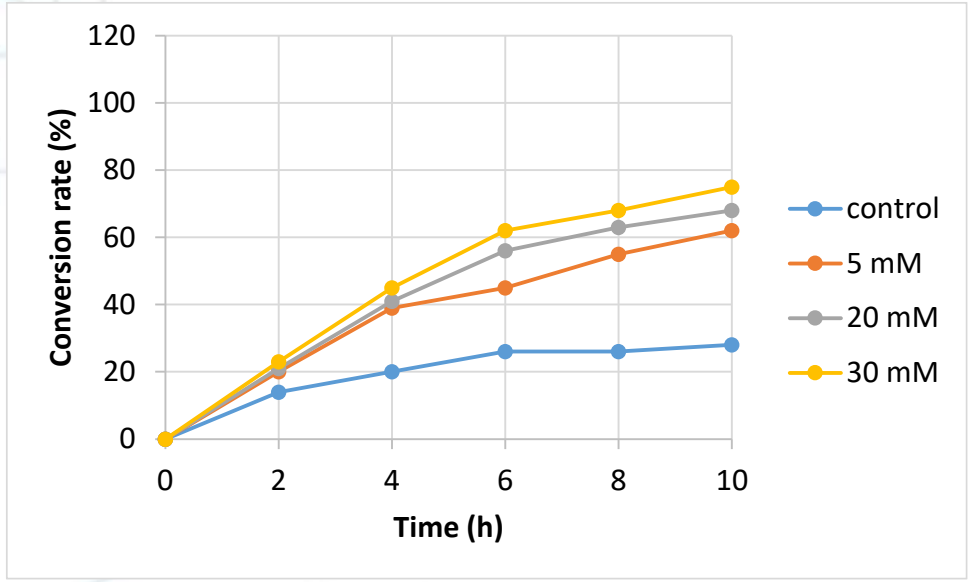
CDs in MICROBIOLOGICAL TRANSFORMATIONS



Cholesterol



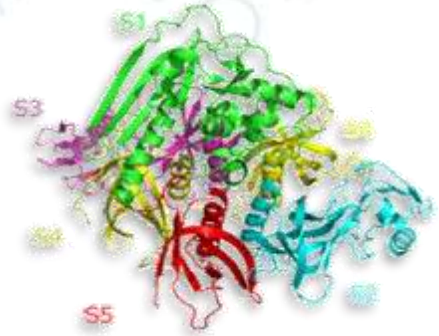
Cholest-4-en-3-one



Effect of DIMEB concentration on the conversi

- Rapid formation of cholesterol complex
- Solubilization
- Enhanced conversion rate
- Decreased product inhibition
- Improved product stability

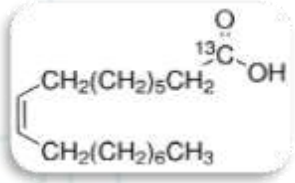
CDs AS „CATALYSTS" IN BIOTECHNOLOGY



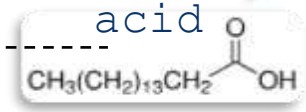
Production

Inhibition

Pertussis toxin



Oleic acid



Palmitic

Bordetella pertussis

Inoculum size cells in 5 µL	0	α	β	γ	DIMEB
10^3	-	-	-	-	++
10^4	-	-	-	-	+++
10^5	-	-	-	-	+++
10^6	-	++	+	+	+++
10^7	-	+++	++	++	+++
- no growth	+ < 100 colonies	++ 10^2 to 10^3 colonies	+++ full growth		

Complexation of fatty acids (growth inhibitors) results in enhanced cell growth and toxin production

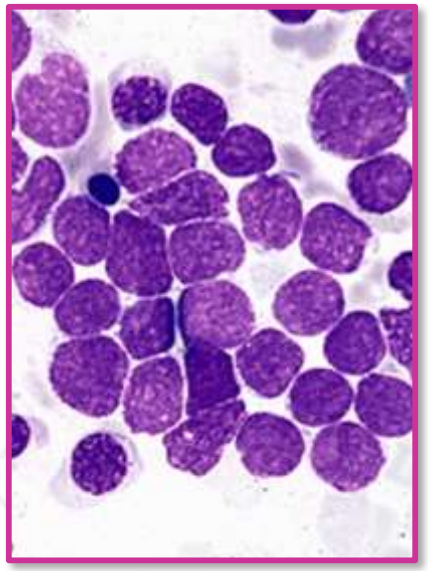
DIMEB increases pertussis toxoid production 100-fold

CDs IN SERUM FREE CULTURE MEDIA

Mycobacterium leprae

Water-soluble lipid/DIMEB complexes:

Cultivation of non-cultivable *Mycobacterium* leprae;
Serum substitutes for lymphoblast cells;



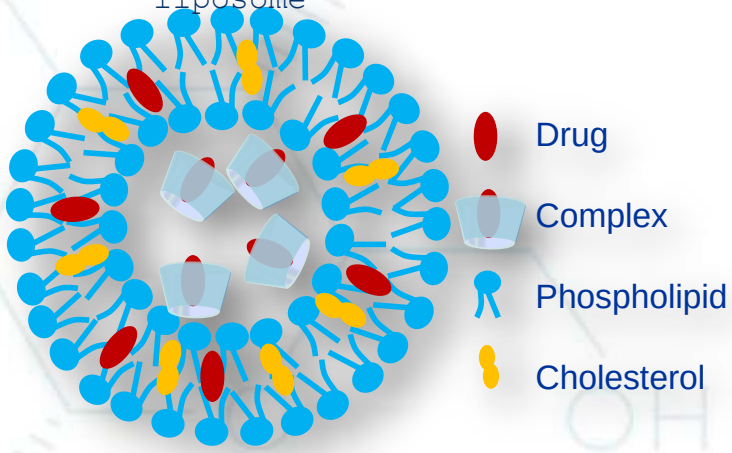
Lymphoblast cells

- Solubilization of lipids (fatty acids, cholesterol, phospholipids)
- No threat of prion proteins

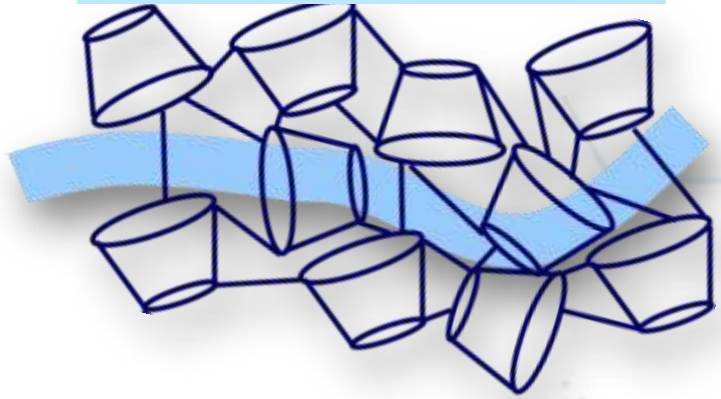
Szente et al.: J. Incl. Phenom. Mol.
Recogn. Chem. 1993, 16, 339-354

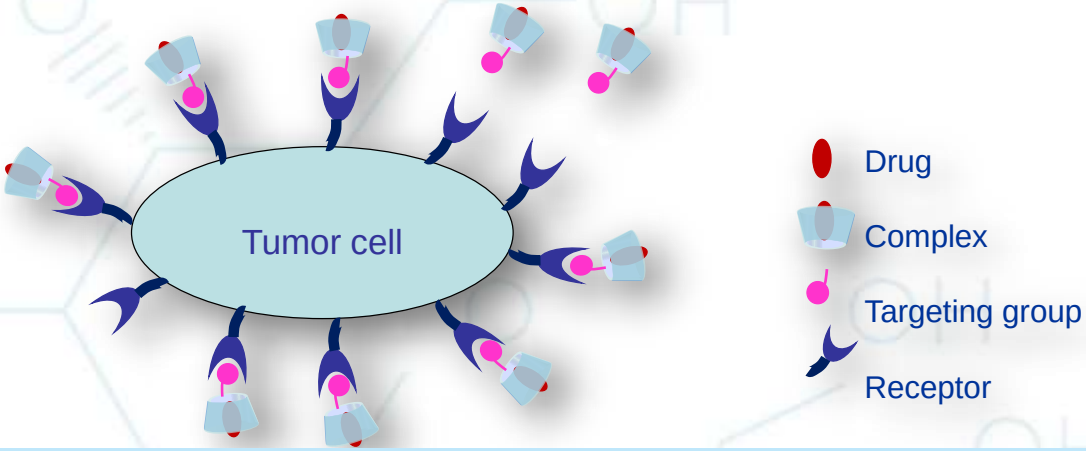
CYCLODEXTRINS IN DRUG DELIVERY SYSTEMS
CONTROLLED AND TARGETED RELEASE

Drug in CD in liposome

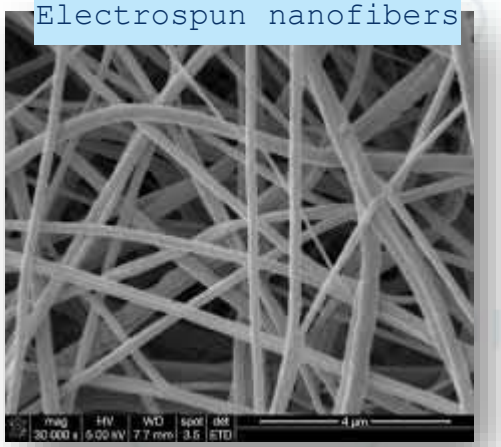


CD is immobilized on polyester mesh for local and prolonged delivery





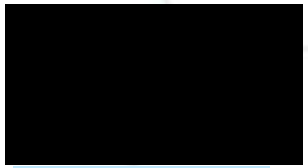
Electrospun nanofibers



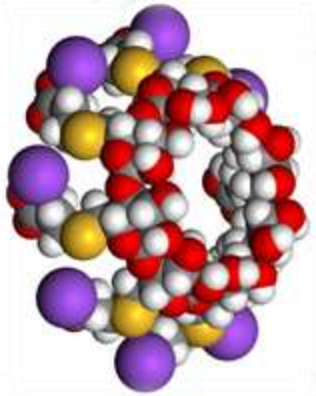
Tumor targeting by folate and/or mannoside moieties; cell-penetrating peptide-conjugated CD

CYCLODEXTRINS AS APIs
SUGAMMADEX

Rocuronium



Pipecuronium



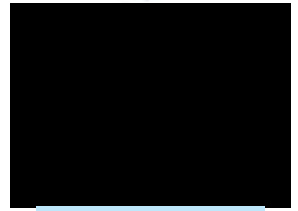
The 1st selective relaxant binding agent to reverse NMBA induced neuromuscular blockade

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

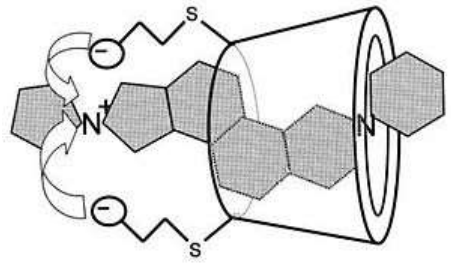
One of the strongest fits among CDs and guests – the rocuronium is unavailable to bind the receptor

Reduced/eliminated adverse effects compared to neostigmine

(lower) Affinity for vecuronium, pipecuronium and pancuronium, yet still working clinically



Vecuronium



CYCLODEXTRINS AS ANTIDOTES
CYCLODEXTRIN-ASSISTED DETOXIFICATION

Pioneering role of an eminent NIH scientist: Josef Pitha

(J.Pitha and L.Szente: Rescue from hypervitaminosis A or potentiation of retinoid toxicity by different modes of cyclodextrin administration, Life Sci., 32 (7), 719-23, 1983)

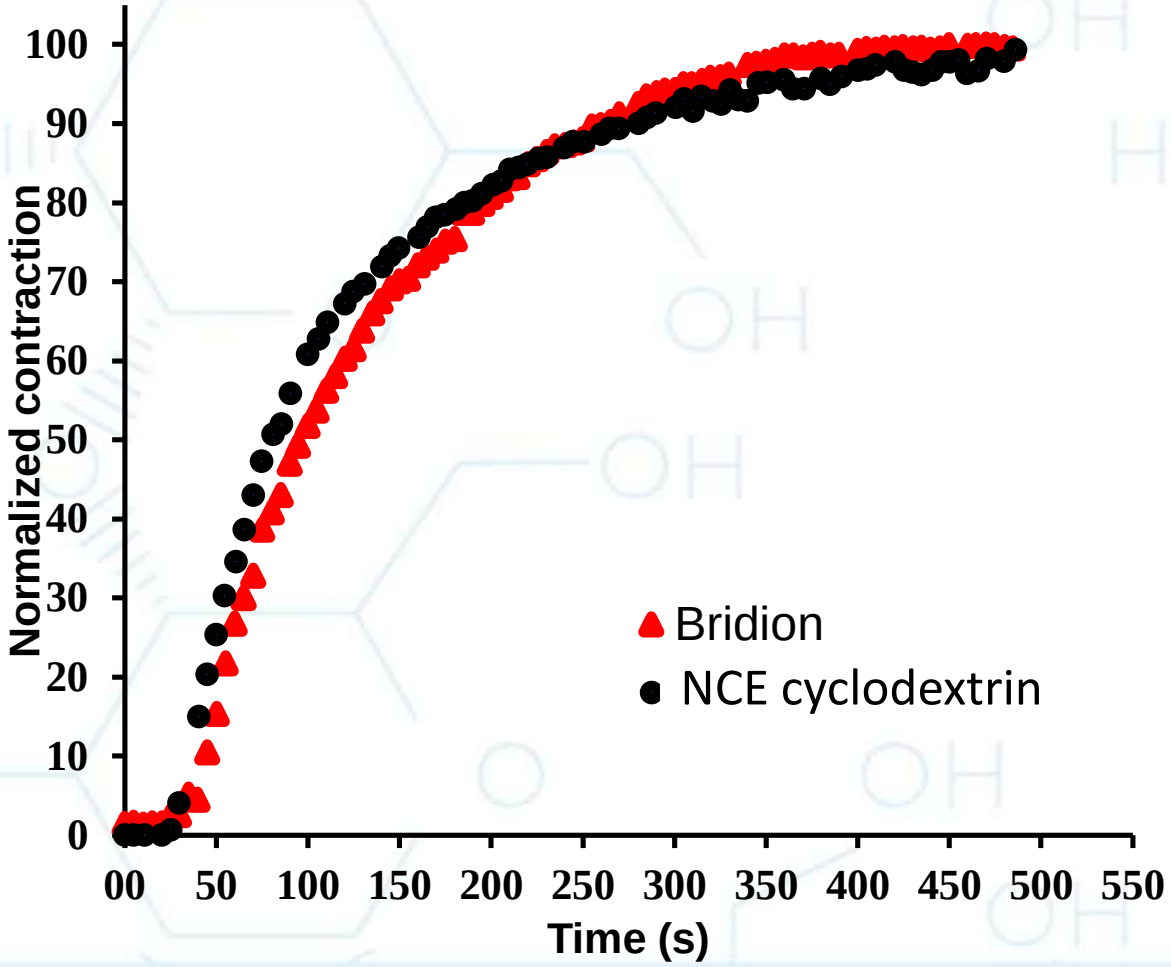
Proof of his concept: first clinical life saving action: rescue from retinoid intoxication in 1987

(J. Pitha and Carpenter T. Hypervitaminosis A in Siblings J. of Pediatrics 111 507, **1987**.)

Father of CD-based clinical detoxication

CYCLODEXTRINS AS APIs
ANTIDOTES

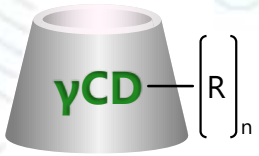
Time elapsed until the reversal of neuromuscular blockade induced with pipecuronium

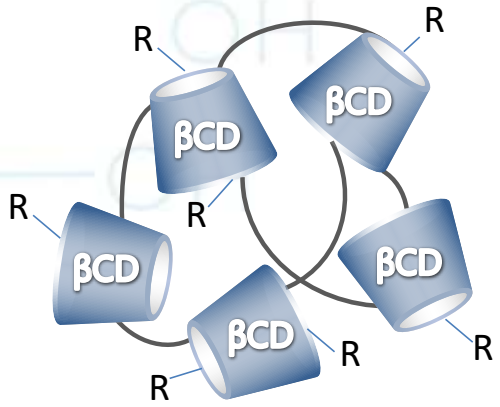


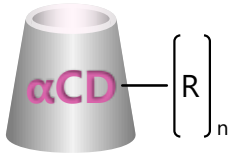
Possibilities:

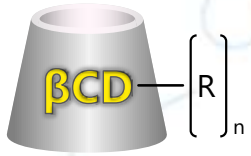
- LMWH antidote
- Toxin/poison antidotes (jellyfish, conotoxin, etc.)
- Retinoid intoxication
- AMD – lipofuscin removal

CycloLab developed a new family of cyclodextrins having huge affinity for different types of low-molecular-weight heparins









Interaction studies

NMR TLC

CE ITC

Dynamic Light Scattering

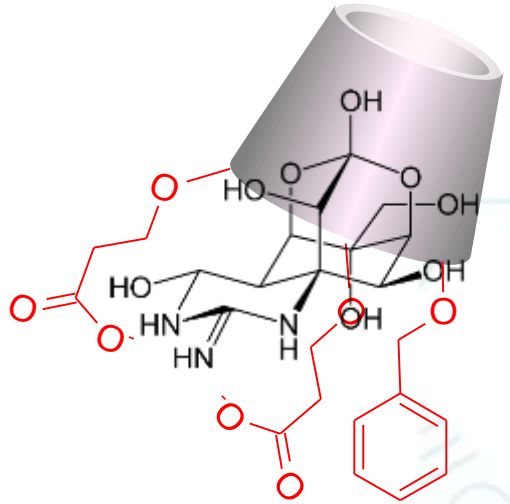
Ex vivo human blood

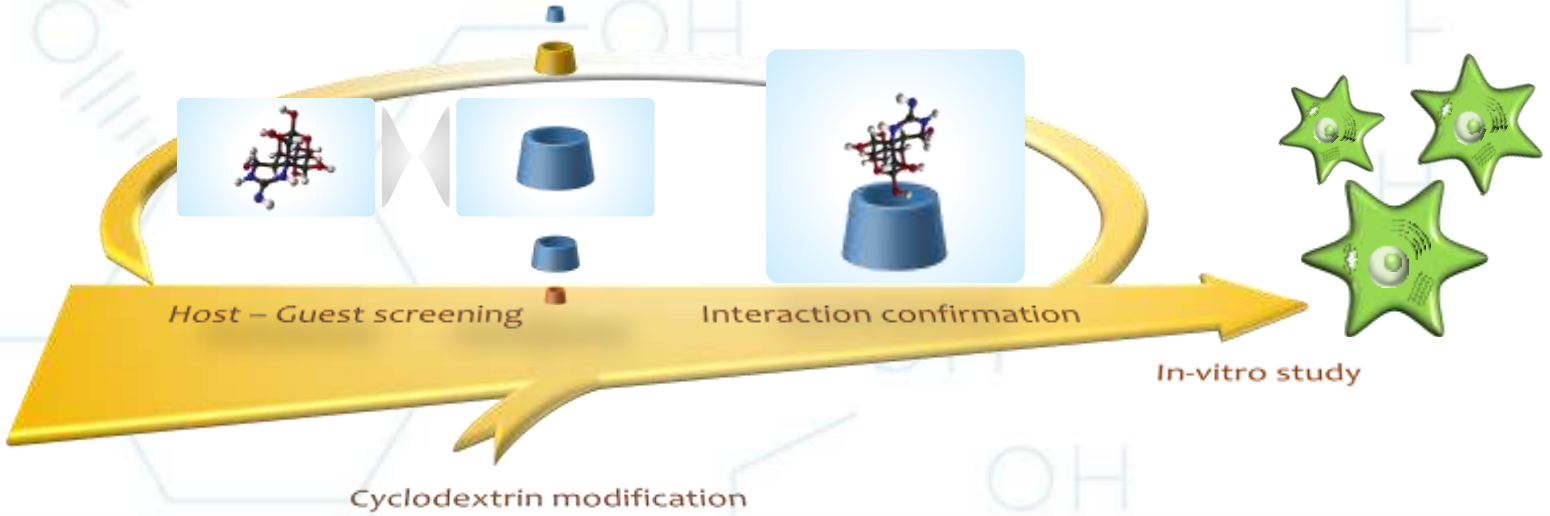
ANTIDOTES - TETRADOTOXIN

Selective and efficient antidotes could be developed for a wide variety of toxins

Cyclodextrins have shown great safety profile for all types of administration

Unique CDs can be designed for each toxin with a selective binding





CYCLODEXTRINS AS APIs
NEURODEGENERATIVE DISEASES

PNAS

Cyclodextrin overcomes deficient lysosome-to-endoplasmic reticulum transport of cholesterol in Niemann-Pick type C cells

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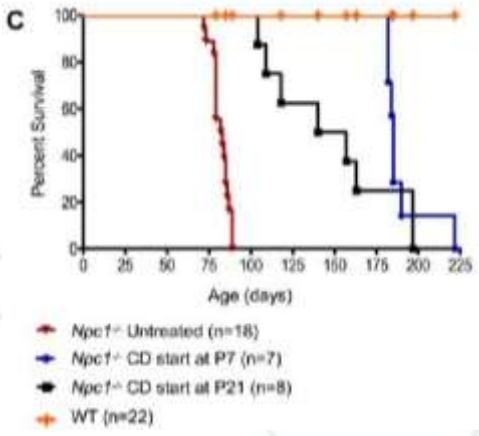
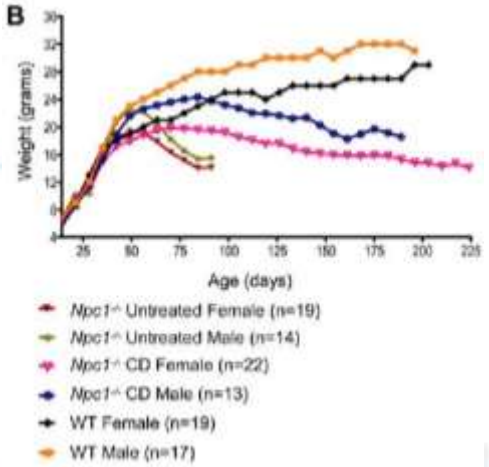
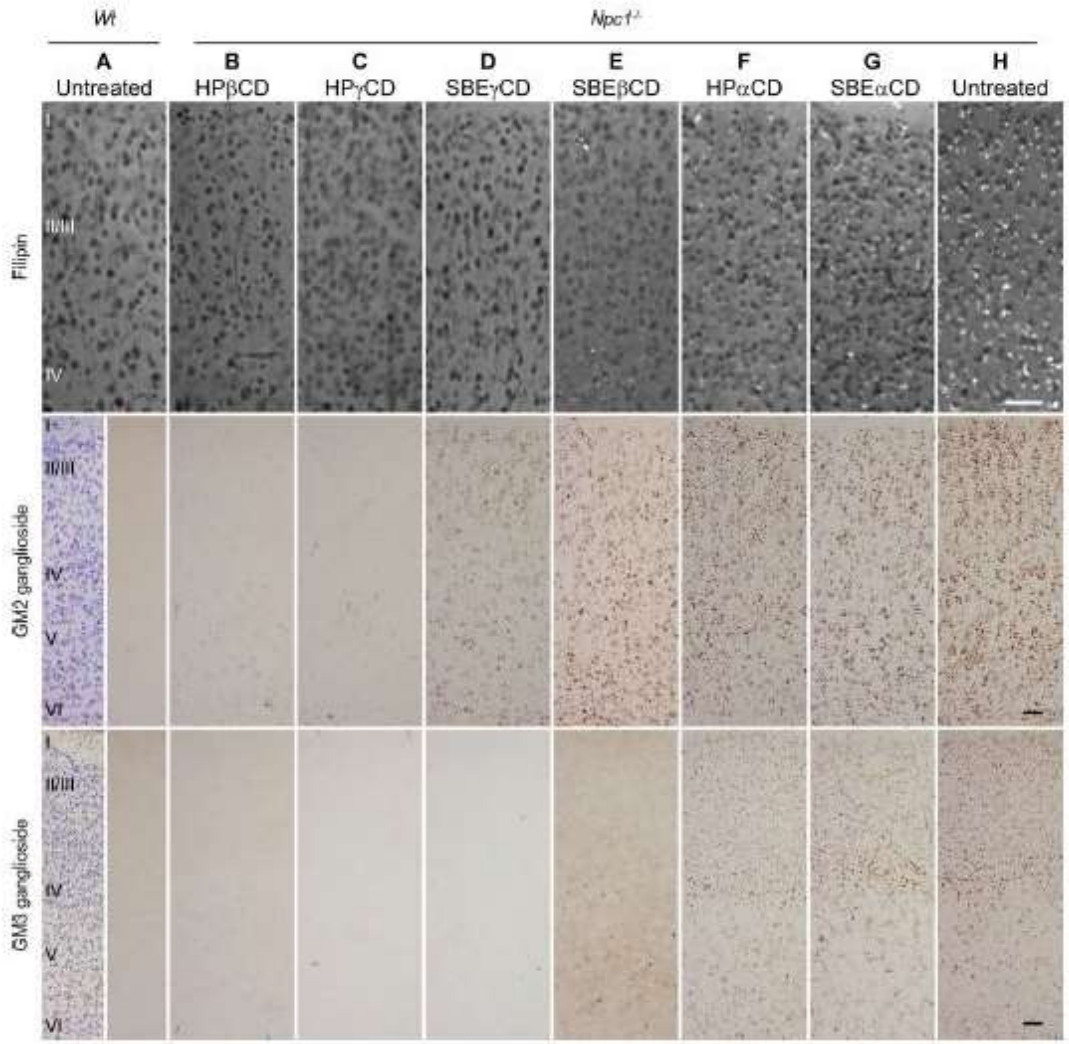
Contributed by Joseph L. Goldstein, September 23, 2009 (sent for review September 15, 2009)



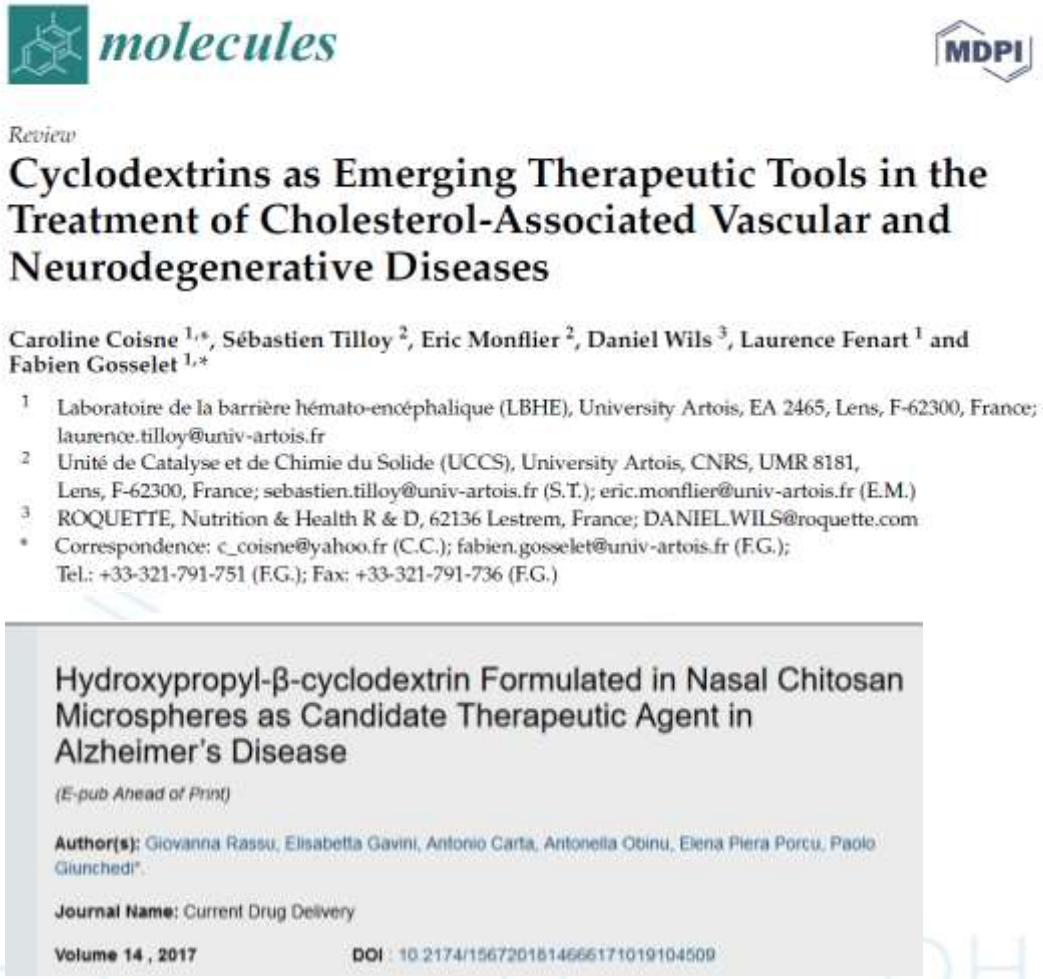




CYCLODEXTRINS AS APIs
NEURODEGENERATIVE DISEASES

The Nobel Prize in Physiology or Medicine 1985 was awarded jointly to Michael S. Brown and Joseph L. Goldstein "for their discoveries concerning the regulation of cholesterol metabolism”

CYCLODEXTRINS AS APIs
NEURODEGENERATIVE DISEASES



molecules

MDPI

Review

Cyclodextrins as Emerging Therapeutic Tools in the Treatment of Cholesterol-Associated Vascular and Neurodegenerative Diseases

Caroline Coisne [1,*], Sébastien Tilloy [2], Eric Monflier [2], Daniel Wils [3], Laurence Fenart [1] and Fabien Gosselet [1,*]

1 Laboratoire de la barrière hémato-encéphalique (LBHE), University Artois, EA 2465, Lens, F-62300, France; laurence.tilloy@univ-artois.fr
2 Unité de Catalyse et de Chimie du Solide (UCCS), University Artois, CNRS, UMR 8181, Lens, F-62300, France; sebastien.tilloy@univ-artois.fr (S.T.); eric.monflier@univ-artois.fr (E.M.)
3 ROQUETTE, Nutrition & Health R & D, 62136 Lestrem, France; DANIEL.WILS@roquette.com
* Correspondence: c_coisne@yahoo.fr (C.C.); fabien.gosselet@univ-artois.fr (F.G.); Tel.: +33-321-791-751 (F.G.); Fax: +33-321-791-736 (F.G.)

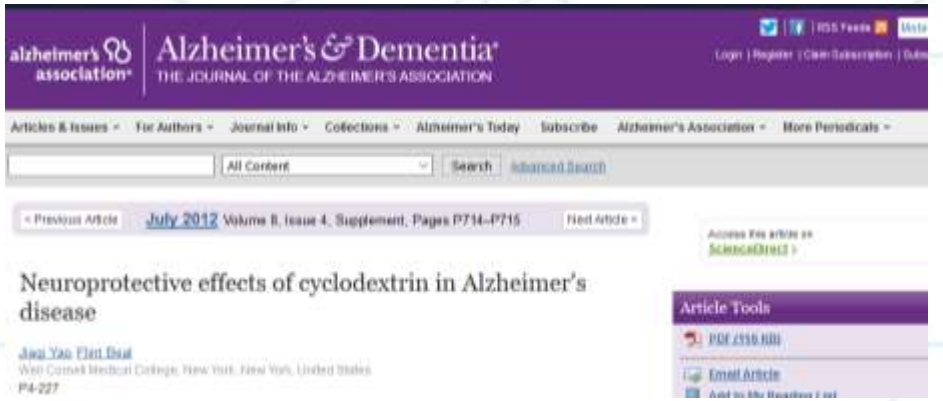
Hydroxypropyl-β-cyclodextrin Formulated in Nasal Chitosan Microspheres as Candidate Therapeutic Agent in Alzheimer's Disease

(E-pub Ahead of Print)

Author(s): Giovanna Rassu, Elisabetta Gavini, Antonio Carta, Antonella Obinu, Elena Piera Porcu, Paolo Giunchedi*.

Journal Name: Current Drug Delivery

Volume 14 , 2017 **DOI** : 10.2174/1567201814666171019104509



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July 2012 Volume 8, Issue 4, Supplement, Pages P714–P715

Neuroprotective effects of cyclodextrin in Alzheimer's disease

Jiagi Yao, Flint Beal

P4-227

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Article

Neuroprotection by cyclodextrin in cell and mouse models of Alzheimer disease

Jiagi Yao, Daniel Ho, Noel Y. Calingasan, Nina H. Pipalia, Michael T. Lin, M. Flint Beal

DOI: 10.1084/jem.20121229 | Published December 3, 2012

Article | Figures & Data | Info | Metrics

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The success of NPC therapy opened up a lot of opportunities for other diseases like Alzheimer's, lysosomal and several neurodegenerative diseases

CARDIOVASCULAR

Since the mechanism of action is not completely clarified, this led to a lot of successful research in other areas.

ANTICANCER

CYCLO A B


BioMed Research International

IMPACT FACTOR 2.48

A Comprehensive Review on Cyclodextrin-Based Carriers for Delivery of Chemotherapeutic Cytotoxic Anticancer Drugs

Rina Gidwani and Amber Vyas*


ORIGINAL RESEARCH

Induction of mitophagy-mediated antitumor activity with folate-appended methyl-β-cyclodextrin

Abstract | Fulltext | Metrics | Get Permission

Authors Kameyama K, Motoyama K, Tanaka N, Yamashita Y, Higashi T, Arima H

Received 20 January 2017


BEILSTEIN JOURNAL OF NANOTECHNOLOGY

Development of polycationic amphiphilic cyclodextrin nanoparticles for anticancer drug delivery

Gamze Varan[1], Juan M. Benito[2], Carmen Ortiz Mellet[3] and Erem Bilensoy*[1,4]


Full Research Paper

Open Access

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[1]Department of Nanotechnology and Nanomedicine, Graduate School of Science and Engineering, Hacettepe University, Ankara, 06800, Turkey, [2]Institute for Chemical Research, CSIC - University of Sevilla, Av. Américo Vespucio 49, Sevilla, 41092, Spain, [3]Department of Organic Chemistry, University of Sevilla, C/ Prof García González 1, Sevilla, 41012, Spain and [4]Department of Pharmaceutical Technology, Faculty of Pharmacy, Hacettepe University, Ankara, 06100, Turkey

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Beilstein J. Nanotechnol. 2017, 8, 1457–1466.
doi:10.3762/bjnano.8.145

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Accepted: 14 June 2017
Published: 13 July 2017

This article is part of the Thematic Series "Nanomaterial-based cancer theranostics".

Guest Editor: V. Sivakov


SCIENTIFIC REPORTS

Altmetric: 3 Citations: 26 More detail

Article | OPEN

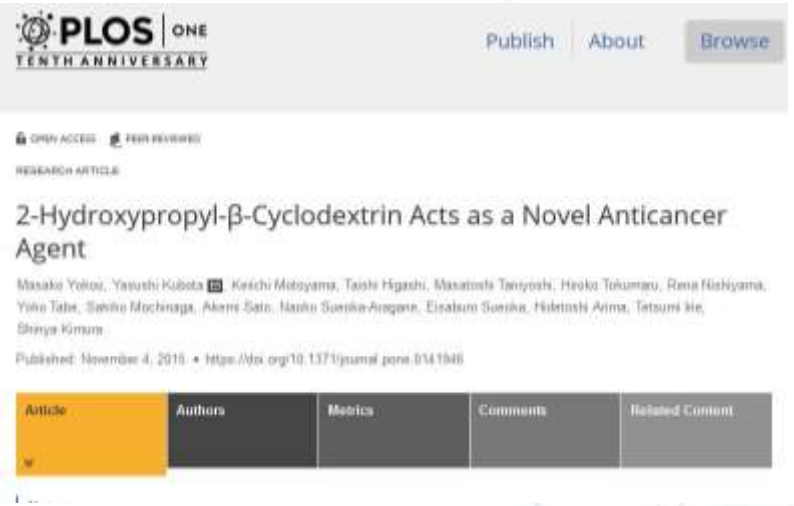
Potential use of Folate-appended Methyl-β-Cyclodextrin as an Anticancer Agent

Risako Onodera, Keiichi Motoyama, Ayaka Okamatsu, Taishi Higashi & Hidetoshi Arima

Scientific Reports 3, Article number: 1104 (2013)
doi:10.1038/srep01104
Download Citation

Cancer immunotherapy | Chemotherapy | Drug development | Targeted therapies

Received: 27 September 2012
Accepted: 10 December 2012
Published online: 22 January 2013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RESEARCH ARTICLE

2-Hydroxypropyl-β-Cyclodextrin Acts as a Novel Anticancer Agent

Masako Yokoo, Yasushi Kubota, Keiichi Motoyama, Taishi Higashi, Masatoshi Taniyoshi, Hiroko Tokumaru, Rena Nishiyama, Yoko Tabe, Seisho Mochinaga, Akemi Sato, Naoko Sueoka-Aragane, Eisaburo Sueoka, Hidetoshi Arima, Tetsumi Ike, Shinya Kimura

Published: November 4, 2015 • https://doi.org/10.1371/journal.pone.0141946

Article | Authors | Metrics | Comments | Related Content

DEXOLVE™

ANTIBACTERIAL

US 20060247208A1

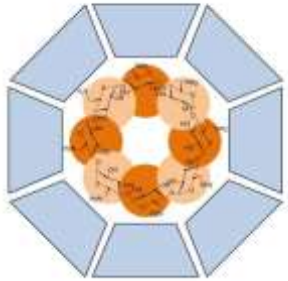
(19) **United States**

(12) **Patent Application Publication** (10) **Pub. No.: US 2006/0247208 A1**

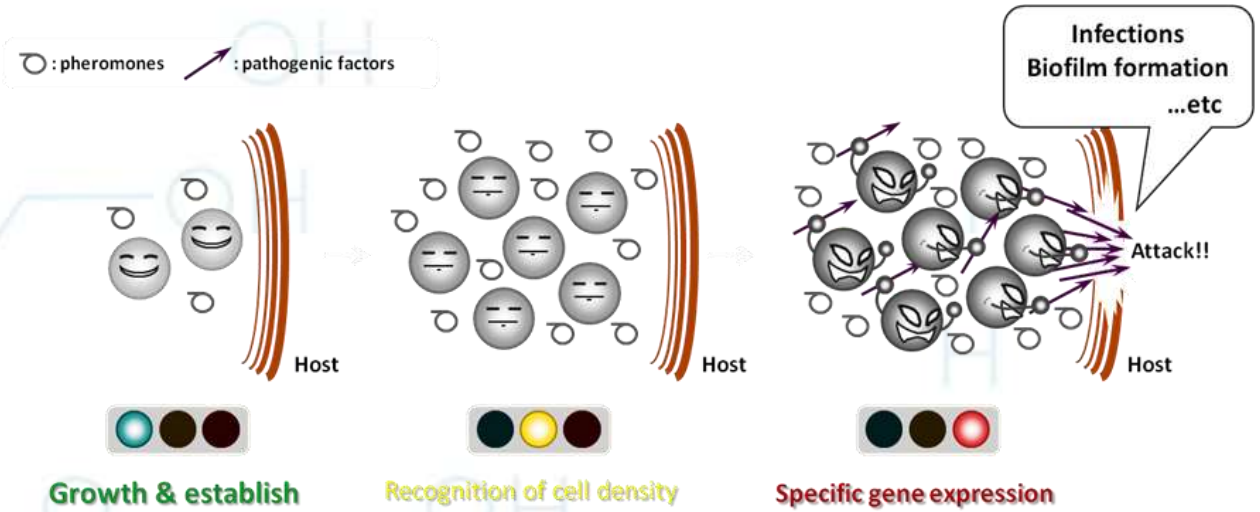
Karginov et al. (43) **Pub. Date: Nov. 2, 2006**

(54) **B-CYCLODEXTRIN DERIVATIVES AND THEIR USE AGAINST ANTHRAX LETHAL TOXIN**

Publication Classification



(54) Title: BLOCKERS OF PORE-FORMING VIRULENCE FACTORS AND THEIR USE AS ANTI-INFECTIVES



Cell density dependent gene expression in quorum sensing (e.g. virulence expression)

CYCLODEXTRINS AS APIs
PRECLINICAL DEVELOPMENTS

CNS diseases

- Alzheimer's disease
- Parkinson's disease
- Neurodegenerative lysosomal storage diseases

Cardiovascular diseases

- Atherosclerosis

Oncology

- Anticancer agents

Infectious diseases

- Antivirals (SARS-CoV-2, Zika, Dengue, HIV, Herpes, Influenza, RSV)
- Antibacterials (Anthrax, MRSA, Clostridium, Pseudomonas)

Respiratory diseases

- Asthma
- COPD
- Cystic fibrosis

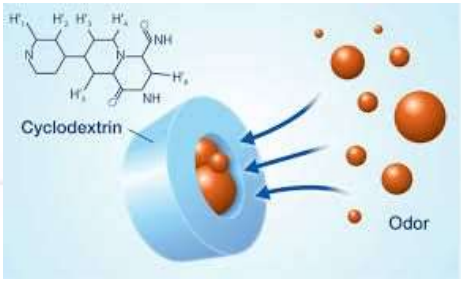
NON-PHARMA USES OF CDs

Food/Nutraceuticals

- α-CD, β-CD, γ-CD are all on the GRAS list
- Solubilization, fat absorption
- Emulsifier
- Powdered coconut milk or alcohol
- Cholesterol removal

Cosmetics

- Similar uses as for pharma (solubilization, stabilization)
- Odor control (controlled release)
- Smell removal in toiletries (Febreze, Bounce)



Agriculture

- Stabilization, controlled release of pesticides

WHO ARE WE AT CYCLOLAB?

The world's only all-round CYCLODEXTRIN company with experience in CD-technology since 1991

in pharmaceutical-, cosmetics-, food-, environmental- and analytical applications

Experience

Over 540 technical/scientific papers and 950 technical reports to customers

200 different cyclodextrin derivatives

130 patents/applications

40 products on the market

Drug Master Files (USA type IV) and eCTD

Over 20,000 citations to CYCLOLAB's papers

Expertise & Technology

Custom synthesis

Drug solubilization and stabilization

Further industrial applications

Cyclodextrin-related analytics

Stability testing

GMP-conform manufacturing

Feasibility studies

TEAM AND RESOURCES

Team

18 qualified cyclodextrin scientists

7 PhDs

2 MBA

3 members in the QA

chemists

chemical engineers

biologists

pharmacists

12 qualified technicians and operators

sales, business development, logistics, HR, administration

Resources

2,000 m^2 (own property) facility

1 galenic/technology lab

3 analytical labs (GC/CE, HPLC and QC)

1 synthetic chemistry lab

150 m^2 cGMP compliant clean room

350 m^2 cGMP compliant production area (Spray-drying unit)

Freeze-drying units

Quality systems

ISO 9001:2015

cGMP (OGYÉI/22915-11/2022)

CYCLOLAB PRODUCT PORTFOLIO

GMP Manufacturing

Betadex Sulfobutyl Ether Sodium

Dexolve ™

Custom cGMP synthesis of CDs, CD complexes, investigational medicinal products

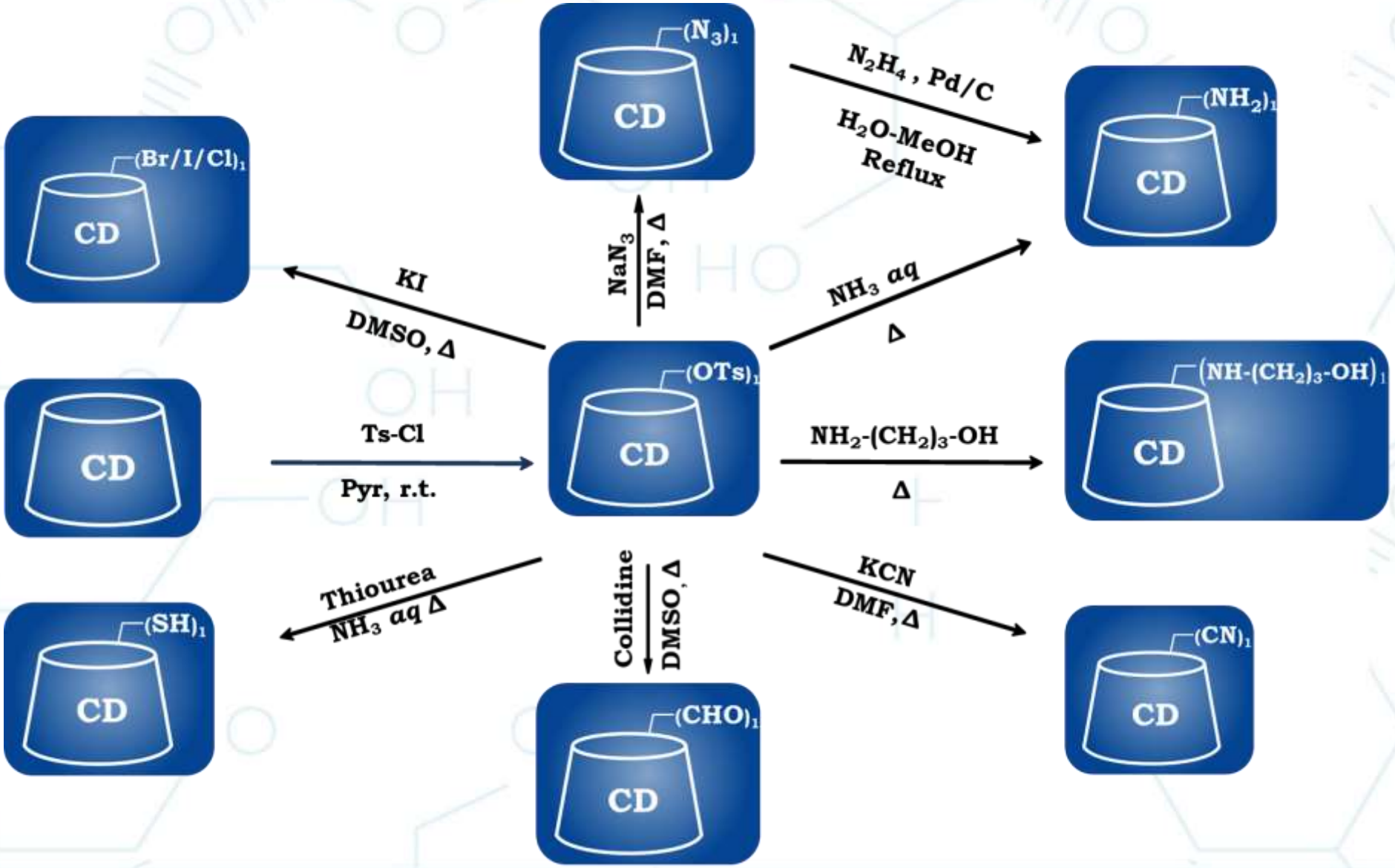
Preparation/filing of regulatory dossier

Products

- Pharma grade CDs
- Fine chemical grade CDs
- Standard grade CDs
- Single isomer CDs
- Fluorescent derivatives
- Maltooligomers
- CD complexes
- Analytical standards
- Sugammadex impurities
- CD polymers
- Special HPLC columns

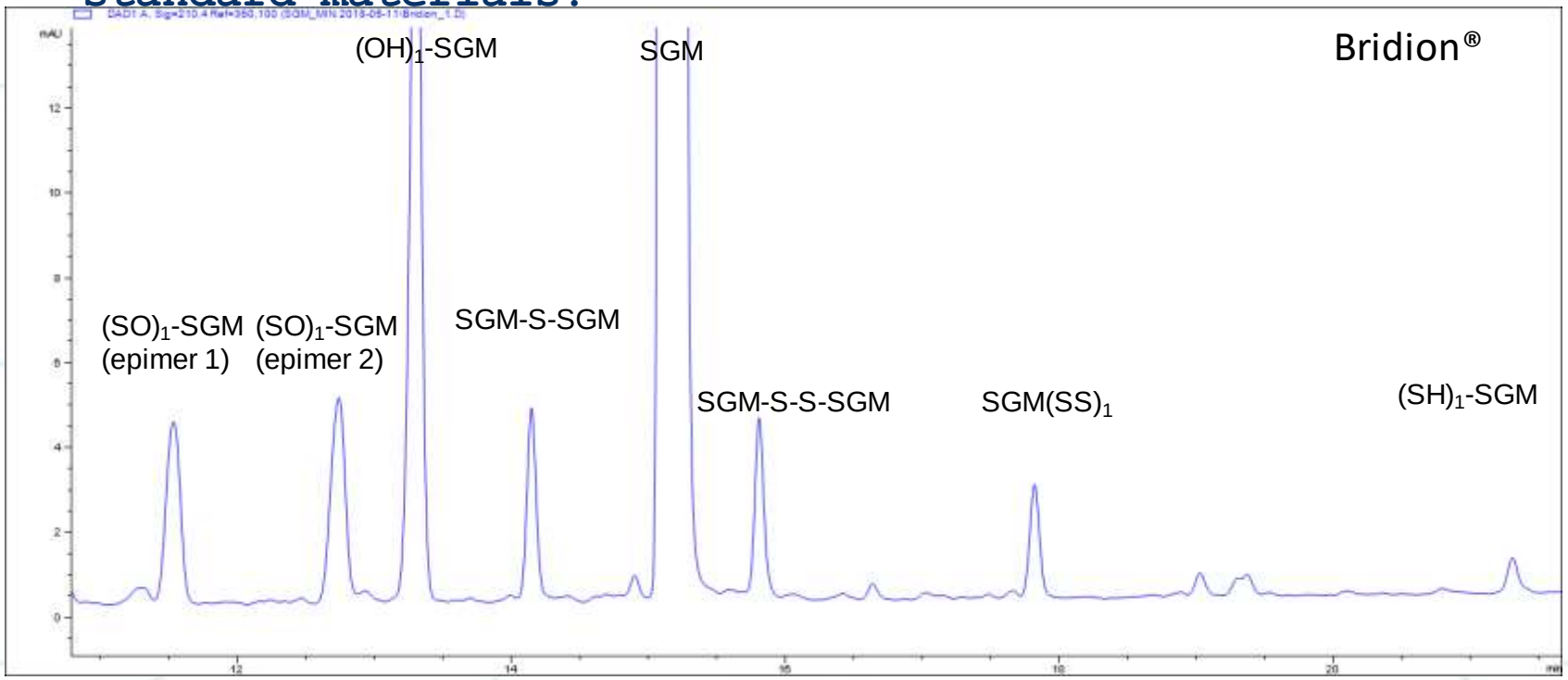
SINGLE ISOMER CYCLODEXTRINS

The key intermediate is the *6-monotosyl-CD*



SUGAMMADEX
TECHNOLOGY AND ANALYSIS

Bridion itself is claimed to potentially contain >20 cyclodextrin related impurities (public regulatory information), while other synthetic approaches generate just as many different ones. The accurate analysis of such an API is not possible without proper methods and standard materials.



SUGAMMADEX AND RELATED IMPURITIES

Cyclolab has vast experience in the production of per-6-halogen-gamma-CD intermediates and has developed Sugammadex (SGM) and related compounds via various process routes and related compounds, supported by sensitive analytical tools to characterize the products.

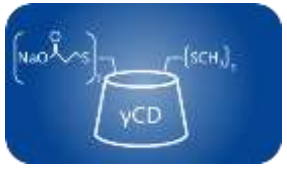
We have in stock several high purity, process related starting materials, standards and impurities.

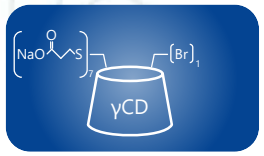

Monochloro


and monoiodo SGM


Monodisulfide SGM


Monoanhydro SGM

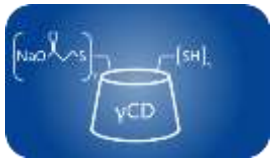

Monomethylthio SGM


Monobromo SGM


Monosulfoxide SGM (mixture and epimers separatley)


Monomethylester SGM

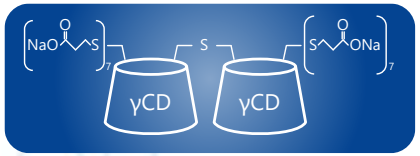

Monoethylester SGM


Monothio SGM


Disulfide-sugammadex dimer


Monoamino SGM


Exometylene SGM


Monosulfide SGM dimer


Monothio and monohydroxy SGM


Mono- SGM


and dihydroxy

Further 20+ derivatives are under development!

CYCLOLAB PRODUCT PORTFOLIO
DEXOLVE ™

DEXOLVE™

CycloLab Ltd. is the producer of the first generic USP and EP-conform Betadex Sulfobutyl Ether Sodium (SBECD = Dexolve™)

>350 kg/batch USP N.F. / EP

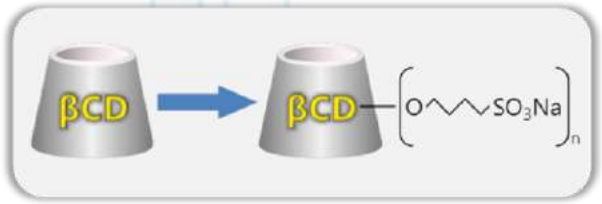
Global presence and distribution

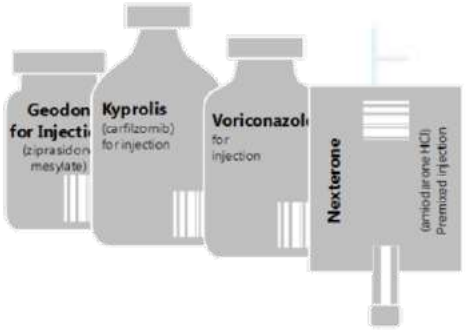
cGMP certified OGYÉI/22915-11/2022

60-month stability data

>250 batches manufactured

Annual capacity over 30.000 kgs





SAMPLES FREE SAMPLES

No down payment

no royalty

no milestone payment

GMP MANUFACTURING PRACTICE GOOD

CANADA HEALTH

EudraGMDP

FDA REGISTERED

CFDA

MFDS KOREA

DEXOLVE™

There are 17 APIs on the market and at least 150 further in development in formulations containing SBECD including

- Voriconazole (Vfend, Pfizer)
- Carfilzomib (Kyprolis, Amgen)
- Amiodarone (Nexterone, Baxter)
- Ziprasidone (Geodon, Pfizer)
- Maropitant (vet., Cerenia, Zoetis)
- Aripiprazole (Abilify, BMS)
- Posaconazole (Noxafil, MSD)
- Carbamazepine (Carnexiv, Lundbeck)
- Melphalan (Evomela, Spectrum)
- Delafloxacin (Baxdela, Melinta)
- Brexanolone (Zulresso, Sage)
- Remdesivir (Veklury, Gilead)
- Fosphenytoin (Sesquient, Sedor)
- Alfaxalone (Phaxan, Drawbridge)
- Docetaxel (Docetaxel inj., Meridian)
- Levothyroxine (Levothyroxine inj., Laucadia)
- Posaconazole (Noxafil, Merck)

- Mebendazol
- Topiramate
- Omeprazole
- Clopidogrel
- Meloxicam
- Allopregnanolone
- Iohexol
- Busulfan
- Alphaxalone

Several other nitrogen containing APIs are in various clinical phases

Main regulatory / QA / sales aspects:

Maintained DMF Type **IV** for SBECD in US and Canada since 2008, in China since 2019, in Korea since 2021.

Prepared via a self-developed proprietary, patented technology with a process independent from any existing patents (expires in 2031)

60-month stability data

Successful production of over 250 subsequent USP compliant batches – no OOS result in the production

Dedicated production facility, with 30000+ kg annual capacity producing up to 360+ kg batches

Quality system compliant to ISO 9001 and GMP requirements (regularly audited)

~100 APIs of over 500 partners in development using Dexolve in commercial and development phases

Flexible business model, technical and regulatory support on development

CYCLOLAB SERVICE PORTFOLIO
RELATED SERVICES - R&D

Early phase drug development

Customization of CD enabled formulations

Investigation of changes in physico-chemical properties

Life cycle management

Custom cyclodextrin synthesis

Exclusive manufacture, unique synthetic routes

Self-tailored products and characteristics

In vitro bioequivalence studies

Design and performance of in vitro studies to support bioequivalence of a CD enabled formulation

Analytical services

Method development, validation; cGMP release testing of pharma grade CDs

HPLC, GC, CE, UV, MS, NMR, IR, Micro and BET content methods

Stability studies

CD-guest interaction studies

CD-based chiral separations

Assay, impurity tests

Bioanalytical investigations

IP services and consultation

Experience in the compilation of CD-related patents (synthesis, application, etc.), patent claim analysis, and consultancy in CD-related projects since 1991.
Over 62.000 CD related papers

DEXOLVE™

CYCLOLAB SERVICE PORTFOLIO
RELATED SERVICES - R&D

Feasibility study

Running a short feasibility study with your molecule

free of charge

Proof of concept to consider CD based formulations

CycloLab Grant

CycloLab offers a unique possibility to collaborate on creating novel and interesting cyclodextrins under the terms of the CycloLab Grant

The proposal after application is thoroughly evaluated by CycloLab

If the application is approved, the cyclodextrin is provided free of charge for the beneficiary

PIPELINE FOR PARTNERING

Formulations

Pediatric and geriatric reformulation

Injectable repurposing: oral drugs reformulated as injectables

Cyclodextrins as NCEs

Antivirals (SARS-CoV-2, Zika, Dengue), protective gear

Lysosomal storage diseases (Niemann Pick C)

Neurodegenerative diseases (Alzheimer's)

Antibacterials (Quorum quenching)

Sugammadex (technology, analytical support and impurity supply)

Drug delivery systems

Platform for selective and targeted anticancer therapy with unmodified APIs

Platform for improving BBB penetration

PIPELINE FOR PARTNERING

Sugammadex

Our main efforts are driven into technical and analytical support for companies developing generic Bridion and supply of a wide variety of process impurities

CDs in biological formulations

CDs to be applied as artificial chaperones in mAb and other protein formulations to control folding and prevent aggregation, improve stability, replacing detergents

CDs as new class of antibiotics

A family of CD molecules that may prevent Quorum sensing of bacteria in combination products and as single APIs

GLOBAL FOOTPRINT OF CYCLOLAB

EUROPE 97

Executed R&D projects: 97
Key market for Cyclolab's Dexolve

NORTH AMERICA 48

Executed R&D projects: 48
Key market for Cyclolab's Dexolve,
DMF in U.S. and Canada

SOUTH-AMERICA 9

Executed R&D projects: 9
Emerging market for Cyclolab's Dexolve

AFRICA 1

Executed R&D projects: 1
Emerging market for Cyclolab's Dexolve

ASIA 44

Executed R&D projects: 44
Key market for Cyclolab's Dexolve,
DMF in China, South Korea

AUSTRALIA 2

Executed R&D projects: 2
Emerging market for Cyclolab's Dexolve

DEXOLVE™: BETADEX SULFOBUTYL ETHER SODIUM (SBECD)
2016 - 2022 NUMBER OF EXECUTED R&D PROJECTS: 201

COMPANY CONTACTS

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Web: http://www.cyclolab.hu

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